503B Outsourcing Market Overview

Industry Bulletin

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Introduction

Healthcare providers today are challenged to do more with less while trying to improve patient care. Managing a hospital or surgery center pharmacy in today's complex regulatory environment can be a daunting task. Drug shortages, recalls, supply procurement, staff shortages and space constraints are just a few of the challenges faced on a daily basis. Outsourcing compounded sterile preparations (CSP's) is an effective business strategy to alleviate some of these concerns.

This industry bulletin will provide a general overview on outsourcing facilities, benefits to your pharmacy operation and some general considerations for selecting a trusted partner.

In-house Hospital Compounding

Healthcare institutions utilize a variety of medications throughout the patient care journey. These medications come in a variety of containers such as bottles, IV bags, pain pumps, syringes and vials.

Typically, the procurement process for these types of CSP's is to either compound and package them in-house or outsource to an external provider. Healthcare institutions that perform sterile drug compounding in-house continue to face new, heightened quality requirements and intense regulatory oversight to ensure compliance with regulatory guidelines for the sake of patient safety. As regulations continue to evolve, it is becoming more challenging for healthcare institutions to safely and effectively compound drugs in house.

Due to these in-house challenges, many healthcare institutions are electing to outsource their sterile compounding and drug repackaging to U.S. Food and Drug Administration (FDA) registered 503B outsourcing facilities. But what exactly is a 503B outsourcing facility and how does a healthcare institution evaluate and select the right partner?

CHALLENGES INCLUDE:

- **Heightened and ever-changing regulatory oversight**
- **Continuing drug shortages and escalating drug costs**
- **Shorter in house shelf life and large procurement containers that can lead to medication waste and revenue loss**
- **Allocating pharmacy staff to devote to compounding preparations**
- **Costly investments in equipment**
- **Robust and ongoing staff training to ensure compliance and patient safety**

The Birth of FDA-registered 503B Outsourcing Facilities

An outbreak of fungal meningitis at the New England Compounding Center in September 2012 focused the attention of the FDA and Congress on how drugs are compounded in the United States – specifically, how we can be assured that compounded drugs are safe, effective and commercially available, and how we can more easily track drugs through the supply chain.

An important consequence of the outbreak was the Drug Quality and Security Act (DQSA), signed into law in November 2013. The DQSA created two distinct types of compounding categories in sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act.

1. **Section 503A** applies to licensed physicians and pharmacists who compound for individual patients based on a prescription. 503A compounders are defined as traditional small batch compounding pharmacies, where medications can be produced for short-dated use, prescribed either for specific individual patients or in limited quantities before receipt of a prescription.

2. **Section 503B** established a new category, outsourcing facilities. Outsourcing facilities are FDA-registered locations where sterile drugs may be compounded (including repackaging) as long as certain conditions are met. Unlike 503A providers that compound medicines for a specific patient prescription, outsourcing facilities produce CSP's in bulk for healthcare institutions. The following must be completed to qualify as an outsourcing facility:

- **Registration with the FDA**
- **Comply with current good manufacturing practice (CGMP) requirements**
- **Be inspected by FDA according to a risk-based schedule**
- **Meet certain other conditions, such as reporting adverse events and providing FDA with certain information about the products they produce**
- **Comply with all requirements set forth by the FDA in section 503B**

By virtue of meeting these conditions, human drug products compounded by an outsourcing facility are exempt from Federal Food, Drug, and Cosmetic Act requirements concerning approval of drugs under New Drug Application's (NDA's) and Abbreviated New Drug Application's (ANDA's), labeling of drugs with adequate directions for use, and drug supply chain security requirements. For additional information, please visit the FDA website[1] to review all requirements set forth in section 503B of the Federal Food, Drug, and Cosmetic Act.

Serving the Healthcare Industry

Typically, outsourcing facilities provide CSP's to healthcare providers across the continuum of patient care including hospitals and health systems, ambulatory surgery centers, clinics and doctor's offices.

Outsourcing facilities produce CSP's to meet needs that traditional drug manufacturers and commercially available drugs do not meet. For example, an outsourcing facility may offer unique dosages or provide the drug in a "ready to use" package, such as a pre-filled syringe or IV bag to assist in reducing medication errors.

Also outsourcing facilities serve healthcare institutions by assisting the market when drug shortages occur. Outsourcing facilities are prohibited by the 503B statute from compounding any drug that is essentially a copy of one or more FDA-approved drugs. However, when a drug shortage occurs and an FDA-approved drug is placed on the FDA drug shortage list[2], 503B facilities are allowed to compound and supply the drug in order to assist during the shortage.

Examples of 503B services include:

- **Pre-filled syringes (patient-controlled analgesia (PCA) syringes and Intravenous (IV) injections)**
- **Pre-filled IV bags**
- **Pre-filled elastomeric pain pumps**
- **Pre-filled vials and eye dropper bottles**

While it's important to note that not all 503B vendors provide a full portfolio of compounded sterile preparations, examples of the medication categories offered could include:

- **Analgesics, anesthetics, antibiotics, neuromuscular blockers, ophthalmic preparations, sedatives and vasopressors**

These drugs are commonly used in the surgical and labor and delivery healthcare settings.

Evaluating a Vendor

A common misconception is that if a 503B outsourcing facility is registered with the FDA, it is also in good standing with the FDA, but the reality is that the FDA does not license or otherwise formally approve or disapprove 503B outsourcing facilities. Instead, while the FDA is very active in its inspection of 503B outsourcing facilities, monitoring remediation of observations resulting from those inspections, and issuing Guidance For Industry to clarify FDA policy on an array of detailed 503B matters, the fact that a 503B outsourcing facility is FDA-registered has no correlation with the quality of compounding operations or products at that facility. 503B facilities are expected to comply not only with the 503B statute and cGMP, but also with FDA Guidance For Industry even though the Guidance does not carry the weight of actual law or regulation. As a result, not all 503B outsourcing facilities are equal nor are they all necessarily in good standing with the FDA just because they continue to be registered.

The selection of a 503B vendor is an important decision that requires thoughtful assessment and vetting of any potential vendor. Pharmacy leaders must do their due diligence to fully assess the quality, safety and track record of any potential 503B partner.

Thoroughly evaluating an outsourcing facility may seem overwhelming or unnecessary and some healthcare institutions may be inclined to simply purchase from the lowest cost provider, but this approach is strongly discouraged, particularly with the priority of patient safety in mind.

Selecting a 503B partner that meets all the regulatory requirements and understanding its history with the FDA is critical to the quality and reliability of the product. For example, the likelihood of a pharmaceutical supply chain interruption or drug recall from a 503B vendor with a poor inspection history is significantly higher than one with a strong track record.

Fortunately, there are many widely used industry resources available to help with the 503B audit process.

Resources to Help With Your Evaluation

Many health systems and group purchasing organizations (GPO's) have established robust auditing tools for evaluating a 503B vendor. If you are part of a GPO, please contact them to request their inspection details.

Additional resources publicly available are as follows:

- Visit the ***FDA*** website to review their list of Registered Outsourcing Facilities[3]. Included on this website is also information pertaining to registration dates, inspection dates and inspection findings. Of particular note are the following:
  - Quality observations, or ***Form FDA-483's***, will be outlined on inspection reports and should be reviewed for severity, remediation and response by the outsourcing facility.
  - Pay close attention to facilities that received ***Warning Letters***, as Warning Letters reflect an elevated level of concern by the FDA. Warning Letters are the principal means by which the agency provides prior notice of violations and of achieving voluntary compliance.[4]
  - Additional scrutiny should be employed in circumstances of a ***Regulatory Meeting***. A Regulatory Meeting is a meeting requested by FDA management at its discretion, to inform responsible individuals or firms about how one or more products, practices, processes, or other activities are considered to be in violation of the law.[5]
  - If there are reported ***Warning Letters, Form FDA-483's*** or a ***Regulatory Meeting***, demand that the vendor shares their formal response and resolution strategies.
- As part of their annual license renewal, the ***State of California Board of Pharmacy***[6] performs an annual inspection of any 503B facility that holds a California outsourcing facility license.
  - You may contact them or the 503B facility to inquire about the results of any given inspection.

Additional Resources to Help With Your Evaluation

- The ***U.S. Department of Justice Drug Enforcement Administration (DEA)***[7] makes periodic unannounced inspections to audit registered controlled substance storage locations. In a typical audit, DEA Diversion Investigators ensure that the controlled substance licensee/registrant is compliant with the Controlled Substance Act.
  - If you plan to outsource controlled substances be sure to contact your 503B vendor to inquire about their most recent DEA inspection
- The ***American Society of Health-System Pharmacists (ASHP)*** has a web-based Vendor Assessment Tool[8] to help you evaluate a 503B vendor in the following categories:
  - Regulatory compliance; Quality and patient safety measures; Medication administration safety features and Service excellence
  - Any vendor you are evaluating should be able to provide responses for their facility

A high-quality, compliant and transparent 503B vendor that is in good standing with the FDA, DEA and state boards of pharmacy should willingly provide you with any documentation that you request, as well as allow you to visit their facility to conduct your own onsite inspection.

Available Resources

- ☑ U.S. Food and Drug Administration (FDA)
- ☑ State of California Board of Pharmacy
- ☑ U.S. Department of Justice Drug Enforcement Administration (DEA)
- ☑ American Society of Health-System Pharmacists (ASHP)

Conclusion

While essential to patient care, CSP's can be complicated and arduous to effectively manage in-house. Partnering with a trusted and compliant FDA-registered 503B outsourcing facility can provide many benefits to your facility including:

- **Decrease the compounding burden on pharmacists and pharmacy technicians, allowing them to focus on other important pharmacy tasks and their patients.**
- **Provide a consistent and reliable supply of high-quality ready to administer pre-packaged and labeled CSP's**
- **Inherent safety factor by using repeatable, validated cGMP aseptic processes**
- **Support your facility during drug shortages**
- **Extended Beyond Use Dates (BUD) to enable better inventory management and reduce waste**
- **Documented quality reporting**

When considering outsourcing options and a vendor, it is essential to perform a thorough evaluation of a potential vendor's compliance with regulations. In addition, active and ongoing communication and collaboration with your outsourcing partner is critical to success.

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References:

1,3 U.S. Food and Drug Administration. FDA Registered Outsourcing Facilities; www.fda.gov/drugs/human-drug-compounding/information-outsourcing-facilities

2 U.S. Food and Drug Administration. FDA Drug Shortages; www.accessdata.fda.gov/scripts/drugshortages/default.cfm

4,5 U.S. Food and Drug Administration. Regulatory Procedures Manual; https://www.fda.gov/media/71765/download

6 California State Board of Pharmacy; www.pharmacy.ca.gov/licensees/ask_inspector.shtml

7 U.S. Department of Justice Drug Enforcement Administration; Diversion Control Division; https://www.deadiversion.usdoj.gov/21cfr/cfr/index.html

8 Outsourcing Sterile Products Preparation: Contractor Assessment Tool; https://www.tn.gov/content/dam/tn/health/documents/SterileProductsAssessmentTool.pdf