



FDA Oversight of Interstate Drug Compounding Raises Serious Concerns for Infusion Providers

The Issue

State governments have traditionally regulated drug compounding pharmacies, but in recent years safety issues have raised concerns about the adequacy of these regulations and the extent to which the federal government should be involved in oversight. In response, the U.S. Food and Drug Administration (FDA) has issued a series of documents, including a February 19 draft memorandum of understanding (MOU) addressing the distribution of certain interstate compounded drug products. The language in the MOU raises questions and has important implications for the ability of compounding pharmacies to serve patients with specific needs across state lines. Specifically, the MOU inappropriately treats dispensing and distribution as interchangeable terms and maintains that an “inordinate” number of compounded drug products have been distributed (including dispensed) between states in cases where the number of units of product distributed was equal to or greater than 30% of the number of units compounded by that entity in a given month. While Innovatix applauds the agency’s efforts to bring increased scrutiny to those pharmacies that cross the line from compounding to manufacturing, the implications of combining the definitions of dispensing and distribution, and for choosing 30% as a general rule, raises concerns for our infusion members.

Background

To address the problems underpinning the New England Compounding Center (NECC) fungal meningitis outbreak in 2012 that left 64 dead and over 700 ill, Congress passed the Drug Quality and Security Act (DQSA) of 2013 (H.R.3204), which President Obama



signed into law in November of that year. The law appropriately aims to bring larger compounding manufacturers or those that are now mass-producing products under increased federal regulation.

Specifically, the law creates a voluntary outsourcing facility category under section 503B of the Food, Drug & Cosmetic Act (FDCA). A sterile drug compounding entity that elects to register with the FDA as an outsourcing facility must ensure that its production complies with the FDA’s Current Good Manufacturing Practices and is subject to FDA inspection based on a set of risk factors. Further, such outsourcing facilities must meet certain other conditions, such as reporting adverse events and providing the FDA with requested information about its compounded products. An outsourcing facility must also pay an initial base registration fee of \$15,000, which is subject to inflation.²



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Memorandum of Understanding

In 2015, the FDA issued a draft MOU in accordance with DQSA requirements. The draft MOU is intended to foster communication between the states and the FDA, and to give the latter more control over interstate compounding. Compounding pharmacies must either operate in a state that has signed an MOU with the FDA, or if the state in which they operate has not signed an MOU with the FDA, no more than 5% of a pharmacy's compounded prescription drug orders may be dispensed or distributed to another state. The draft MOU addresses some of the issues that arose from earlier FDA regulations, but certain definitions remain of concern, specifically for the terms distribution and inordinate amounts.

Distribution

In the appendix to the MOU, the definition of distribution includes dispensing to an agent of a patient or to a patient for the patient's own use. Such a definition blatantly exceeds the scope of congressional intent. When Congress added Section 503A to the FDCA in 1997, policymakers intended the words distribute and dispense to be distinct and separate. The aim of regulating pharmacies that enter into manufacturing has consistently been at the forefront of the FDA's regulations, but the terms dispense and distribute need to remain separate in order to make the distinction between mass manufacturers and traditional compounders that compound patient-specific drugs. Home infusion therapy, which is made possible by infusion pharmacies, is a clear example of why the FDA's proposed definitions are problematic. Infusion pharmacies compound patient-specific medications for patients whose medical conditions cannot be treated with oral medications. Not only is home infusion therapy more cost-effective than inpatient treatment in a hospital or skilled nursing facility, but it can allow a patient to resume a normal lifestyle and

work activities while recovering from their illness, and in doing so, provide the patient with the opportunity for a better quality of life. By including dispensing in the definition of distribute, the MOU would potentially interfere with the ability of infusion pharmacies to dispense medically needed drugs to patients across state lines. It is not uncommon for the catchment areas of home infusion providers to include patients in neighboring states, due simply to their proximity. Depending on location, it may actually be faster for a provider located in a neighboring state to serve a patient than for a provider in the same state (but perhaps at a greater distance) to send the medication. Furthermore, though this distinction is not explicitly made in the MOU, its underlying purpose is understood: dispensing is the professional service provided by a pharmacist pursuant to a prescription, with the end-user being the patient. Dispensing is not an element of mass manufacturing nor should it be considered distribution of a drug.

Inordinate Amounts

The question of what constitutes an inordinate amount surfaced after the passage of section 503A of the FDCA. The law requires the FDA to develop a standard MOU for use by the states, and the first draft MOU released in 1998 defined inordinate in terms of both the total number of prescriptions and the individual products. That MOU was never finalized, and the recent draft MOU proposes that an entity has distributed (and dispensed) an inordinate amount of compounded drugs if the number of units distributed interstate is equal to or greater than 30% of the total number of compounded and noncompounded drug products distributed or dispensed during a calendar month. The FDA did not explain how or why 30% is now deemed the appropriate threshold amount nor does it appear to tie to quality concerns, and it remains unclear whether such a number is appropriate for different-sized pharmacies that serve



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individuals with varying medical needs. If a pharmacy meets the strict regulations of its state board of pharmacy and the FDA, the reason why it could distribute 30% of the number of units compounded by that entity in a given month as opposed to 32%, for example, is not clear. The FDA should remove the 30% cap on interstate compounded drug shipments, which may prevent some patients from obtaining specific or specialized medicines that they need and may also create troubling access issues for beneficiaries. Furthermore, the FDA did not include the definition of a unit in the MOU, which makes the policy and the full extent of its impact unclear for stakeholders.

Our Position

Innovatix supports services that enhance the delivery of quality patient care and to that end recognizes that changes are necessary to avoid another tragedy like the one that occurred at the NECC. However, to avoid new adverse health events from occurring, the language in the FDA's MOU needs to take into consideration the full range of patient needs. The FDA overreaches by including dispensing in the definition of distribution, especially since the Congress used them as two different terms in Section 503A of the FDCA. Further, the FDA should remove the 30% unit cap on interstate compounding,

as it neither ties to quality nor considers that pharmacies have different, changing medication demands. If the FDA insists on providing a subjective cap, then at a minimum, the term unit should be clearly defined and easily calculated so that it is understood by all affected entities. Innovatix believes that the draft MOU is a step in the right direction, but we urge the FDA to correct and clarify these areas of concern before finalizing this guidance.

1. Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the State of [Insert State] and the U.S. Food and Drug Administration can be found here: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM434233.pdf>.
2. Regulatory policy information can be found here: <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm166743.htm>.
3. Section 503A provides that a drug product may be compounded in compliance with this section only if the drug product is compounded in a State that has: (i) entered into a memorandum of understanding with the Secretary which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State; or (ii) not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician distributes (or causes to be distributed) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician.