WASHINGTON STRATEGIC CONSULTING

WSC POLICY BRIEF

Compounding Pharmacies Under Sections 503A and 503B of the FD&C Act

Overview

On April 15, 2016, the Food and Drug Administration (FDA) released three new draft guidance documents intending to clarify lingering questions surrounding the application and the enforcement of sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act) that regulate the practice of pharmacy compounding.

Generally, section 503A carves out "traditional" pharmacy compounding from FDA oversight, leaving its regulation to the states. While these facilities are generally required to obtain a patient-specific prescription before compounding a product, the FDA has indicated that it will not take enforcement action in the event that a drug is compounded without a prescription if, among other requirements, the distribution of the drug is limited to patients within facilities under common ownership and control that are within a one-mile radius of the compounding pharmacy.

Section 503B defines facilities that may compound greater quantities of drugs without the receipt of patient specific prescriptions, making them more similar to drug manufacturers. As a result, the FDA has greater oversight of outsourcing facilities, including ensuring that they comply with current good manufacturing practice (CGMP) requirements.

While the April 2016 guidance has yet to be finalized, the FDA has signaled the agency's intention to release further guidance and regulations in 2018 to encourage more compounding pharmacies to register for 530B regulation. In the interim, however, as noted in this policy brief, federal law does not currently empower the FDA to enforce the one-mile radius requirement. Any such enforcement authority would need to be established through the formal rulemaking process. Moreover, the agency has suggested that it intends to continue delegating enforcement of low-volume *intrastate* distribution by 503A facilities to state regulatory authorities.

Facility Definitions

Section 503A, added to the FD&C Act by the Food and Drug Administration Modernization Act in 1997, describes the conditions that must be satisfied for human drug products compounded

by state-licensed pharmacies, among others (known as "traditional compounders")

- Under section 503A, a licensed pharmacist or a licensed physician within a hospital or health system must compound drug products *for an identified individual patient*.
    - The compounding must either take place (a) after the receipt of a valid prescription or order for an identified individual patient or (b) in limited quantities (up to a 30-day supply) in advance of receipt of a valid prescription or order for an identified individual patient, and the drug must be distributed after receipt of the prescription or order.

Section 503B, added to the FD&C Act by the Drug Quality and Security Act (DQSA) in 2013, created a new category of compounders called *outsourcing facilities*.

- A compounder can register as an outsourcing facility if it intends to provide compounded drugs to facilities such as other hospitals or clinics without first obtaining a prescription for an identified individual patient.

- Hospitals and health system compounders that elect to register with FDA as outsourcing facilities must comply with all of the provisions of section 503B, including reporting adverse events, labeling products with certain information, and complying with stricter 'current good manufacturing practice' (CGMP) requirements.

In other words, outsourcing (503B) facilities that meet certain conditions may compound drugs that are not necessarily in response to patient-specific prescriptions, whereas 503A facilities may not.

2016 FDA Guidance

In April 2016, FDA issued draft guidance, "Hospital and Health System Compounding under the Federal Food, Drug, and Cosmetic Act: Guidance for Industry. The guidance describes how FDA intends to apply Section 503A to drugs compounded by licensed pharmacists or physicians in state-licensed hospital or health system pharmacies for use within the hospital or health system.

According to the guidance, a hospital pharmacy may distribute compounded drug products without first receiving a patient-specific prescription or order provided that the drug products are distributed only to healthcare facilities that are **owned and controlled by the same entity** that owns and controls the hospital pharmacy and that are located **within a 1-mile radius of the compounding pharmacy**. Only when non-patient specific medications are compounded and dispensed/distributed is the 1-mile radius requirement at issue.

FDA reasoned that a central pharmacy sending compounded drugs beyond the 1-mile limit would, for all intents and purposes, be operating like a large manufacturing operation (a 503B pharmacy), but without the necessary standards to ensure drug quality. **Hospital-based pharmacies that wish to distribute drugs outside of the 1-mile radius of the pharmacy will need to register with the FDA as a 530B facility** (and therefore be subject to increased FDA oversight).

It is important to note that, in general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidance documents describe the agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

Hospital and Health System Impact

FDA Definition of Compounding

The FDA's definition of compounding differs from the commonly used USP definition of compounding. 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.

> 21 U.S.C. 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.*

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. However, deviating from package labeling (e.g., using a different diluent or using an extended beyond-use date) when preparing medication does fall under FDA's definition of compounding.

503B Registration

Hospitals and health systems may prefer to compound in their own pharmacies under 503A in order to maintain a closed patient care system and to maximize resources. If a hospital compounding pharmacy wishes to distribute compounded medications to affiliated facilities outside, they will need to register as a 503B pharmacy. This can be accomplished using FDA's electronic drug registration system or by sending an email to FDA's drug registration and listing staff with the required registration information.

However, as noted above, **the DQSA did not empower the FDA to enforce the one-mile requirement**, and without a specific regulation to back the guidance up, the guidance document remains a statement of FDA's current thinking on the subject and is not legally enforceable.

According to the American Society of Health-System Pharmacists (ASHP), 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.

What's Next

Final Guidance

As of this writing, the FDA has not updated the April 2016 guidance on 530A and 530B compounding pharmacies.

2018 Compounding Policy Priorities

According to FDA's 2018 Compounding Policy Priorities Plan, the agency plans to issue proposed regulations on CGMP requirements that 503B outsourcing facilities must meet. In the interim, the agency is revising the draft guidance to describe a new flexible, risk-based approach to CGMP requirements for outsourcing facilities. This guidance will consider how CGMP requirements should be applied in light of the size and scope of an outsourcing facility's operations.

The agency's goal is for more compounders to register as outsourcing facilities with the understanding that they can still meet the FDA's core requirements for drug quality, based on the size and scope of their compounding operations.

FDA Partnership with State Regulatory Authorities

The FDA is working closely with state partners on oversight of compounding activities. In the upcoming months FDA plans to issue a significantly revised draft MOU between the FDA and the states regarding compounding under section 503A. Once revised and issued in final form, the MOU will serve as an important mechanism for the FDA and the states to come to a mutual understanding about what types of activities are primarily overseen at the state versus federal level.

FDA plans to focus their inspection and enforcement resources on activities that present the greatest risk to patients across many states, while primarily **leaving to state regulatory authorities routine oversight of those activities that mainly affect patients within their own borders.**

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