DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

January 8, 2014

Dear [Hospital/Purchaser]:

The purpose of this letter is to inform you of the passage of new federal legislation that affects the oversight of human drug compounding and to encourage you to consider requiring compounders from which you purchase compounded sterile drugs to meet the medical needs of patients that cannot be met by FDA-approved products to register with the Food and Drug Administration (FDA) as outsourcing facilities.

Beginning a little over a year ago, a fungal meningitis outbreak tied to contaminated compounded steroid injections made by a Massachusetts firm has been 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. 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).

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 Drug Quality and Security Act on November 27, 2013 (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).

The new legislation creates a new section 503B in the Federal Food, Drug, and Cosmetic Act (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 certain 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, and would be regulated primarily by the states. 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 patients with drugs that were compounded in outsourcing facilities, which are subject to CGMP requirements and increased federal oversight.

As a purchaser of compounded drugs, you can play an important role in improving the quality of compounded drugs by requiring compounding pharmacies that supply drugs to your facility to register as outsourcing facilities. Once they register, you and the patients you serve can be assured that FDA will inspect these 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 require appropriate labeling.

I urge you to consider this in your future purchasing decisions and look forward to working with you to improve the quality of compounded drugs.

Sincerely,

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