DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

January 8, 2014

Dear Colleague:

As you may be aware, on November 27, 2013, the President signed into law the Drug Quality and Security Act (DQSA), legislation that contains important provisions relating to federal and state oversight of compounding of human drugs. I am writing to ask you to consider how you could encourage compounding pharmacies located outside of your state that ship compounded sterile drugs into your state to register with the Food and Drug Administration (FDA) as outsourcing facilities under the new legislation. The registration of pharmacies as outsourcing facilities will help FDA identify and more effectively regulate these facilities.

Beginning a little over a year ago, a fungal meningitis outbreak tied to contaminated compounded steroid injections made by a Massachusetts firm was associated with infections in over 750 individuals and the deaths of 64 people across 20 states. Since the outbreak, FDA has conducted over 70 inspections of compounding pharmacies across the country, both for cause, in response to serious adverse event reports and reports of quality problems, and proactively to identify pharmacies with deficient sterile compounding practices. FDA appreciates the partnership of the states in these efforts; in most cases, our state partners have participated in the inspections, some of which were initiated at the request of a state. Between October 1, 2012, and October 31, 2013, FDA completed 42 for-cause inspections and 31 proactive inspections.

During these inspections, FDA observed serious quality problems, including contaminated products and poor sterile practices that create a risk of contamination. Numerous recalls of sterile products have been conducted, and numerous pharmacies chose to stop sterile compounding after FDA identified problems with their sterile compounding processes. New problems continue to be identified at compounding pharmacies across the country, which number over 15,000. (*2012 NCPA Digest In-Brief.* Retrieved November 14, 2013, from National Community Pharmacists Association (NCPA): http://www.ncpanet.org/pdf/digest/2012/2012_digest_inbrief.pdf).

In December 2012, FDA convened a 50-state meeting to provide an opportunity for state officials to discuss a variety of issues including their views on the role of FDA and the states in the oversight of compounding. FDA received many thoughtful suggestions during that meeting, some of which FDA has implemented, and others which the agency is in the process of implementing. During the meeting, many states expressed the view that their greatest concerns lay with non-resident pharmacies located outside the borders of their states that shipped sterile

drugs to patients and health care facilities in their states, because they did not have the capacity to oversee the operations of out-of-state pharmacies. Some states expressed the view that these pharmacies should be overseen by FDA.

At about the same time, Congress began considering federal legislation to provide FDA with additional tools to regulate compounding to help prevent another outbreak. These legislative efforts culminated in the enactment of the DQSA (Public Law 113-54,127 Stat. 587; for the text of the Compounding Quality Act, which is Title I of the Drug Quality and Security Act, see http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm376732.htm).

This legislation removes certain provisions from section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) related to advertising, promotion, and the solicitation of prescriptions that were found to be unconstitutional by the U.S. Supreme Court in 2002. By removing those provisions, the legislation clarifies that section 503A applies to compounders nationwide.

In addition, the new legislation creates a new section 503B in the FD&C Act under which a facility that compounds sterile drugs can register to become an "outsourcing facility." An outsourcing facility can qualify for exemptions from FDA approval requirements and the requirement to label products with adequate directions for use, but it still must comply with current good manufacturing practice (CGMP) requirements. Outsourcing facilities:

- Must provide FDA with information about the products they compound;
- Must comply with CGMP requirements;
- Will be inspected by FDA on a risk-based schedule; and
- Must meet certain other conditions, such as reporting adverse events and labeling their products with certain information.

Registration as an outsourcing facility is voluntary. If a compounder chooses not to register as an outsourcing facility and satisfy the conditions in section 503B, it could qualify for an exemption from FDA approval requirements, the requirement to label products with adequate directions for use, and CGMP requirements by meeting the conditions in section 503A of the FD&C Act. If a compounded drug does not qualify for an exemption under either section 503A or 503B of the FD&C Act, it would be subject to all of the requirements of the FD&C Act that are applicable to drugs made by conventional manufacturers, including the new drug approval, adequate directions for use, and CGMP requirements. For further information about FDA's plans to implement the new legislation, see http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm.

When a drug is FDA-approved, patients are assured that FDA has reviewed the safety and efficacy of the drug and the adequacy of the manufacturing process to produce a quality product. Because they do not go through the drug approval process, compounded drugs do not provide such assurance and, therefore, should only be used when an FDA-approved product is not available to meet the medical needs of an individual patient. If compounders register with FDA as outsourcing facilities, hospitals and other health care providers that purchase compounded

drugs necessary to meet the medical needs of their patients can provide their patients with drugs that were compounded in outsourcing facilities, which are subject to CGMP requirements and increased federal oversight.

States have a critical role to play in the oversight of pharmacy compounding. One new opportunity afforded states by new section 503B is the ability to encourage compounding pharmacies located outside of the state that ship compounded drugs into the state to register with FDA as outsourcing facilities. Once facilities are registered, states could be assured that FDA will inspect the facilities on a risk-based schedule, hold them to CGMP requirements, monitor the adverse event reports they are required to submit to the agency, and through these activities help improve the quality of drugs compounded at these facilities.

FDA intends to continue to partner with states in the oversight of drug compounding. The agency intends to hold another 50-state meeting in the first quarter of 2014 to discuss our plans for implementation of both sections 503A and 503B. I encourage you to participate in that meeting so that we can continue working together to help prevent another outbreak from contaminated compounded drugs.

Sincerely,

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs