



COMPOUNDING FREQUENTLY ASKED QUESTIONS

1. Where can I find the compounding guidances?

All of FDA’s compounding guidance documents are available at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm452240.htm>.

2. Do the compounding guidance documents apply only to sterile compounding?

No. All current compounding guidances apply to both sterile and non-sterile compounding. FDA does not differentiate on the basis of sterility.

3. If you just mix a commercially-available product according to package instructions are you compounding under FDA’s definition and bound by 503A guidelines?

Preparing a medication in accordance with the package instructions is compounding under USP’s definition but NOT under FDA’s definition. Thus, the compounding guidance documents are not applicable to this type of activity. However, if the pharmacist deviates from the product labeling when preparing the product, FDA would consider the activity compounding, not preparation.

4. How does FDA define compounding for the purposes of the guidance documents?

It is important to note that the FDA’s definition of compounding differs from the commonly used USP definition of compounding. USP’s definition is broader, and encompasses almost any manipulation of a sterile product.

COMPOUNDING DEFINITIONS

FDA	USP
<p>Under Section 503A, FDA specifically defines compounding (21 USC 353a(f)): “As used in this section, the term ‘compounding’ does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling.”</p> <p>FDA’s Compounding FAQ further defines compounding as when a “person under the supervision of a licensed pharmacist, combines, mixes, or alters ingredients of a drug to create a</p>	<p>“The preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug-delivery device, or device in accordance with a licensed practitioner’s prescription, medication order, or initiative based on the practitioner/patient/pharmacist/compounder relationship in the course of professional practice.”²</p>

medication tailored to the needs of an individual patient.” ¹	
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FDA defines compounding to require a change or alteration to a commercially-available drug. Thus, merely preparing a drug according to the product labeling would NOT meet FDA’s definition of compounding. FDA also differentiates repackaging, which involves transferring medication to different containers but making no alterations, from compounding. Below, we’ve provided some examples to illustrate the differences.

- **Repackaging:** Transferring medications from one container to another without making any changes, such as drawing up syringes from a larger container, is repackaging, not compounding. Repackaging is covered by its own [FDA guidance](#). While repackaging is considered compounding under the USP definition, it is NOT compounding under the FDA guidances.
- **Tablet splitting:** Compounding involves changes to a finished dose, and splitting tablets alters the finished dose in a way that simply transferring medication to a different package or container does not. FDA has not yet clarified this issue, but ASHP suggests reviewing the USP standard for splitting doses and checking your state pharmacy regulations for any applicable requirements.
- **Preparing medication for immediate administration:** If no changes are made to the medication and the medication is simply drawn up for immediate administration to a patient, this is not considered compounding or repackaging. This is simply preparation for immediate use and is not specifically regulated by FDA or USP.

5. Can a 503A pharmacy repackage products before receiving an order or prescription for an individually identified patient?

Yes, a pharmacy can repackage products but in a quantity that “does not exceed the amount of drug product that the state-licensed pharmacy or the Federal facility repackaged pursuant to patient-specific prescriptions or written orders in a previous, consecutive 14-day period, and based on a history of receipt of prescriptions or written orders over a consecutive 14-day period for such repackaged drug products.” The pharmacy must also meet the other requirements set forth in the FDA’s repackaging guidance.

² USP, *Chapter <797>: Pharmaceutical Compounding – Sterile Preparations*, (It is important to note that while FDA states that compounding does not include products prepared according to package labeling, FDA-approved labeling (*i.e.*, the product package insert) rarely describes environmental quality (*e.g.*, ISO Class air designation, exposure durations to non-ISO classified air, personnel garbing and gloving, and other aseptic precautions by which sterile products are to be prepared for administration)).

6. Are hospitals/health systems held to the same requirements for anticipatory compounding as community pharmacies that do 503A compounding?

Yes. Unless a hospital/health system meets the 3 requirements of the hospital/health system exception (e.g., distribution within a 1-mile radius, only to healthcare facilities under the hospital/health system's common control, and only for use within the facility's four walls), the hospital or health system may still compound only a 30 days' supply of medication and must not dispense or distribute medication until it receives a patient-specific prescription or order. Hospitals/health systems would also be expected to keep records of their calculation of the 30-day supply amounts and to comply with the other recordkeeping requirements included in the 503A guidance.

7. Does FDA guidance impact other state or federal requirements related to providing medications to affiliated health care facilities?

While the hospital/health system guidance allows hospitals and health systems meeting the hospital exemption to compound non-patient specific medications in one facility and distribute them for administration in a separate facility under common control/ownership, the guidance does not supplant or alter any existing state or federal laws or regulations related to medication distribution. For example, if state regulations prohibit transfer of non-patient specific medications between a hospital and a hospital-owned outpatient clinic, the guidance does not negate the state regulations. The guidance provides a floor for compliance – states may still impose stricter laws.

8. When does the 1-mile radius requirement apply?

Only when non-patient specific medications are compounded and dispensed/distributed is the 1-mile radius requirement at issue. When compounding in anticipation of a prescription or compounding after receipt of a patient-specific prescription, dispensing and distribution are not restricted to a 1-mile radius or to health care facilities under common control/ownership by the FDA guidances (although other state laws may apply). However, when products are compounded in anticipation of an order or prescription, it is important to note that the compounded medications cannot leave the pharmacy until the patient-specific order or prescription is received.

9. Can hospitals continue to purchase non patient-specific compounded products from 503A compounding pharmacies for use in outpatient clinics?

Under the new guidance documents, 503A pharmacies are prohibited from compounding and distributing non patient-specific medications for use in physician offices or clinics. Instead, the draft guidances leave hospitals with two options: 1) purchase non patient-specific compounded medications from 503B outsourcing facilities; or 2) compound products on the hospital campus and distribute them only within the 1-mile radius to facilities under the hospital or health system's common control. ASHP has urged FDA to replace the one-mile radius requirement, which does not mesh with care delivery

models and may negatively impact patient access to care, with a time-based standard keyed to USP <797>.

10. Can you lay out all of the scenarios that occur in a hospital and define how they fall into 503A versus 503B?

Unless a hospital is registered as a 503B outsourcing facility, any compounding it undertakes must be done under 503A. While hospitals can choose to buy compounded product from a 503B (assuming that the 503B will make it), FDA would like to see non patient-specific compounding moved to 503B. Thus, while hospitals can compound and distribute non patient-specific medications within a 1-mile radius and only to healthcare facilities under their common control, non-hospital 503A pharmacies are completely prohibited from compounding any non patient-specific medications for use in physician offices and clinics.

For commercially-available determinations, it's impossible to lay out every scenario that could occur in a hospital/health system and an outsourcing facility. FDA included a decision tree in the 503B guidance document to assist 503Bs in determining when a product is considered a copy. For hospitals and health systems, the first question should be whether you are actually compounding under FDA's definition (e.g., making a change to a medication) or if you are merely preparing medication for administration, which is not compounding. If you are compounding under FDA's definition, then you would need to determine if the product you're compounding is currently commercially available (e.g., is it on the shortage list or has it been withdrawn or removed from the market?). If it is commercially available, you would then need to determine if the product would be a copy of an approved drug (same strength, API, and route of administration). You may still be able to compound a copy if it's a one-off or an unusual circumstance, but it may be beneficial to retain documentation justifying that choice.

11. How will compounding in Pyxis™ machines be treated under the guidances?

ASHP has asked FDA to clarify how Pyxis and other automated dispensing machines (ADMs) will be treated under the framework laid out in the draft guidances. FDA has indicated that they will be providing clarifying information about how these technologies will be treated.

12. How do 503B Outsourcing Facilities fit into the compounding framework laid out in the guidances?

ASHP strongly supports the creation of a robust 503B outsourcing facility program – we believe 503Bs play an essential role in the provision of safe, quality compounded medications. Many of our members rely on these outsourcers to provide compounded products in hospitals and health systems. However, as ASHP has emphasized to FDA, 503Bs cannot currently meet all patient needs. Our understanding is that 503Bs do not have the immediate capacity to fill the compounding needs of every hospital and health system nor can they compound every requested product. Further, hospitals/health systems may prefer to compound in their own pharmacies (i.e., insource) under 503A in order to maintain a closed patient care system (facilitating outcomes/quality tracking and reducing liability risk) and to maximize

resources. Thus, ASHP advocates for compounding framework that ensures the continued ability of hospitals and health systems to insource to meet the needs of their patients.

Additionally, some hospitals and health systems are exploring 503B registration, but are concerned that the broad definition of “facility” would, realistically, preclude registration of facilities on a hospital campus that includes other pharmacy facilities. For instance, a hospital with a sterile compounding lab in one building and a smaller, non-sterile facility next door could register the sterile compounding lab, but under the new 503B guidance, would be required to meet 503B CGMP standards for products produced in the non-sterile facility as well.

13. Can a single facility be dually licensed as a 503A and 503B?

No. Under the current facility guidance, anything produced in a facility registered under 503B (and this now includes any building nearby or close to the registered facility) must meet 503B standards, regardless of whether those product could normally be produced by a 503A pharmacy (e.g., a prescription for an individually identified patient).

14. Are products sold by 503B outsourcing facilities considered commercially available?

This is an excellent question – and one that FDA hasn’t explicitly addressed. FDA considers a drug product is commercially available if it is a “marketed drug product.” Given that FDA created the guidance documents to protect the drug approval process, including the monographs, it seems unlikely that FDA would consider a product sold by a 503B “commercially available” for the purposes of the copying guidances. FDA generally considers products compounded under both 503A and 503B to be “unapproved new drugs.”

15. Does the "copies" guidance consider the use of a different container (e.g., a syringe versus a bag) sufficient to keep a compounded product from being considered a copy?

It depends on whether the change would be considered a different route of administration. Under 503A, for a product to be considered a copy, it must have the same strength, API, and route of administration as the approved product. If the route of administration differs, then compounding a product that can be administered differently would not be copying if the commercially available version cannot be administered via the route of administration required by the patient.

503B outsourcing facilities have more flexibility in what they can compound. Under the guidance, for a product to be a copy, it must have the same strength, API, route of administration, dosage form, and excipients. Using the example provided, it seems possible that compounding a syringe when only a bag is commercially available would change, at minimum, the route of administration, but could also impact the dosage form.

16. Do the “copies” guidances require hospitals to use premixed bags if they’re commercially available?

ASHP does not interpret the guidance to mean that only premixed bags can be used and we are requesting that FDA further clarify this issue. However, if you are preparing a bag from commercially-available products according to the package label and insert, you are not compounding under FDA’s definition and the guidance requirements are not applicable. Preparation of a product according to package labeling for administration to a patient is not compounding or copying for the purposes of FDA’s guidance documents. However, if you are using a bulk substance (not a commercially-available approved product) to make the bags, then you are compounding under 503A. Further, if you are not making some other change necessary for a patient (e.g., different strength, API, route of administration), then you would be copying under the copies guidance.

17. We use a diluent that is not listed in the product labeling when preparing some medications. Is this compounding?

Deviating from package labeling (like using a different diluent or using an extended beyond-use date) when preparing medication falls under FDA’s definition of compounding. If there is a clinical justification for using a different diluent, then you could continue to compound the product, but you would need to document that the change creates a significant difference for the patient.

18. Is cost allowed to be factored into a hospital’s decision to compound a product?

No. FDA does not consider price/cost alone to be sufficient justification to compound a product. However, it’s important to note again that if you are purchasing commercially-available product and then preparing it according to labeling instructions, the FDA compounding guidances do not apply. Further, if you are making a change to the product that produces a significant difference for the patient, then you can compound the product if you document the justification for the change.

OTHER RESOURCES:

Compounding FAQ:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339764.htm#what>

Repackaging Guidance: <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm434174.pdf>