

January 26, 2018

TO: Members, Subcommittee on Health

FROM: Committee Majority Staff

RE: Hearing on “Examining Implementation of the Compounding Quality Act”

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## **I. INTRODUCTION**

The Subcommittee on Health will hold a hearing on Tuesday, January 30, 2018, at 11:00 a.m. in 2123 Rayburn House Office Building. The hearing is entitled “Examining Implementation of the Compounding Quality Act.”

## **II. WITNESSES**

### **Panel I**

- Scott Gottlieb, M.D., Commissioner, U.S. Food and Drug Administration;

### **Panel II**

- Jenn Adams, Senior Vice President and President, Clinical Product Solutions, PharMEDium Services;
- Bruce Brod, M.D., Chair, Congressional Policy Committee, American Academy of Dermatology;
- Nancy Dargan, Patient of New England Compounding Center;
- Shawn Hodges, Vice President, International Academy of Compounding Pharmacists;
- Elizabeth Jungman, Director, Public Health, The Pew Charitable Trusts;
- Jacob Olson, President and CEO, Skywalk Pharmacy, on behalf of National Community Pharmacists Association;
- Molly Ventrelli, Vice President, Regulatory Affairs, Fresenius Kabi; and
- George Williams, M.D. President Elect, American Academy of Ophthalmology.

### **III. BACKGROUND**

#### **Drug Compounding**

Drug compounding is the process of combining, mixing, or altering pharmaceutical ingredients to create medication customized to the needs of a patient, or for whom an approved drug may not be appropriate. The Food and Drug Administration (FDA) does not review or approve compounded drugs prior to marketing for safety, effectiveness, or quality. However, the Federal Food, Drug, and Cosmetic Act (FFDCA) authorizes FDA to regulate their manufacture and sale.

Compounded drugs can serve important clinical needs when an FDA-approved product may not be an option for a patient. For instance, a patient who is allergic to a certain dye may need a compounded alternative to an FDA-approved product, or child or elderly patient or who cannot swallow a tablet may need a medicine in liquid form.

There are certain known risks associated with compounding that are balanced with the public health needs they meet. Poor compounding practices can result in serious drug quality problems, such as contamination or medications that do not possess the strength, quality, and purity they should. This can lead to serious patient injury and death.

Drug compounding has historically been overseen by state regulatory bodies such as boards of pharmacy or medicine. As a growing number of entities began engaging in the practice, and the scope of the practice expanded, concerns arose about compounding pharmacies functioning like traditional drug manufacturers, without the stringent oversight and standards adhered to by traditional manufacturers.

In 1997, Congress passed the Food and Drug Administration Modernization Act, which attempted to clarify FDA's authority to regulate compounded drugs. The act established section 503A in the FFDCA, which set forth the conditions that must be met for a compounded drug to be exempt from certain statutory requirements related to new drug approval.

In 2012, the New England Compounding Center (NECC) in Massachusetts shipped over 17,000 vials of a compounded steroid medication contaminated by fungal meningitis to patients and health care providers in 23 states across the country. The drugs were injected into patients' spines and joints. More than 750 people in 20 states developed fungal infections, and over 60 people died as a result. The scale of the outbreak was one of the worst and most fatal drug safety incidents in our country's history, and led to a series of investigations and actions by the Committee on Energy and Commerce.<sup>1</sup>

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<sup>1</sup> COMM. ON ENERGY & COMMERCE, FDA'S OVERSIGHT OF NECC AND AMERIDOSE: A HISTORY OF MISSED OPPORTUNITIES? (2013), available at <https://archives-energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/analysis/20130416Meningitis.pdf>

## **The Drug Quality and Security Act**

Following the NECC event, Congress passed the Compounding Quality Act (CQA) as Title I of the Drug Quality and Security Act (DQSA). The CQA clarified FDA's authority to regulate pharmacy compounding practice under section 503A of FDCA, and added a new section 503B creating a category of drug compounders termed outsourcing facilities. These outsourcing facilities compound sterile drugs in circumstances that go beyond what section 503A compounding pharmacies may do. Unlike section 503A compounding pharmacies, outsourcing facilities must comply with current good manufacturing practices (CGMPs) and are subject to certain registration, reporting, and inspection requirements.

Since enactment of the DQSA, FDA has issued numerous draft and final guidance documents, proposed and final rules, and a draft memorandum of understanding (MOU) to implement the CQA compounding provisions.<sup>2</sup> Most recently, FDA issued its 2018 Compounding Policy Priorities Plan, which outlines key priorities the agency will pursue as it continues to implement the CQA.<sup>3</sup> The plan lays out how FDA will address the quality standards for outsourcing facilities; regulate compounding from bulk drug substances; restrict compounding of drugs that are essentially copies of FDA-approved drugs; solidify the FDA's partnership with state regulatory authorities; and provide guidance on other activities that compounders undertake.

### **Issues for Consideration**

#### *Patient-Specific Prescriptions and Compounding for Office Use*

To qualify for the exemptions under section 503A, a compounded drug product must satisfy certain statutory conditions. Generally, a drug product may be compounded upon the receipt of a valid prescription for an identified patient, or in limited quantities before the receipt of a prescription for an identified patient, based on a history of prescription orders within an established relationship between the pharmacist, patient, and prescriber. This second practice is commonly referred to as anticipatory compounding.

Anticipatory compounding refers to compounding done in limited quantities before the receipt of a patient-specific prescription. In contrast, office-use refers to compounding that is not for an identified, individual patient pursuant to a prescription, but rather to have compounded drugs in stock for use by health care providers in the delivery of care. For example, a provider may prefer to administer a compounded drug to a patient immediately rather than writing a prescription and waiting for the drug product to be compounded and shipped to the provider.

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<sup>2</sup> FDA, COMPOUNDING PROGRESS REPORT: THREE YEARS AFTER ENACTMENT OF THE DRUG QUALITY AND SECURITY ACT (2017), *available at* <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm536549.pdf>.

<sup>3</sup> FDA, 2018 Compounding Policy Priorities Plan, <https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm592795.htm> (last visited Jan 26, 2018).

FDA has generally taken the position that section 503A pharmacies should be limited to anticipatory compounding and may not compound for office-use. Instead, health care practitioners should obtain non-patient-specific compounded drugs to keep in stock for office-use from outsourcing facilities.<sup>4</sup> This policy is intended to differentiate traditional compounding by licensed pharmacists or physicians from compounding by registered outsourcing facilities, which are subject to additional FDA standards and oversight, including compliance with CGMPs, registration, reporting, and inspections.

### *Interstate Distribution of Compounded Drugs*

Section 503A prohibits distribution of compounded drug products outside of the state in which they are compounded in quantities that exceed 5 percent of the total prescription orders dispensed or distributed by that pharmacy or physician, unless the state in which the compounding is performed has entered into a memorandum of understanding (MOU) with the Secretary of Health and Human Services.

FDA issued a draft MOU, which would establish an agreement between FDA and a state regarding the distribution of inordinate amounts of compounded human drug products interstate.<sup>5</sup> The draft MOU defines inordinate amounts and addresses how states would handle complaints about products compounded by pharmacies within their borders. The draft MOU proposes a 30 percent upper limit for section 503A pharmacies operating in a state that enters into the MOU, as opposed to the 5 percent threshold set in the CQA.<sup>6</sup> The interstate distribution restrictions do not apply to registered outsourcing facilities under section 503B.

Some have taken issue with FDA's inclusion of patient-specific dispensing across state lines in calculating whether a pharmacy or physician meets the distribution threshold. These concerns stem from the fact that *dispensing* of compounded drugs has traditionally been overseen by state regulators. Thus, the limit should only apply to compounded products distributed without a patient-specific prescription.

FDA's takes the position that section 503A pharmacies, unlike outsourcing facilities, are primarily overseen by the states, are exempt from CGMP requirements and are not required to register with FDA. If a substantial proportion of drugs compounded by section 503A pharmacies are distributed outside of a state's borders, adequate regulation of those drugs can be challenging and may make it more difficult to investigate and address multistate outbreaks. For instance, the interstate distribution of contaminated compounded drug products in 2012 resulted in an outbreak of fungal meningitis, with an estimated 14,000 patients receiving injections from lots of contaminated drug product.

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<sup>4</sup> FDA, PRESCRIPTION REQUIREMENT UNDER SECTION 503A OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT: GUIDANCE FOR INDUSTRY (2016), *available*

at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM496286.pdf>.

<sup>5</sup> FDA, *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*, *available at* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM434233.pdf>.

<sup>6</sup> FDA recently announced that the threshold would be raised to 50 percent in the final MOU, based on the feedback the Agency received.

### *Pharmacy Inspections*

Section 503A compounding pharmacies are not subject to CGMP requirements, are not required to register with FDA, and are not routinely inspected by the agency. These pharmacies are subject to the prohibition on preparing drugs under insanitary conditions, and FDA has the authority to inspect these facilities within certain limitations. Since enactment of the DQSA, FDA has undertaken hundreds of inspections of both section 503A and 503B facilities, with the majority being 503A pharmacies.

In the wake of these inspections, some pharmacy groups have raised concern over FDA inspecting section 503A compounding pharmacies under CGMP standards. FDA has stated that CGMP deficiencies are only noted when the agency has evidence to suggest that the compounding pharmacy does not qualify for the exemptions under section 503A because it does not meet the statutory requirements. In an effort to address this concern, FDA issued a notice regarding a change in inspection procedures of section 503A pharmacies, indicating that the agency will make a preliminary assessment regarding compliance with section 503A before closing an inspection.<sup>7</sup>

### *Copies of FDA-Approved Products and Bulk Substances*

The FDCA prohibits compounding drugs that are essentially copies of FDA-approved or commercially available products. This restriction is intended to ensure that drugs are not compounded for patients who could use an available, FDA-approved product to protect both public health and the premarket approval process.

Because they are subject to a lower regulatory standard, compounded drugs should only be distributed to meet the needs of patients whose medical needs cannot be met by an FDA-approved drug. Furthermore, this restriction is intended to protect the incentives for conventional manufacturers to pursue FDA approval of new and generic drugs.

Pharmaceuticals can be compounded either by starting with an FDA-approved, finished drug and modifying it for administration; or by using “bulk” forms of an active pharmaceutical ingredient and preparing a new drug. While the latter is less costly, it carries greater risk of reduced quality or contamination. Section 503A facilities may compound drugs using bulk drug substances that comply with existing United States Pharmacopeia (USP) or National Formulary monograph standards; are components of FDA-approved drugs; or appear on a list developed by the FDA through regulation, after consultation with USP and the Pharmacy Compounding Advisory Committee. Section 503B outsourcing facilities may use a bulk drug substance to compound a drug if the FDA has determined there is clinical need to compound with the substance and places it on the 503B bulks list, or if the drug compounded appears on the FDA’s drug shortage list.

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<sup>7</sup> FDA, FY2018 Justification of Estimates for Appropriations Committees, p. 251, <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM559923.pdf>.

FDA has been subject to criticism that its interim policy should not have included some bulk substances and that it was too lax in enforcement. FDA announced that it would take action on its interim policy in March 2018.<sup>8</sup>

#### **IV. STAFF CONTACTS**

If you have any questions regarding this hearing, please contact Danielle Steele or Paul Edattel of the Committee staff at (202) 225-2927.

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<sup>8</sup> FDA, 2018 Compounding Policy Priorities Plan, <https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm592795.htm> (last visited Jan 26, 2018).