How NABP Drug Distributor Accreditation can help Outsourcing Facilities demonstrate their commitment to the U.S. Drug Supply Chain

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Summary Overview

Although FDA-registered outsourcing facilities are a significant link in the U.S. drug supply chain, the compounded drugs provided by them are exempt from track and trace requirements created by the Drug Supply Chain Security Act (DSCSA). By obtaining a Drug Distributor Accreditation from the National Association of Boards of Pharmacy (NABP), outsourcing facilities can still demonstrate their procedures and practices are compliant with track and trace. ***Yet fewer than 15% of outsourcing facilities have obtained this accreditation.***†

In This Article

Past events that uncovered weaknesses in the U.S. Drug Supply Chain

Four years before vials of compounded betamethasone precipitated a deadly multi-state meningitis outbreak in 2012, an FDA-registered drug manufacturer distributed injectable heparin contaminated with chondroitin throughout the United States, sickening hundreds of patients and killing eighty-one.[1] The source for the betamethasone was a single compounding pharmacy in New England. The

Heparin source, however, spanned all the way back to an offshore-produced Active Pharmaceutical Ingredient (API), compromising confidence in multiple links in the drug supply chain.

Drug distribution can often seem like more of a tangled web than a straightforward path. In 2010, Canada Drugs (a drug distribution company from across the northern border) introduced counterfeit Avastin into the United States. Canada Drugs then purchased and used other companies' customer lists, brand names, and inventories,[2] allowing further fraudulent drug transactions and complications concerning traceability. Eventually, at the end of the supply chain where patients are treated, up to 19 clinics in California, Texas, and Illinois may have purchased injectable Avastin—*which contained no Avastin whatsoever*.[3]

After the meningitis outbreak of 2012, Congress passed the **Drug Quality and Security Act (DQSA)** in 2013, which strengthened federal oversight over drug compounding and drug distribution. Title I of DQSA (the Drug Quality Act) added section 503B to the Federal Food, Drug, and Cosmetic Act (FD&C Act), creating a new type of FDA-registered drug compounding establishment—the outsourcing facility. Title II of DQSA (the Drug Supply Chain Security Act [DSCSA]), added section 582, enhancing track and trace requirements during drug distribution.

How Section 582 Strengthens the U.S. Drug Supply Chain

What are some of the track and trace requirements in section 582? One is for manufacturers or repackagers to add a standardized product identifier on packages or homogenous cases of prescription drug products. These identifiers—which are comprised of the NDC number, serial number, lot number, and expiration date—must be in both human-readable and machine-readable formats.[4] On drug packages (e.g. cardboard trays of injectable heparin vials), the machine-readable format must be a 2D data matrix barcode. On homogenous cases, barcodes may be linear.

Displaying a standardized product identifier is just the foundational first step toward

full implementation of section 582. The ultimate pathway laid out by the DSCSA requires authorized trading partners to exchange transaction information, transaction statements, and transaction histories as the drug packages change ownership along the supply chain. Some purchasers may notice, however, that standardized product identifiers are not components on packages of compounded drugs received from outsourcing facilities. This is because section 503B exempts compounded drugs from section 582 requirements.

In fact, outsourcing facilities are not even referenced in section 582. The statute only defines five types of entities in the prescription drug supply chain: manufacturer, repackager, dispenser, wholesale distributor, and third-party logistic provider,[5] none of which perfectly fit the role of the outsourcing facility. Many outsourcing facilities, for example, will never directly dispense prescription drugs to patients, and none are allowed to wholesale.[6] If one further incorporates the different rules and regulations from the various states, the official role of the outsourcing facility in the drug supply chain becomes even more muddled. Arkansas, for example, requires outsourcing facilities to be licensed under its wholesale distribution regulations, and Arizona requires a manufacturer's permit.

No matter how inconsistently defined from state to state, all outsourcing facilities have a critical obligation to remain faithful to the intent of the DSCSA because the drug supply obtained for compounding ultimately becomes the drug supply used to treat patients. According to a 2021 survey by Pharmacy Products and Purchasing, 60-77% of hospital respondents reported purchasing compounded drugs from an outsourcing facility.[7] **By obtaining a Drug Distributor Accreditation from NABP, an outsourcing facility can demonstrate its commitment to ensuring a trustworthy drug supply, however only fewer than 15% currently have this accreditation**[8] (table 1).

Table 1 – NABP Accreditation Status of FDA-registered Outsourcing Facilities	
Total number outsourcing facilities listed on FDA website	**75**
Total number of FDA-listed outsourcing facilities that are also listed with NABP as having drug distributor accreditation.	11 (14.7%)
Total number of FDA-listed Outsourcing facilities that are not listed with NABP drug distributor accreditation.	64 (85.3%)

These results were determined on November 24, 2021 by comparing the FDA website of registered outsourcing facilities to the NABP list of accredited drug distributors.

How NABP drug distributor accreditation can demonstrate that outsourcing facilities are compliant with section 582

NABP will first takes steps to ensure that their accreditation program is relevant to each outsourcing facility that it surveys. Before it begins the on-site survey, NABP will confirm that the outsourcing facility is fully operational, that it maintains proper storage requirements for drugs and devices, that it identifies as being compliant with section 582, and that it has processes and systems in place to detect and prevent the receipt and distribution of suspect drug products.

Identifying and preventing the distribution of suspect drug products is a critical component in section 582. A suspect product is defined as one for which there is suspicion of any of the following:

- Product is potentially counterfeit, diverted, or stolen
- Product is potentially adulterated
- Product is potentially the subject of a fraudulent transaction
- Product appears otherwise unfit for distribution.[9]

Identifying and acting on a suspect product must also be a core strength of an outsourcing facility's procedures and practices. Among the many focus points covered during the NABP accreditation survey, there are three especially relevant to having a reliable drug supply: "Authorized Trading Partners (Sources and Vendors)," "Product Tracing," and "Reporting and Notifications."

1. Survey Focus Point: Authorized Trading Partners (Sources and Vendors)
Because outsourcing facilities must meet all the conditions in section 503B, they are only allowed to prepare compounded drugs from approved drug products or, under limited circumstances, from bulk drug substances (ie. API). When

compounding with approved drug products, outsourcing facilities must only use products purchased from authorized manufacturers, authorized repackagers, or authorized wholesale distributors.

During the accreditation survey, the inspector will examine procedures and practices for authorized trading partner verification, due diligence, and sourcing drug products. By successfully meeting these criteria, an Outsourcing Facility demonstrates its commitment to preventing illegitimate drug products from entering its drug supply.

2. Survey Focus Point: Product Tracing

To comply with section 582, outsourcing facilities should not accept ownership of a drug product unless the prior owner has also provided the drug's transaction history, transaction information, and transaction statement.

The NABP surveyor will examine samples of these transactional records during the Outsourcing Facility's accreditation inspection, and will also review inventory adjustment records, recall records, distribution records, and destruction records. Possessing adequate documentation provides assurance that the approved drug products used in compounding are fully traceable back to an authorized source.

3. Survey Focus Point: Reporting and Notifications

One of the most important objectives of section 582 is to ensure that suspect or confirmed illegitimate drug products are identified and quarantined. If illegitimate drug products are suspected or confirmed, outsourcing facilities must conduct timely investigations, perform product dispositions, and take appropriate and reasonable steps to assist any impacted customers with their own product dispositions.

During accreditation, the NABP surveyor will review policies and procedures for illegitimate product determination and reporting, FDA requests for verification of suspect product, illegitimate product notifications from FDA trading partners, and suspect product investigations.

Conclusion

There are some limitations in the scope of an NABP survey. A survey does not equate to a full Current Good Manufacturing Practices (CGMP) inspection. NABP is not the FDA.

Also, it's important to note that section 582 only applies to drug products. It does not apply to any API obtained from bulk drug substance suppliers in the drug supply chain. Therefore, it's critical outsourcing facilities only compound from API when it's legally allowable. Fortunately, section 503B only allows compounding from API under two circumstances: 1. If the drug appears on the FDA's drug shortage list; 2. When the API appears on an FDA list of bulk drug substances for which there's a clinical need (i.e. The 503B Bulks List).[10] However, because the FDA is still evaluating 216 nominated substances that are also components of an approved drug product, outsourcing facilities often have to limit themselves (Table 2).

Table 2

In certain respects, healthcare organizations must rely on faith when selecting an outsourcing facility. Unlike approved drug products, compounded drugs will not come with a transaction history, transaction information, or a transaction statement. Alternatively, an NABP accreditation certificate can provide some objective evidence of faithfulness to the drug supply chain and to the safety of the patients treated at the end.

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Elevate Your Sterile Compounding Program

The first step is simple. Connect with our sterile compounding consultant, Eric Bauer, RPh, BCSCP, and find out how our programs can be customized to meet your needs.

Connect

† See footnote 8.

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4. Product Identifiers under the Drug Supply Chain Security Act Questions and Answers. FDA Guidance for Industry. June 2021.
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10. Interim Policy on Compounding Using Bulk Drug Substances under section 503B of the Federal Food, Drug, and Cosmetic Act. FDA Guidance for Industry. March 2019.
11. Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act (Pages 2 to 5); https://www.fda.gov/media/94164/download; Updated June 7, 2021.