Your Generics and Biosimilars Industry

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Introduction

Chairman Burgess, Ranking Member Green and members of the subcommittee, thank you for the invitation to testify today. My Name is Molly Ventrelli and I am Vice President of Regulatory Affairs for Fresenius Kabi USA. I am testifying today on behalf of Fresenius Kabi USA, a member of the Association for Accessible Medicines, or AAM, which represents companies that develop and market generic and biosimilar medicines. Fresenius Kabi is a leading provider of generic sterile injectable medicines in the U.S., and proud of the important role generic and biosimilar medicines play in helping patients and reducing costs in the U.S. health care system.

AAM is the nation's leading trade association for manufacturers and distributors of FDA-approved generic and biosimilar prescription medicines. AAM members employ more than 36,700 individuals at nearly 150 facilities and manufacture more than 61 billion doses in the United States every year. AAM's core mission is to improve the lives of patients by advancing timely access to affordable generic and biosimilar medicines. Generic medicines represent greater than 89 percent of all prescriptions dispensed in the U.S., but only 26 percent of expenditures on prescription drugs, saving patients and payers nearly $5 billion every week.

Fresenius Kabi Background and Experience

Fresenius Kabi is a global health care company – with more than 30,000 employees around the world - specializing in lifesaving medicines and technologies for infusion, transfusion and clinical nutrition. Our portfolio consists of more than 400 injectable drugs administered predominately in hospitals and other clinical settings. These include chemotherapeutics, analgesics and anesthetics used in surgery, and a wide range of anti-infective and critical care drugs. We manufacture these products in three

states – Illinois, New York and North Carolina – and we employ approximately 3,000 people in the U.S. in research and development, manufacturing, distribution and other related functions.

Additionally, Fresenius Kabi operates 18 compounding centers around the world, and we are in the process of launching our first U.S.-based, 503B compounding center in suburban Boston. It is from these various experiences that I share my perspective with you today.

We commend FDA's implementation of the Drug Quality and Security Act of 2013 (DQSA). As you know, this bipartisan legislation was passed by Congress in response to a fungal meningitis outbreak that sickened over 700 Americans and killed 64. This was caused by the compounding of sterile medications under insufficient quality standards and in violation of federal law. In order to avoid future tragedies like this, FDA must continue to enforce the strong protections of the DQSA against illegal compounding activity, including federal prohibitions on compounding without an individual prescription by pharmacies that do not comply with FDA regulations and do not meet quality standards designed to better protect and ensure patient safety.

Drug Compounding Background

Drug compounding plays an important role in health care. In particular, it allows a pharmacist, through a patient specific prescription, to tailor a therapy for an individual's unique needs – for instance, to add flavor to a child's medication or provide the medication in a liquid instead of solid form. But it is critical for us all to ensure the safety of patients who receive compounded medications, specifically, outsourcing facility compounded products as the 2012 outbreak demonstrated. Compounding should not be used for widespread manufacturing and distribution as a substitute to the FDA generic drug review process gold standard.

Congress recognized this when crafting the DQSA, and established two regulatory structures for the oversight of drug compounding: 503A and 503B. Pharmacies that operate under 503A are those that compound according to specific prescriptions unique to a patient ("one patient, one prescription") and under state board of pharmacy oversight. They do not compound large quantities of product in advance of a patient prescription.

However, Congress also recognized that some hospitals and healthcare providers may need supplies of medications not made by pharmaceutical manufacturers, or not made in a specific form, combination, or strength that is medically required for patients. These products, which need to be on

hand, often referred to as "office stock," present unique safety concerns due to the amount of time between compounding and administration of the drug to the patient. This risk is increased as these products are typically made in large volumes. Therefore, if they do become contaminated, or are produced incorrectly, more patients are exposed to the risk. To mitigate the higher risk associated with producing stock supplies of compounded drugs, Congress created the outsourcing facility category, governed by section 503B of the Food Drug and Cosmetic Act (FDCA). Congress required that these facilities adhere to current Good Manufacturing Practices (cGMP)—rigorous requirements enforced by FDA that describe a full-set of quality standards for the manufacturing, processing, packing, storage and testing of pharmaceutical products. Generic manufacturers are held to these robust standards to ensure the safety and efficacy of our products. To protect patients from another tragedy, outsourcing compounders must also be held to these rigorous standards as Congress intended.

Quality Standards

Compounded medications produced under conditions that guarantee potency and stability and are free of contamination can help patients in need and have a place in the U.S. healthcare system. Therefore, compounders registered under 503B of DQSA must comply with standards consistent with cGMPs that apply to regulated drug manufacturers. Recent history has proven the need for clear and strong regulation of standards for this space.

503B facilities, called "outsourcing facilities", allow for appropriate FDA regulation of mass production of compounded products. If these outsourcing facilities elect to register with FDA, and agree to meet critical regulatory and quality standards, they may provide hospitals and clinics with standing supplies of non-patient-specific compounded medicines that are regularly prescribed, when an FDA-approved product is not available. It is important to note that compounders registered under section 503B may not make a drug that is essentially a copy of an approved medicine except under certain highly limited circumstances. One of the primary reasons Congress was so clear in drafting 503B this way was to preserve incentives for traditional manufacturers to continue to pursue FDA approval through the current NDA and ANDA process. It is critical that this standard be upheld.

We support the FDA's efforts to ensure patient safety by inspecting compounders under the new 503B category in a timely fashion, and issuing guidance to make clear how 503B facilities should comply with federal law. We also commend the FDA for its continued risk-based inspections of compounding pharmacies not registered with the FDA that may not be in compliance with the provisions of 503A or 503B. One lesson learned from the fungal meningitis outbreak is that some licensed pharmacies operated outside the bounds of traditional, patient-specific compounding pharmacy practice. As

Congress has repeatedly noted, the FDA has the authority to address facilities that are illegally manufacturing drugs in violation of federal law. These facilities are not entitled to any of the exemptions that apply to compounding pharmacies; and are therefore subject to the requirements placed on manufacturers including adherence to cGMPs. FDA must be allowed to enforce federal law to prevent compounding activities that increase safety risks to patients.

FDA's enforcement of 503A is also important to ensure that facilities that are essentially acting as outsourcers, i.e., selling significant amounts of commercially unavailable compounded sterile drugs in absence of patient prescriptions, register as FDA 503B outsourcers. Congress' intent under DQSA was for this kind of larger-scale, non-patient specific compounding to be conducted not by traditional pharmacies but by 503B registered facilities that meet higher quality standards and submit to FDA oversight.

We also note that Congress did not alter the law prohibiting the repackaging or compounding of biologics without FDA oversight, and encourage FDA to include such activities in its enforcement priorities.

Additionally, a compounding pharmacy that seeks to compound a copy of a commercially available drug on the drug shortage list should be overseen by the FDA and should not only notify FDA, but also be inspected by the FDA prior to beginning the compounding of that product. In the interest of protecting public health, the safety and manufacturing standards of compounders producing commercially available products on the drug shortage list should not be lowered below the standards required of pharmaceutical manufacturers.

Protecting the FDA approval process

Another key to protecting patients is safeguarding the FDA approval process for new drugs. To uphold patient safety, Congress sought to ensure that FDA-approved drugs would be used whenever possible, including in the rare circumstances in which FDA-approved ingredients might be necessary in the use of compounded formulations. Under the DQSA, compounders should not use an active pharmaceutical ingredient (API) from any source, except those available through an FDA-approved source, unless doing so would produce a clinical difference for an identified patient. This is commonly referred to as patient-prescription specific compounding. In addition, the DQSA prohibits the compounding of drugs that are essentially a copy of an FDA-approved medicine, unless FDA has placed that drug on the drug shortage list. It is critical that these provisions be enforced to avoid a disincentive to invest in new drug approvals and in the production of approved versions of drugs. While compounded drugs are an

important option when approved drugs cannot meet a patient's clinical needs, products that have been evaluated and approved through FDA's approval process are the gold standard.

State Boards of Pharmacy quality standards applied to pharmacies are appropriate for patient-specific preparations, but not for outsourcing facility operations at a larger scale, where significantly more individuals are exposed. We must ensure that flexibility for outsourcing facilities does not compromise patient safety.

Drug Compounding is Not the Appropriate Response to Rising Drug Prices

Despite what some might argue, drug compounding – whether conducted under 503A or 503B – is not a solution to the issue of high drug prices. Congress has clearly recognized that the solution to high drug prices is greater competition from lower cost FDA-approved generic and biosimilar medicines. In the past year, Congress has taken important steps to encourage greater availability of generics – including in therapeutic areas without generic competition – through enactment of the Generic Drug User Fee Act. Moreover, FDA Commissioner Gottlieb continues to prioritize generic competition as part of the FDA Drug Competition Action Plan. And multiple legislative proposals are under consideration in Congress that would lead to greater competition through generic and biosimilar medicines. In contrast, seeking to use mass drug compounding as a solution for more drug competition ignores the tragic events of 2012-2013 and more recent warnings of the safety of compounded drugs – including some that FDA has called out even since the enactment of DQSA as having significant quality problems.

Conclusion

On behalf of Fresenius Kabi and member companies of AAM, I extend our gratitude to the subcommittee for holding today's hearing. I'd also like to thank the FDA and Commissioner Gottlieb for the steps the Agency has taken to-date to strengthen the oversight of compounding, and for clarifying today FDA's path forward. We recognize the role compounders play in delivering special care to patients, but as we know all too well, it should not be done at the expense of quality and patient safety.