DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

APR 26 2013

The Honorable John D. Dingell
House of Representatives
Washington, D.C. 20515-2215

Dear Mr. Dingell:

Thank you for your letter of October 9, 2012, concerning the fungal meningitis outbreak associated with methylprednisolone acetate, a steroid injectable product distributed by the New England Compounding Center (NECC). This outbreak has had devastating effects on individuals and families across the country.

The Food and Drug Administration (FDA or the Agency) believes that pharmacists engaging in traditional compounding provide a valuable medical service that is an important component of our health care system. The history of this issue shows that there is a need for appropriate and effective oversight of this evolving industry. It is clear that the industry and the health care system have evolved and outgrown the law, and FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients has been hampered by gaps and ambiguities in the law, which have led to legal challenges to FDA's authority to inspect pharmacies and take appropriate enforcement actions.

The fungal meningitis outbreak has caused the Agency to review our past practices with regard to our oversight of compounding pharmacies. We have established an Agency-wide steering committee to oversee and coordinate our efforts, and we have taken several important steps to identify and inspect high-risk pharmacies that are known to have engaged in production of sterile drug products.

The Administration is committed to working with Congress to address the threat to public health from gaps in authorities for effective oversight of certain compounding practices. To that end, FDA has developed a framework, discussed below, that could serve as the basis for the development of a risk-based program to protect the public health.

We have restated your questions below in bold, followed by our responses.

1. **Although the investigation is still ongoing, FDA has discovered fungal contamination of sealed vials of methylprednisolone acetate collected at NECC. How many vials of this steroid has NECC produced? How many vials of this steroid produced by NECC have been distributed? How many facilities have received vials of this steroid produced by NECC? Where are these facilities located? When were the vials linked to the outbreak distributed? How many patients have received injections of this steroid produced by NECC thus far?**

As part of the public health investigation into the outbreak, FDA has learned that, among the three suspect lots of methylprednisolone acetate (MPA) produced by NECC, there are 17,676 total vials. These lots were distributed to facilities in 23 states (California, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Maryland, Michigan, Minnesota, North Carolina, New Hampshire, New Jersey, Nevada, New York, Ohio, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Virginia, West Virginia), between the date of preparation of the first lot (May 21, 2012) and the date on which the suspect lots were recalled (September 26, 2012). After the recall of NECC steroid medications on September 26, state and local health departments identified almost 14,000 people in 23 states who were potentially exposed to the implicated MPA; of these, an estimated 11,000 individuals received spinal or paraspinal injections.

2. **Who first discovered the contamination of vials of methylprednisolone acetate? When was the contamination first discovered? Where was the contamination first discovered? How was contamination discovered? When was the contamination first reported to FDA? How did this contamination occur?**

   As part of the public health investigation into the outbreak, FDA has learned that, on September 21, 2012, the Centers for Disease Control and Prevention (CDC) was notified by the Tennessee Department of Health of a patient with the onset of meningitis approximately 19 days following epidural steroid injection at a Tennessee ambulatory surgical center. On September 25, 2012, CDC notified FDA that it was working with the Tennessee Department of Health to investigate a cluster of meningitis cases at a single clinic, which might be associated with product contamination. On October 18, 2012, FDA and CDC announced that "CDC and FDA have confirmed the presence of a fungus known as *Exserohilum rostratum* in unopened medication vials of preservative-free methylprednisolone acetate (80mg/ml) from one of the three implicated lots from NECC (Lot #08102012@51, BUD 2/6/2013). The laboratory confirmation further links steroid injections from these lots from NECC to the multistate outbreak of fungal meningitis and joint infections."

   Due to the ongoing criminal investigation, FDA cannot comment further.

3. **NECC has issued a voluntrary recall of the methylprenisolone acetate products and has voluntarily shut down. When was the voluntary recall first initiated? How many lots have been recalled? How many doses were included in the recall? When did NECC shut down its facility?**

   As part of the public health investigation into the outbreak, FDA worked with NECC to initiate a voluntary recall of the suspect lots of MPA on September 26, 2012. At the time, three lots (17,676 vials) were included in the recall; however, since that time, the recall was expanded to include all products made by NECC. FDA was notified that NECC ceased production on October 3, 2012, and has not recommenced production.

4. **Are any vials of methylprednisolone acetate from NECC still available on the market? If yes, how many vials remain on the market?**

As of October 6, 2012, all products compounded and distributed by NECC were recalled by the firm. NECC posted notice of the recall on their website, *www.neccrx.com*. As of January 30, 2013, as part of the public health investigation into the outbreak, FDA had completed 1,155 audit checks with customers who received NECC products. FDA found no unexpired product remaining for use with any of the customers, and all customers had knowledge of the recall either through NECC, CDC, state health departments, the media, or other sources.

5. What alerts regarding methylprednisolone acetate has FDA issued to health professionals? What alerts regarding methylpredinsolone acetate has FDA issued to consumers? How have these alerts been transmitted to these parties?

As part of the public health investigation into the outbreak, FDA issued two MedWatch alerts in October 2012 (with updates through November 2012), advising health care professionals and consumers of the risks associated with drug products produced by NECC, including MPA acetate, and providing updates as FDA's investigation progressed. Links to the MedWatch alerts on FDA's website are provided below.

FDA issued an alert on October 5, 2012 (updated on October 6, 2012), advising that FDA had observed fungal contamination in a sealed vial of methylprednisolone collected from NECC, and recommending that health care professionals and consumers not use any product produced by NECC. The alert indicated that although the investigation into the source of the outbreak was ongoing, it was possibly associated with preservative-free MPA acetate produced and distributed by NECC. This alert is available at *http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm322849.htm.*

FDA issued another MedWatch alert on October 15, 2012, which was updated multiple times. The initial alert dated October 15, 2012, advised of a patient with possible meningitis associated with triamcinolone acetonide, and two transplant patients (revised on October 16, 2012, to one transplant patient) with *Aspergillus fumigatus* infections following administration of cardioplegic solution made by NECC. The alert was updated on October 18, 2012, noting that CDC and FDA confirmed the presence of *Exserohilum rostratum* in unopened vials of preservative-free MPA acetate made by NECC. Further updates, dated October 22, 2012, informed that FDA was making available lists of customers who received products shipped on or after May 21, 2012, from NECC, and dated October 24, 2012, was to provide an updated list of customers. The final update, dated November 1, 2012, advised that two additional products recalled by NECC, preservative-free betamethasone and cardioplegia solution, tested positive for bacterial contamination. This alert is available at *http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm323946.htm.*

FDA communicated throughout its investigation with the media, Congress, state health officials, health care professionals, and the public to keep them apprised of important findings and developments as our investigation proceeded. FDA's website was updated on a frequent basis to provide broad access to any new public information. This information was further disseminated through the Agency's electronic listservs and through Twitter and

Facebook. Along with CDC, FDA provided health care professionals with information they needed on an ongoing basis, and as new information came to light, to advise and treat patients affected by this situation.

Targeted alerts were sent to 150 health care professional organizations, including the national specialty-specific societies that work with spinal injections, such as the American Society of Anesthesiologists, the American Academy of Physical Medicine and Rehabilitation, and the North American Spine Society, and also to all state medical, pharmacist, nursing, and physicians' assistant societies, as well as all state boards of pharmacy. Regular phone updates were provided to state health departments, in collaboration with CDC, and written updates were also distributed to national pharmacy and ophthalmology professional organizations. FDA also contacted patient and health care professional groups and consumer groups and worked with the American Hospital Association as part of our response.

FDA pharmacists fielded calls from the public and extended their hours of availability for several weeks to help respond to the public's concerns. We also continued to respond to calls and e-mails from health care professionals, hospitals and clinics, and others with questions about the NECC and Ameridose recalls.

6. **With what federal and state agencies has the FDA been working on this investigation?**

FDA cannot comment at this time.

7. **It has been reported that Massachusetts Board of Registration in Pharmacy has had at least four previous complaints about the sterility of NECC's products- in 2002, 2003, 2011, and one complaint is currently being investigated. Were these complaints shared with the FDA? If yes, when were these complaints shared?**

FDA received three adverse event reports in 2002 suggesting sterility concerns associated with MPA acetate compounded by NECC. These reports came directly to FDA via the MedWatch reporting system from the hospital that treated the patients. The Agency is not aware that the Massachusetts Board of Registration in Pharmacy (MBRP) provided any report of these adverse events to FDA. FDA's investigations of these reports were, however, communicated to the Massachusetts' Board of Registration in Pharmacy (MBRP). The inspection beginning in 2002 regarding the adverse event reports associated with methylprednisolone was conducted jointly by FDA with MBRP.

FDA does not have a record of having received from MBRP reports of any complaints or adverse events in 2002, 2003, or 2011, regarding sterility of NECC's products.

8. **What has been the inspection history of the NECC facility? When was the NECC facility in Framingham last inspected? What were the results of that inspection?**

See enclosed document entitled "Timeline of FDA Interactions with NECC and Ameridose" that was provided to the House Energy and Commerce Committee on January 4, 2013.

9. Does FDA have the authority to inspect compounding pharmacies? If yes, when was the last time FDA officials have inspected NECC's facility? What were the results of that inspection?

Under FDA's current inspection authority in section 704 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA's authority to inspect records at a pharmacy depends upon knowing certain facts about the pharmacy's operations that oftentimes can only be determined through inspection of records. The first of three criteria for being exempt from having records inspected is whether the pharmacy is operating in conformity with state law, a determination most readily made by a state and, in any case, likely dependent upon examining certain records. The second criterion is whether the pharmacy is dispensing prescription drugs without a prescription, but in many cases, FDA must be able to inspect records to determine that fact. Similarly, the third criterion is whether the pharmacy is compounding drugs for sale other than in the regular course of its retail business, which is also something that would be difficult to determine without a full inspection of the facility, including an inspection of appropriate records. So the authority is circular, and compounding pharmacies have cited this language in opposing FDA's efforts to inspect.

In addition, the records exemption for pharmacies can present an obstacle to FDA in determining the source of a complaint or outbreak associated with a compounded drug that may be adulterated or misbranded under the FD&C Act. FDA's ability to inspect in a timely manner any firm producing drugs is critical for effective oversight and regulation. Therefore, FDA strongly recommends that the provision in section 704 of the FD&C Act that limits the Agency's ability to inspect a pharmacy's records be removed. It is critical that FDA have clear authority to inspect pharmacies to determine the scope and nature of their operations to determine whether they are operating as compounding pharmacies or conventional drug manufacturers. The determination of whether a compounding pharmacy is engaging in conventional drug manufacturing is fact-specific, and FDA must be able to fully inspect pharmacies, and review their records, to gather the facts to make this determination.

Therefore, FDA should have clear ability to examine records such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding, respond to public health threats, and enforce federal standards.

See enclosed document entitled "Timeline of FDA Interactions with NECC and Ameridose," which was provided to the House Energy and Commerce Committee on January 4, 2013, for additional information.

10. It has been reported that more than 17,000 vials compounded by NECC have been recalled thus far. What does FDA consider to be legitimate forms of pharmacy compounding? What volume does FDA consider to be legitimate uses of pharmacy compounding?

Due to the ongoing criminal investigation, FDA cannot comment on NECC specifically.

With regard to compounding generally, FDA issued a Compliance Policy Guide (CPG) in 2002 (CPG Sec. 460.200) that describes the factors FDA considers in determining whether to take enforcement action against a compounding pharmacy. The CPG recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon receipt of a valid prescription for an individually identified patient from a licensed practitioner, and states that this traditional activity is not the subject of the CPG. In its simplest form, this compounding may involve reformulating a drug, for example, by removing a dye or preservative in response to a patient allergy. Or it may involve making a suspension or suppository dosage form for a child or elderly patient who has difficulty swallowing a tablet. FDA believes that pharmacists engaging in traditional compounding provide a valuable medical service that is an important component of our health care system.

Section 503A of the FD&C Act, added to the law in 1997, also attempts to draw a line between pharmacy compounding and conventional manufacturing using different but similar factors to draw the line. That statute was challenged in court and the compounded product, consistent with the factors set forth in section 503A, is exempt from three key provisions of the FD&C Act: the requirement of premarket review for safety and effectiveness, the requirement to provide adequate directions for use, and the requirement that the drug meets Current Good Manufacturing Practice standards. The statute contains some ambiguous provisions that make it difficult to draw a clear line between compounded drugs that are subject to exemptions from the above provisions of the Act and those compounded drugs which are not.

Further, regulating certain types of compounding pharmacies as conventional manufacturers is not a good fit for the evolving category of outsourcer pharmacy, which provides drugs for hospitals and other health care entities. The Administration is committed to working with Congress to address the threat to public health from gaps in authorities for effective oversight of certain compounding practices. To that end, FDA has developed a framework that could serve as the basis for the development of a risk-based program to protect the public health.

FDA has suggested that legislation be enacted to create a new framework for regulating compounding. FDA suggests Congress create a new category of non-traditional compounding, subject to appropriate federal standards, which may be based on certain Current Good Manufacturing Practice (CGMP) requirements in 21 *Code of Federal Regulations* (CFR) Parts 210 and 211, and oversight to ensure consistent product quality standards are applied to sterile compounding done in advance of or without a pharmacy receiving a prescription where the compounded product is then shipped across state lines. FDA believes that there are other authorities that would be important to support this new regulatory paradigm. For example, FDA should be given clear, full authority to collect and test samples of compounded drugs and to examine and collect records in a compounding pharmacy, just as the Agency does when inspecting other manufacturers. FDA should have clear statutory authority to examine records, such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to

determine when a pharmacy exceeds the bounds of traditional compounding to respond to public health threats and to enforce federal standards.

11. Do compounding pharmacies, like NECC, register with FDA? If yes, how many compounding pharmacies are currently in operation?

Generally, pharmacies are exempt from registration under section 510 of the FD&C Act, provided they meet certain conditions (510(g) of the Act). Such conditions include operating under applicable local laws regulating the practice of pharmacy and medicine, regularly dispensing drugs upon a valid prescription, and not compounding drugs other than in the regular course of dispensing drugs at retail. As a result, FDA does not know all of the compounding pharmacies in the United States, and FDA does not conduct regular surveillance inspections of pharmacies as it does with typical drug manufacturers.

According to the International Academy of Compounding Pharmacists (IACP), there are an estimated 28,000 pharmacies that compound, including 7,500 pharmacies that specialize in compounding. About 3,000 of these pharmacies compound sterile products.

An accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with state regulators. Under FDA's proposed framework, certain sterile compounding facilities should be subject to federal oversight to ensure that the compounding of sterile drug products at those facilities can be done without putting patients at undue risk. These requirements would include federal registration of the compounding facilities that will be subject to federal quality standards, so that FDA knows where they are and what drug products they are making.

12. Do compounding pharmacies list their products with FDA? If yes, how many products produced by compounding pharmacies are currently on the market?

Because pharmacies that meet certain criteria generally are not required to register or list, FDA does not have a list or count of marketed compounded products.

An accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with state regulators. Under FDA's proposed framework, requirements would include federal registration of the compounding facilities that will be subject to federal quality standards, so that FDA knows where they are and what drug products they are making,

13. Does FDA approve products produced through compounding pharmacies? Are drug products made through pharmacy compounding required to meet the safety and efficacy standard set by FDA?

Under section 503A of the FD&C Act, compounded drugs that meet certain criteria are provided an exemption from three key provisions of the Act, including the drug approval requirements of section 505. The CPG on pharmacy compounding, CPG Sec. 460.200 Pharmacy Compounding, sets forth factors that FDA considers in determining whether to

exercise enforcement discretion in applying the drug approval requirements of section 505 of the FD&C Act. Thus, under either section 503A or the CPG, compounded drugs are not approved by FDA and lack an FDA finding of safety and efficacy.

14. Does FDA have sufficient authority to oversee compounding pharmacies, such as NECC, now? If so, please explain why. If no please explain why.

With regard to compounding generally, FDA is working with Congress, states, industry, and other interested stakeholders to develop a basic framework to help the Agency effectively oversee firms engaged in widespread distribution of sterile compounded drug products in advance of or without receiving a prescription. In the proposed framework, FDA believes that certain sterile compounding facilities should be subject to federal oversight to ensure that the compounding of sterile drug products at those facilities can be done without putting patients at undue risk, including requiring:

- Compliance with federal quality standards that are appropriate for the compounding of riskier products and exposure of larger numbers of patients
- Federal registration of the compounding facilities that will be subject to federal quality standards, so that FDA knows where they are and what drug products they are making; and
- These higher-risk compounding pharmacies to report to FDA serious adverse reactions to their drugs, of which they become aware, so that we can act quickly on potential problems that may be associated with compounded drugs.

And for all pharmacy compounding, FDA believes certain basic protections should be in place. These include:

- Clear authority to examine a pharmacy's records to more quickly locate the cause of an outbreak or other violations of the law
- Requirements for clear label statements that identify the nature and source of compounded products, providing prescribers and consumers with valuable information about the products they are using, so that they can make informed judgments about their use; and
- Prohibiting compounding of the most complex and highest-risk products—drugs and biologics that should only be made for patients by an FDA-registered drug manufacturer under an approved new drug application in which the manufacturer has demonstrated that the product is safe and effective and that it can be safely made according to the highest-quality standards.

This proposed framework requires legislative action. We look forward to continuing to work with Congress to enact an oversight framework to protect the public health before an outbreak.

15. Does FDA need additional authority to oversee compounding pharmacies? If yes, please explain why and list the authorities needed. If no, explain why.

There is a need for appropriate and effective oversight of this evolving industry. It is clear that the industry and the health care system have evolved and outgrown the law, and FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients has been hampered by ambiguities in the law, which have led to legal challenges to FDA's authority to inspect pharmacies and take appropriate enforcement actions. The Administration is committed to working with Congress to address the threat to public health from limitations in authorities for effective oversight of certain compounding practices. To that end, FDA has developed a framework that could serve as the basis for the development of a risk-based program to protect the public health.

Recognizing the history of compounding practice, FDA supports the long-standing policy that all compounding should be performed in a licensed pharmacy by a licensed pharmacist (or a licensed physician) and that there must be a medical need for the compounded drug.

Further, there should be a distinction between two categories of compounding: traditional and non-traditional. Traditional compounding would include the combining, mixing, or altering of ingredients to create a customized medication for an individual patient with an individualized medical need for the compounded product, in response to a valid patient-specific prescription or order from a licensed practitioner documenting such medical need. Traditional compounding, while posing some risk, plays an important role in the health care system, and should remain the subject of state regulation of the practice of pharmacy.

Non-traditional compounding would include certain types of compounding for which there is a medical need, but that pose higher risks. FDA proposes working with Congress to define non-traditional compounding based on factors that make the product higher risk such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the state in which it was produced. Non-traditional compounding would be subject to federal standards adequate to ensure that the compounding could be performed without putting patients at undue risk, and FDA would inspect against and enforce these federal standards. Such a definition focuses on the highest-risk activities and offers a uniform degree of protection across all 50 states, for highest-risk compounding activities.

Non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight. Sterile products produced in advance of or without a prescription and shipped interstate should be subject to the highest level of controls, established by FDA and appropriate to the activity, similar to CGMP standards applicable to conventional drug manufacturers.

In addition, with noted exceptions, certain products are not appropriate for compounding under any circumstances. These products would include: 1) what are essentially copies of FDA-approved drugs, absent a shortage justification based on the drug appearing on FDA's shortage list; and 2) complex dosage forms, such as extended release products; transdermal patches; liposomal products; most biologics; and other products as designated by FDA. Producing complex dosage forms would require an approved application and compliance with CGMP standards, along with other requirements applicable to drug products made by conventional manufacturers.

There are other authorities that would be important to support this new regulatory paradigm. For example, FDA should have clear ability to collect and test samples of compounded drugs and to examine and collect records in a compounding pharmacy, just as the Agency does when inspecting other manufacturers. FDA should also have clear ability to examine records, such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding to respond to public health threats and to enforce federal standards.

An accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with state regulators. In addition, FDA looks forward to working with Congress on potential improvements that may include label statements and adverse event reporting that have proven useful in other areas.

Thank you, again, for contacting us concerning this important matter. If you have further questions please let us know.

Sincerely,

Michele Mital

Michele Mital
Acting Associate Commissioner
for Legislation

Enclosure

Timeline of FDA Interactions with NECC and Ameridose

Background

Please find below an overview of certain facts related to the Food and Drug Administration's (FDA, or the Agency) past interactions with the New England Compounding Company (NECC) and Ameridose. No information related to FDA's ongoing investigations of these companies is included. The information in these timelines is representative of our current understanding, based upon the records and information we have been able to review to date. We continue to collect information related to our history with these companies. We would be pleased to provide additional information if and when it becomes available.

Timeline for NECC

- According to the records FDA has reviewed to date, our earliest record of contact with NECC was an April 2002 inspection to follow-up on two adverse event reports submitted to FDA associated with betamethasone compounded by NECC. On April 16, 2002, FDA issued a Form FDA 483, which included three observations voicing concerns regarding NECC's process for producing sterile drugs.

- From October 24, 2002, until February 10, 2003, FDA and the Massachusetts Board of Pharmacy (MABP) conducted a jointly coordinated inspection to follow-up on adverse event reports received in July and August 2002 of bacterial meningitis associated with methylprednisolone compounded by NECC.

- In a meeting held on February 5, 2003, toward the end of the 2002-2003 inspection, FDA and MABP jointly decided that MABP would take the lead in enforcement and inspections of NECC's compounding operations since NECC was functioning as a compounding pharmacy. On February 10, 2003, FDA issued a 483 closing out its inspection. The firm responded on February 26, 2003, and supplemented its response on May 20, 2003, describing the corrective steps the firm was taking in response to the 483.

- FDA inspected NECC from September 23, 2004, until January 19, 2005, in a focused inspection related to a competitor's complaint that NECC had compounded a drug using bulk active ingredients that were not a component of an FDA-approved drug. FDA subsequently approved another firm's application to market the drug, and FDA issued a Warning Letter in December 2006 to NECC stating the firm was compounding copies of commercially available products; compounding standardized anesthetic drug products, which was outside the scope of traditional pharmacy compounding; and repackaging Avastin. The Warning letter charged that the copies of the FDA approved drugs and the anesthetic cream were misbranded and that the repackaged Avastin was an unapproved new drug. The Warning Letter did not pertain to sterility failures at NECC. During the 2004-05 inspection, FDA reviewed NECC's procedures in light of the February 10, 2003 483 and concluded that corrective actions had been implemented.

- In January 2006, NECC entered into a consent agreement with the Commonwealth of Massachusetts related to inadequacies in the firm's sterile and non-sterile compounding

practices. The consent agreement required NECC to hire a consultant and take corrective actions, which would be verified by the consultant. In June 2006, MABP notified NECC that the firm had fulfilled the terms of the consent decree.

- In January 2007, NECC responded to the 2006 Warning Letter.

- FDA responded to NECC's Warning Letter response in October 2008.

Timeline for Ameridose

- Ameridose first registered with FDA in September 2006, but never listed any drugs.

- FDA and MABP conducted a jointly coordinated inspection of Ameridose in December 2007 to follow-up on a complaint related to the company making IV solutions without receipt of patient-specific prescriptions and to gather facts since the firm had recently registered with FDA. FDA advised the firm to validate and verify its aseptic processes since it was making sterile products.

- FDA performed a second inspection of Ameridose seven months later (July-Aug. 2008). This was an inspection to review the firm's "good manufacturing practices." The agency issued the firm a 483 on August 6, 2008, citing several observations, such as not confirming the sterility of products before distribution. Ameridose responded in August 2008 stating that it would take corrective actions to address FDA's observations in the 483.

- During the 2008 inspection, FDA also collected samples of Fentanyl (a strong pain medication), which was found to be super-potent, leading to a Class I recall in September 2008.

- In September 2008 and November 2008, FDA returned to the firm to review shipping records specific to the super-potent Fentanyl, to review the firm's corrective and preventative actions since the September 2008 recall, and to follow-up on questions discussed during the prior inspection.

- In June 2010, FDA received a commercial complaint related to the compounded product nicardipine and conducted at the same time as MABP a limited inspection in response. In January 2011, FDA was informed that the complainant and Ameridose reached amicable resolution. Massachusetts officially dismissed the complaint in June 2011.