

Preliminary Recommendations for Aligning Federal and State Regulation of Compounders Registered as Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act

I. Overview

Clear and consistent regulation of outsourcing facilities is important to their success, and by extension, successful implementation of the Drug Quality and Security Act (DQSA). FDA recognizes that both its own regulation and state regulation have a significant impact on the success of outsourcing facilities.

FDA-State regulation alignment is particularly important in three specific areas: licensure and registration, filling of patient-specific prescriptions, and compliance with current good manufacturing practice (CGMP) requirements.

Below we describe current federal and state regulations applicable to these topics; the challenges that could arise if state and federal requirements were to differ; and opportunities to advance a more harmonized regulatory approach that will enhance oversight, clarity, and consistency, and support the compliance and success of outsourcing facilities.

II. Current Federal and State Regulation of Outsourcing Facilities

A. Overview of Section 503B and Federal Regulation of Outsourcing Facilities

Compounders in the United States that have not registered with FDA as outsourcing facilities may produce drugs that are eligible for the exemptions under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act). Section 503A describes the conditions that must be satisfied for drug products compounded by a licensed pharmacist in a State-licensed pharmacy or a Federal facility, or by a licensed physician, to be exempt from federal statutory requirements for FDA approval, CGMP, and the labeling of drug products with adequate directions for use.

In 2013, the DQSA added a new section 503B to the FD&C Act, creating a new type of compounding entity called outsourcing facilities. While drugs compounded by outsourcing facilities that meet the conditions of section 503B are eligible for exemptions from FDA approval and certain labeling requirements, they are not exempt from CGMP requirements. Outsourcing facilities must register with FDA and must be inspected according to a risk-based schedule. They are also subject to a number of statutory conditions that do not apply to section 503A compounders, such as product labeling and reporting requirements. FDA endeavors to inspect outsourcing facilities within two months following their initial registration, if they have not had a recent FDA inspection.

Under federal law, as long as a facility remains registered with FDA as an outsourcing facility, all of its drugs must be compounded in accordance with CGMP requirements and must meet the conditions of section 503B to qualify for the exemptions in that section.

Under federal law, outsourcing facilities may hold a pharmacy license and may fill patient-specific prescriptions. Section 503B(d)(4) of the FD&C Act states that an outsourcing facility is not *required* to be a licensed pharmacy, and section 503B(d)(4)(C) states that outsourcing facilities *may* or may not obtain prescriptions for identified individual patients prior to distribution of compounded drug products. In addition, section 503B(a) requires that compounding at an outsourcing facility be done by or under the direct supervision of a licensed pharmacist.

B. Overview of State Laws and Regulation of Outsourcing Facilities

States bear the primary oversight responsibility for state-licensed pharmacies (that are not registered as outsourcing facilities) and licensed physician compounders. States regulate compounding by, for example: imposing licensure or registration requirements; conducting inspections, often annually; and imposing quality requirements, often United States Pharmacopeia (USP) Chapters <795> and <797>.

Since creation of the outsourcing facility category in 2013, states have been working to adapt their existing oversight systems to accommodate this new type of compounder. A few states have established licensure or registration categories specific to outsourcing facilities, but most states have so far licensed or registered outsourcing facilities under existing regulatory categories, including pharmacies, wholesalers, or manufacturers, each with their own set of regulatory requirements.

State requirements that apply to federally registered outsourcing facilities may differ from state to state. Outsourcing facilities are generally subject to state licensure or registration requirements in the state in which they are located, as well as all the states into which they ship drug products. Because most outsourcing facilities ship interstate, heterogeneity in state requirements can cause licensure or registration challenges for outsourcing facilities. If state requirements were also to differ from requirements in federal law, that would create additional challenges and confusion. Such challenges have the potential to undermine the development of outsourcing facilities as a source of compounded drugs that are prepared subject to higher quality standards.

C. Examples of Problems Outsourcing Facilities Encounter under the Current Landscape

1. State licensure and registration requirements

Variations in state licensure or registration categories and related regulatory requirements for outsourcing facilities can both impose burdens on outsourcing facilities and impede their ability to distribute drug products in certain states. For example, one state may require an outsourcing facility that sends compounded drugs into the state to be licensed as a pharmacy in its state of residence, but the state in which the outsourcing facility is located may prohibit the outsourcing facility from being licensed as a pharmacy. Such differing state requirements would effectively prevent the outsourcing facility from doing business in both states.

2. Filling patient-specific prescriptions

Certain state laws may not provide for outsourcing facilities to fill patient-specific prescriptions. However, under federal law, an outsourcing facility may or may not obtain prescriptions for identified individual patients (section 503B(d)(4)(C) of the FD&C Act). If a state law were to prohibit an outsourcing facility from being licensed as a pharmacy, and if pharmacy licensure were required in the state in order for a facility to fill patient-specific prescriptions, an outsourcing facility could be prevented from engaging in this practice in that state.

3. CGMP requirements

Under federal law, an outsourcing facility, whether or not it is licensed as a pharmacy, must meet CGMP requirements for all compounding of human drugs in that facility, even when compounding drugs to fill patient-specific prescriptions. This affords patients and providers an option to source compounded products made under more stringent quality standards. Compliance with CGMP requirements also provides an important public health protection to the relatively large number of patients that may receive compounded drug products made by an individual outsourcing facility. State regulations that require compliance with quality standards other than CGMP requirements for entities registered with FDA as outsourcing facilities could cause confusion lead an outsourcing facility to believe that they do not need to comply with CGMP standards. .

III. FDA's Recommendations for State Regulation of Outsourcing Facilities

A. States Should Adopt Requirements that Conform to Provisions in Section 503B

FDA recommends that states: 1) license or register outsourcing facilities as “outsourcing facilities”; 2) permit outsourcing facilities to fill patient-specific prescriptions; and 3) require compliance with CGMP requirements for all human drug compounding activity at an entity that is registered with FDA as an outsourcing facility. These recommendations are described in further detail below.

Greater alignment between federal and state requirements, and among states' requirements, will reduce and possibly even eliminate the potential for direct and indirect conflicts, burdens, and

confusion experienced by outsourcing facilities. This in turn will help foster the success of the outsourcing facilities, which the DQSA created to help to address national concerns about oversight and quality of compounding practices.

Further, state regulation of outsourcing facilities that conforms to key provisions of federal law will enhance collaborative enforcement options. While FDA is the primary entity that regulates outsourcing facilities and will pursue enforcement action when necessary, states may have the ability to use different tools and act more rapidly than FDA to stop unsafe activity when identified, such as through immediate state licensure suspension.

B. FDA makes the following specific recommendations to states:

1. State licensure and registration requirements

We recommend that states create a licensure or registration category specific to outsourcing facilities. Requiring these facilities to be primarily licensed as “manufacturers,” “wholesale distributors,” or pharmacies can result in conflicts with other states’ laws. Compliance with federal law applicable to outsourcing facilities should be a condition of state licensure or registration under this category.

2. Filling patient-specific prescriptions

We recommend that states allow entities that are licensed or registered with states as outsourcing facilities to fill patient-specific prescriptions.

We understand that the most practical way for many states to allow this may be to license the outsourcing facility as a pharmacy in addition to primary licensure as an outsourcing facility. State pharmacy licensure would allow the outsourcing facility to fill prescriptions and the state to enforce applicable state pharmacy practice requirements. We request that states adopting this approach take care to address any state pharmacy requirements that, if applied to outsourcing facilities, could conflict with federal law. Most importantly, we recommend that state laws make clear that outsourcing facilities, even when licensed as a pharmacy, remain subject to CGMP and other applicable federal requirements.

We also recognize that updating regulations takes time. In the interim, we recommend that states consider differences between their requirements and other states’ requirements that may prevent an outsourcing facility from doing business in both states, and make efforts, where reasonable, to address such barriers.

3. CGMP requirements

We recommend that states make clear that as a condition of licensure or registration as an outsourcing facility, regardless of additional licensure as a pharmacy, all compounding activity

that occurs at an outsourcing facility, including patient-specific compounding, is subject to CGMP requirements. Drugs compounded at an outsourcing facility registered with FDA under section 503B are subject to CGMP requirements, and while the outsourcing facility remains registered such drugs cannot qualify for exemptions from CGMP under section 503A. This would be true even if, for example, a facility registered with FDA as an outsourcing facility loses its state outsourcing facility license or registration for failure to comply with state requirements.

IV. Conclusion

Collaboration and alignment between FDA and the states are fundamental to instituting complementary compounding oversight programs. While FDA is primarily responsible for oversight of outsourcing facilities, state oversight also plays an important role. Alignment of oversight systems will help support the success of the outsourcing facilities by reducing regulatory confusion or potential conflict for compounded drug products in interstate commerce. State licensure or registration of outsourcing facilities also allows the state to define the set of tools it may use to address an outsourcing facility's noncompliance, which may supplement or be more agile than those available to FDA.

FDA will continue to perform inspections of outsourcing facilities as required under section 503B(b)(4) of the FD&C Act, communicate as closely as possible with states regarding inspections in their jurisdictions, and provide states with the opportunity to accompany FDA on these inspections.