Sterile Compounding Versus Outsourcing Premixed Solutions: Making Informed Decisions

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Introduction

This article explores the advantages and disadvantages of insourcing and outsourcing sterile compounding. The decision to outsource often comes down to cost, but many other factors must be considered. The United States Pharmacopeia defines compounding as "the process of combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug product or bulk drug substance to create a sterile preparation."[1] In an ideal world, pharmacies would not compound and be able to source all sterile pharmaceuticals in commercially available, ready-to-administer forms from a supplier who contracts with a manufacturer.

Affordable, commercially available, ready-to-administer products alleviate the burdens of constant monitoring, preparation and compliance with compounding standards and regulations within the healthcare facility.

Unfortunately, in today's environment, the answer is not whether to insource or outsource, but rather, maintaining the flexibility to do both depending on the need.

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Advantages and Disadvantages of Insourcing Sterile Compounding

Insourcing sterile compounding refers to compounding sterile medications within your pharmacy. Compounding means pharmacists and pharmacy technicians control the entire process, from sourcing the ingredients to final delivery to the patient. To safely and effectively insource sterile drug compounding, pharmacists and pharmacy technicians must be well-trained on current compounding standards. One of the advantages of compounding sterile preparations is increased control and customization over the formulation to meet individual patient needs.

But increased control and customization may also be a disadvantage, as many pharmacists may not know all the considerations in making non-standard formulations, nor be familiar with the General Chapter <797> Pharmaceutical Compounding – Sterile Preparations, which is considered the minimal standard for sterile compounding.[1] They may lack the training or expertise to make crucial decisions regarding proper ingredients, selecting an appropriate container closure system or assigning the appropriate beyond-use dates (BUDs). USP 797 was revised in 2022, and the new revision was effective on November 1, 2023.

A lack of sterile compounding expertise can increase risk, especially when dealing with complex compounds such as those compounded with non-sterile starting ingredients.

Compliance with current standards of sterile compounding can be complex and time-consuming, requiring dedicated personnel and continuous monitoring. With staffing shortages and turnover common, this is a significant challenge. An ASHP survey conducted in late 2021 found that hospital and health-system pharmacy administrators experienced turnover rates of at least 21-30% in 2021, and nearly 1 in 10 had lost 41% or more of their pharmacy technicians.[2] Sterile compounding is an advanced skill for pharmacy technicians and pharmacists and requires in-depth training of new staff and can take anywhere from weeks to months of training depending on the baseline level of knowledge. Since sterile compounding can require significant investments in personnel, training and equipment it may come with financial challenges.

Outsourcing Sterile Compounding Versus Use of Commercially Available Sterile Products

Outsourcing compounding involves partnering with a specialized compounding pharmacy, which could be a 503A pharmacy or 503B outsourcing facility, to prepare sterile compounds on behalf of the healthcare facility or pharmacy. A 503A pharmacy can provide compounds for patient-specific orders only whereas a 503B outsourcing facility may provide a bulk supply to facilities (without a patient-specific order) as well as compounds for patient-specific orders.[3] Outsourcing may also include purchasing a sterile compound that is commercially available and ready-to-administer. Both outsourcing options allow pharmacies to focus on core functions like clinical work, while relying on outsourcing providers for safe compounding services or commercially ready-to-administer products.

Outsourcing compounding or commercially available products may help to reduce investments in sterile compounding facilities, equipment, training, and personnel, making it a cost-effective solution for pharmacies.

Although it is not likely that a pharmacy will be able to outsource all premixed solutions, less frequent in-house compounding frees pharmacists and pharmacy technicians to perform other pharmacy duties, which is especially important in today's labor environment.

Outsourced compounds typically have greater stability exhibited through longer expiration dates, allowing pharmacies to stock them for extended periods near locations where they are administered.[4] Extended storage near administration sites reduces the pharmacy technician's workload by limiting the exchange of expired products and allows for quick retrieval by those administering the medications, which is especially important in critical care areas such as the emergency room, operating room, and intensive care units. Studies conducted on behalf of 503B outsourcers and manufacturers will show that many of their compounds or products can be safely stored at room temperature.[4,5] Room temperature storage of internally prepared compounded products is difficult to manage due to short BUDs (see Table 1 for comparison).

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When nurses can retrieve these medications at their unit, it decreases phone calls and notifications to the pharmacy, and avoids last-minute preparation, especially of critical care medications such as norepinephrine and fentanyl, which cause strain on pharmacy staff and delays which can affect patient care.

Table 1

Norepinephrine	Compounded in-house	503B Provider	Commercially Manufactured
Beyond Use Date or Expiration and Storage Requirement	10 days BUD refrigerated/4 days BUD at room temperature (USP 797 2023)[1]	90 days BUD at room temperature (CAPS May 2023 catalog)[5]	Up to 24 months expiration at room temperature[4]

In addition, commercially manufactured products generally have color-differentiated labels, which provides an additional visual cue compared to compounds produced in-house or by 503B outsourcing facilities, which typically all have the same color of labels.[6]

Outsourcing facilities are not held to as high of a standard as pharmaceutical manufacturers.[7] Manufacturers, as described in more detail in "Considerations for Sourcing Premixed Pharmaceuticals," are held to the highest standard and must follow CGMPs.[8]

Choosing an Ideal Premix Through Outsourcing

Outsourcing sterile compounding requires using pharmaceutical manufacturers or reputable 503B facilities. When choosing an ideal premix sterile preparation or product, consider these steps:

1. Look for an available, manufactured premix first since manufacturers are required to comply with the highest level of safety standards.[8] Also, manufactured premixes generally have extended shelf-life as noted in Table 1, which can help to reduce waste.[4]

2. If no commercially manufactured premix is available, a 503B outsourcing facility should then be considered.[9] As with manufactured premixes, the outsourcing facility's reputation, recalls or other FDA issues should be researched.

The American Society of Health-System Pharmacists created an Outsourcing Sterile Products Preparation Vendor Assessment Tool to guide your facility through this assessment of the outsourcing facility.[9] Pharmacies are responsible for ensuring the outsourcing facility meets pharmacy regulations and standards. If outsourcing through a 503B facility, it is crucial to perform audits to ensure all testing is in place (quality control testing of preparations, certification of primary and secondary engineering controls, calibration/verification of the accuracy of equipment, environmental monitoring, personnel sampling, standard operating procedures, etc.) and it's crucial to have a quality agreement in place.

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Conclusion

The decision to insource or outsource sterile compounding is not a simple one. While insourcing provides increased control and customization over formulations, it also requires extensive training, compliance with compounding standards, and significant investments in personnel and equipment. On the other hand, outsourcing offers cost-effective solutions, reduces investments in facilities and personnel, and provides access to commercially available, ready-to-administer products with longer expiration dates. This allows pharmacies to focus on core functions and improves efficiency in critical care areas.

Manufacturers are subjected to the highest level of regulation, therefore, when outsourcing, we should always check first to see what is commercially available. While they are not held to the same high standard as pharmaceutical manufacturers, reputable 503B facilities can still be a viable option when a commercially manufactured premix is not available. It is crucial to research the reputation and FDA compliance of outsourcing facilities. The American Society of Health-System Pharmacists has created a helpful assessment tool for evaluating outsourcing facilities. Pharmacies should also perform audits and have quality agreements in place when outsourcing through a 503B facility to ensure the highest level of safety and quality.

Ultimately, maintaining the flexibility to do both insourcing and outsourcing depending on the need is crucial in today's environment. By carefully considering the advantages and disadvantages of each approach, pharmacies can make informed decisions that prioritize patient safety and optimize their operations.

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