November 20, 2014

The Honorable Margaret Hamburg
Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Boulevard
Silver Spring, Maryland 20993

Re: FDA oversight of drug compounding and enforcement of federal law

Dear Commissioner Hamburg,

The below signed organizations have come together to voice strong support for FDA's commitment to protecting patient safety through the robust enforcement of the federal law on drug compounding. In particular, we commend FDA's implementation of the Drug Quality and Security Act of 2013 (DQSA), which was passed in response to an outbreak of fungal meningitis—resulting in over 60 deaths—caused by the compounding of sterile medications under insufficient quality standards and in violation of federal law. Current federal law, as amended by DQSA, will help to avoid a repeat of the meningitis tragedy, but only if FDA is free to proactively enforce against illegal compounding activity. In particular, FDA should not be impeded by efforts to carve out exemptions to the law that could allow compounding without prescriptions, outside of limited amounts in anticipation of a prescription, by pharmacies that do not comply with FDA regulations and do not meet appropriate quality standards. As outlined below, compounded medications produced under conditions that guarantee potency, stability and freedom from contamination can help patients who have a specific and prescribed medical need for a drug formulation that is not commercially available. Compounders that create standing supplies of non-patient-specific compounded drugs should be subject to strict FDA regulation and meet standards consistent with current Good Manufacturing Practices (cGMPs) that apply to regulated drug manufacturers.

Background

Compounded drugs can help patients who have a medical need for a drug formulation that is not commercially available. However, these medicines must be produced in a manner that fully complies with applicable FDA regulations and under conditions that guarantee potency, stability and freedom from contamination. When compounded products are not made according to strict quality standards appropriate for their scale of production, the results can be deadly and widespread as was the case with the nationwide outbreak of fungal meningitis in 2012 and 2013 linked to contaminated compounded injections.

Responding to this crisis, Congress passed the DQSA in 2013, which established a new category of compounders under section 503B of the FDCA called "outsourcing facilities". If these outsourcing facilities may elect to register with FDA and agree to meet higher regulatory and quality standards in order to 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. Compounders registered under section 503B may not make a drug that is essentially a copy of an approved medicine

unless it appears on the drug shortage list. These 503B facilities must also not compound a drug using an API that is in an FDA-approved medicine unless there is a change made in the compounded drug that produces a clinical difference for an identified individual patient.

DQSA also made clear that longstanding law on compounding, section 503A of the FDCA, is enforceable throughout the country by removing a provision of that section that had been challenged in some courts. Section 503A describes the traditional compounding activities that are permitted under federal law, which includes compounding drugs pursuant to a prescription, or in limited quantities in advance of a prescription based on a history of such prescriptions.

Support for the FDA's Current Risk-based Approach to Compounding

We support the FDA's efforts to ensure patient safety by inspecting compounders under the new 503B category in a timely fashion and issuing interim 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 from the fungal meningitis outbreak is that some licensed pharmacies operated outside the bounds of traditional, patient-specific pharmacy practice. As Members of Congress have repeatedly noted, the FDA has the authority to address facilities that are illegally manufacturing drugs in violation of federal law. These plants, if they choose not to register as an FDA-regulated compounder, are not entitled to any of the exemptions that apply to compounding pharmacies, and are therefore subject to the requirements placed on manufacturers. These requirements include adherence to cGMPs. FDA must be allowed to enforce federal law to prevent compounding activities that increase risk to patients.

FDA's enforcement of 503A is also important to ensure that facilities that sell significant amounts of commercially unavailable compounded sterile drugs in absence of patient prescriptions participate in the new FDA 503B regulatory category. 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 facilities that meet higher quality standards and submit to FDA oversight.

We support the FDA's targeting of resources by prioritizing oversight of 503B compounding facilities, as well as those not registered under 503B that present the highest risk to patients—specifically, larger operations selling sterile products that are not meeting the standards necessary to ensure patient safety. Such enforcement is necessary to prevent the unsafe compounding of significant amounts of medicine in facilities that are not subject to the newly enacted registration requirements designed to protect patients, and to make sure these facilities do not compound copies of FDA-approved, commercially available drugs in violation of federal law. 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.

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The development of the Drug Quality and Security Act was a broad multi-stakeholder effort that resulted in a carefully crafted law designed to balance access to compounded medicines with the need

for updated oversight to make sure those drugs are safe and meet high quality standards. While the new regulatory paradigm for compounding will take time and resources for stakeholders to implement, FDA should be commended and supported for its continuing, robust efforts to realize the potential of this law. Doing so will help protect patients for years to come.

Sincerely yours,

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