United States Senate
Health, Education, Labor, and Pensions Committee

The Case for Clarifying FDA Authority: Large-Scale Drug Compounding and the Ongoing Risk to Public Health

Committee Staff Report

May 22, 2013

CONTENTS

Executive Summary

- This is the second HELP Committee staff report of the Committee's investigation into the nationwide outbreak of fungal meningitis traced to injections of contaminated drugs prepared by the Massachusetts-based New England Compounding Center. The report is based on a review of more than 30,000 pages of internal Food and Drug Administration ("FDA") documents over a six month period, as well as publicly available documents.

- Drug compounding is a traditional and longstanding activity of pharmacies, and serves an important role in our health care system. However, over the last 10 to 15 years, a number of large-scale drug compounding companies have started to produce large batches of high-risk drugs for national sale.

- Despite a scope of operations that makes these companies much more similar to drug manufacturers than pharmacies, they primarily face oversight similar to a state-licensed community pharmacy, rather than the more rigorous quality standards governing traditional drug manufacturers.

- The New England Compounding Center ("NECC") and the co-owned compounding company, Ameridose, both have lengthy track records of producing drugs of questionable sterility and potency, and both have been the subject of repeated adverse event reports and consumer complaints.

    - The Committee review of FDA documents indicates that, between 2002 and 2012, NECC was the subject of at least 52 adverse event reports that demonstrate the dangers created by its hazardous compounding practices. Documented issues include: the failure to ensure the sterility of equipment and products; the distribution of drugs containing particulate matter; the manufacture of super-potent and sub-potent drugs; the mislabeling of drugs; inaccurate beyond use dating; and the illegal distribution of drugs in the absence of patient-specific prescriptions.

    - Similarly, internal FDA documents dated between 2007 and 2012 indicate that Ameridose was the subject of at least 18 adverse event reports, with inspections documenting that Ameridose-compounded drugs displayed issues relating to sterility, potency, mislabeling, and adulteration.

- In tests of compounded drugs conducted by the FDA in 2001 and 2006, 34 and 33 percent of the drugs sampled *failed* one or more standard quality tests.

- FDA documents indicate that, between 2001 and 2011, at least 25 deaths and 36 serious injuries, including hospitalizations, were linked to large-scale drug compounding companies, including 13 deaths in 2011 alone. These numbers likely understate the actual number of adverse events, as current law does not require reporting of these events.

- Large-scale drug compounders *continue* to pose a serious risk to public health. In the eight months since the NECC-caused meningitis infections, at least 48 compounding companies have been found to be producing and selling drugs that were contaminated or created in unsafe conditions. Ten drug compounders have issued national recalls because of concerns about contamination, and 11 drug compounders have been ordered by state licensing agencies to stop producing some or all drugs.

- To reduce the risk to the public health from compounded drug products, it is essential that a clear statutory framework be enacted – one that requires compounding manufacturers to engage in good manufacturing practices, to better ensure the drugs produced are sterile and contain the correct amount of the active pharmaceutical ingredient.

Introduction

Beginning in the summer of 2012, 379 people in 19 states were infected with a rare form of fungal meningitis.[1] Fifty-five of those people died.[2] Rapid epidemiological investigative work by the Tennessee Department of Health and the Centers for Disease Control and Prevention ("CDCP") likely averted additional fatalities.[3] However, many of those infected continue to suffer debilitating side effects from the infection and the powerful drugs required to save their lives.[4] Those effects include loss of feeling in limbs, nightmare-like hallucinations, intense chronic pain, and the risk of organ failures.[5] One woman who received an injection in Michigan stated that she had been hospitalized seven separate times for a total of 75 days as a result of the infection she contracted.[6] A Florida woman remained hospitalized four months after developing meningitis.[7] Three hundred sixty-two additional cases of spinal and joint infections have also been documented.[8] The CDCP has linked those infections to injections of a fungus-contaminated drug prepared by the New England Compounding Center ("NECC"), a pharmacy based in Massachusetts.[9]

The contaminated drug linked to this outbreak was manufactured in large batch doses and distributed nationally. Neither the FDA nor the state of Massachusetts acted to enjoin the actions of the company. Because the FDA lacked clear authority over this type of pharmacy, the agency did not act to require the company to meet the good manufacturing practices or the quality standards that would have better ensured that the drugs produced were safe. Even in the wake of the NECC outbreak, and despite increased awareness of the risks posed by pharmacies operating like manufacturers, large-scale drug compounders continue to pose a serious risk to public health. Since the NECC outbreak, at least 10 separate companies have recalled compounded drugs, and at least 11 companies were ordered to stop producing some or all drugs.[10] Besides NECC and Ameridose, at least 48 other pharmacies have been found by the FDA or state regulators to be producing and selling drugs that are contaminated, were created in unsafe conditions, or otherwise violate state licensing requirements.[11]

What is Drug Compounding and How is it Regulated?

Compounding medicines is a traditional activity of pharmacies and serves an important role in our health care system. When compounding, the pharmacist alters medicines to adjust the dosing or modify the form to meet a patient-specific need. For instance, if an infant needs an antibiotic that is normally produced as a pill, a pharmacist could convert it to a liquid to be taken orally. That traditional compounding practice, by which a drug is produced in response to an individual prescription, or at most in small batches based on reasonably anticipated need, is regulated by the states. Drugs that are manufactured, in contrast, are regulated by the FDA.[12] Those drugs must be manufactured following rigorous quality controls to ensure that the drugs are not contaminated and that the dosage of the active ingredient is correct.

Over the last 10 to 15 years, a number of pharmacies have expanded operations far beyond the traditional compounding role, at least in part in response to hospital and consumer demand for otherwise unavailable drugs. Dozens, and possibly hundreds, of these large-scale drug compounding companies produce large batches of high-risk drugs, including preservative-free steroid injections and triple

anesthetic creams, for national sale. Some have specialized to become suppliers of commonly used hospital intravenous (IV) drugs like heparin, oxytocin, hydromorphone, and sodium chloride. Despite a scope of operations that makes these companies much more similar to drug manufacturers than pharmacies, they primarily face oversight similar to a state-licensed community pharmacy rather than the rigorous quality controls Americans would expect. Meanwhile, the FDA has been faced with a lack of clarity over the scope of its authority and an industry willing to challenge that authority on a regular basis. There also existed within FDA a bureaucracy hesitant to act on instances of apparent misconduct.

Over the last 10 to 15 years, dozens, and possibly hundreds, of large-scale drug compounding companies have started to produce large batches of high-risk drugs for national sale.

Congress and federal regulators have made previous efforts to establish an enforceable policy that clearly differentiates between traditional pharmacy compounding and compound drug manufacturing, but those efforts have proved to be complicated. Although Congress passed legislation designed to delineate these practices in 1997, the Supreme Court found certain provisions of this law unenforceable in 2002, and federal circuit courts split over whether the rest of the law was enforceable.[13] Also in 2002, the FDA issued a Compliance Policy Guidance setting forth when it would consider bringing an enforcement action against a compounding pharmacy.[14] However, trade associations and individual drug compounding companies continued to initiate challenges when the FDA sought to bring an enforcement action against large-scale drug compounders.[15] These cases further complicated the enforceability of the 1997 law in different parts of the country.

Although the FDA was faced with a lack of clarity in the law, and with an industry willing to challenge its authority on a regular basis, the agency responded poorly to those challenges. Officials responsible for enforcing the drug compounding guidance appear to have lacked defined inspection criteria and tracking procedures for building a strong evidentiary record for these cases. These uncertainties contributed to long delays when cases were brought to the agency Chief Counsel's office for approval, a required step before a Warning Letter or an injunction could be issued for a compounding pharmacy.[16] At least in actions relating to NECC and its co-owned compounding pharmacy, Ameridose, the Chief Counsel's office delayed decisions until the matter was so stale that it was no longer pursued.[17] Even when the agency did issue Warning Letters, as it ultimately did in the case of NECC, the agency's promised follow-through to injunction often did not materialize.[18]

By 2008, the jurisdictional issues had become so unclear that the agency appeared to be unable to balance the risk of litigation against the public health risk posed by the large-scale compounders, even though the agency continued to receive regular reports of serious adverse events, complaints from state boards of pharmacy, and consumer complaints. The result was an agency that lacked effective internal guidelines, procedures, and the leadership consensus required to regulate high-risk compounders like NECC and Ameridose.

In 2009, FDA leadership set out to develop a clear and enforceable policy that reflected the limitations of the multiple court decisions and the resulting differences in authority in various parts of the country.[19] In the fall of 2012, almost three years later, and despite additional complaints, the agency was finally

close to issuing that policy through revised Compounding Pharmacy Guidance, when the NECC-linked fungal meningitis outbreak occurred.[20]

However, had the FDA successfully implemented the revised guidance, it still would have faced serious challenges to ensuring that large-scale compounders were producing safe and effective drugs. Even under the proposed guidance, high-risk compounders would not have been required to register with the FDA, they would not have been subject to regular inspections (only to inspections following an adverse event or complaint), and additional rulemakings would have been necessary to define significant terms in the 1997 law, including what constituted compounding "regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available product."[21] It also likely would have had to litigate further to determine which circuit court's interpretation of the 1997 law would prevail.

Moreover, although the FDA's ability to inspect and bring enforcement actions against individual high-risk compounding operations would have been clarified, it is not clear that the guidance would have led many of the large-scale drug compounders that were engaged in the equivalent of manufacturing to improve quality standards. As demonstrated by the continuing safety violations documented over the past seven months, Congress needs to take action to ensure clear lines of responsibility for oversight of these companies. Drug compounding companies that are manufacturing batches of drugs in the absence of a prescription, and shipping those products to states across the country, need to adhere to an appropriate level of good manufacturing practices as determined by the FDA. These requirements are the linchpin that ensures that drugs are not contaminated and that the dosage of the active ingredient is correct.

The Public Health Risk Posed by NECC and Ameridose

As large-scale compounding manufacturers have grown over the last decades, so have concerns about the quality of the drugs produced by some of those companies. Documents produced to the Committee indicate that both NECC and co-owned Ameridose have lengthy track records of producing drugs of questionable sterility and potency, and both were the subject of repeated adverse event reports and consumer complaints.

NECC

Between 2002 and 2012, NECC was the subject of at least 52 adverse event reports exemplifying the dangers created by its hazardous compounding practices.[22] Also during this time, NECC's threat to public health was conclusively established by investigations undertaken by the FDA and state regulators, both as routine measures and in response to reports of NECC's unsafe compounding practices.[23] NECC's unsafe operations were repeatedly highlighted in the complaints of doctors, state boards of pharmacy, competitors, and consumers, some of whom suffered meningitis-like symptoms after receiving steroid injections made by NECC.[24]

As evidenced by these persistent complaints, NECC's compounding practices posed a public safety risk that was both broad in scope and egregious in nature. Among the many issues documented were

NECC's failure to ensure the sterility of equipment and products, including the distribution of drugs containing particulate matter; the manufacture of drugs that were overly strong or not strong enough ("super-potent" and "sub-potent"); the mislabeling of drugs; the inaccurate use of expiration dates (or "beyond use dates"); and the illegal distribution of drugs in the absence of patient-specific prescriptions.[25]

These deficient and unsafe practices compromised the integrity of a broad range of NECC-compounded drugs, including steroids administered for pain relief such as betamethasone epidural injections and methylprednisolone acetate injections; repackaged Avastin, a drug used to treat age-related macular degeneration; Trypan Blue, a drug used for capsular staining during cataract surgery; methotrexate; and topical anesthetic creams. Ultimately, these dangerous practices appear to have caused more than 50 patients to suffer serious illnesses, often requiring hospitalization, years in advance of the 2012 meningitis outbreak.[26] As previously documented by the Committee, both the FDA and the Massachusetts Board of Registration in Pharmacy took action against NECC, respectively issuing a Warning Letter and a Consent Decree, but neither agency moved effectively to enjoin the company from practices that placed the public health at risk.[27]

When the FDA and Massachusetts Board inspectors returned to NECC in the wake of the 2012 meningitis outbreak, their findings only amplified NECC's long history of unsound practices. The inspection demonstrated that NECC failed to comply with sterility procedures outlined in USP <797>, a widely accepted quality standard for smaller-scale compounders, and documented visible black particulate matter in vials of recalled methylprednisolone acetate.[28] Further, the FDA determined that NECC's environmental monitoring system documented 61 instances between January and August 2012 in which bacteria or mold existed in concentrations surpassing action-level thresholds.[29] Additional findings included "greenish yellow discoloration" lining one of two autoclaves used to sterilize various components and equipment; "yellow residue lining the rear return of Weigh Station 2 Hood and greenish residue lining the rear return of Weigh Station 3 Hood" which were used to "weigh active ingredients and other raw materials"; residual powder in the powder hood; tacky mats, which were used to prevent potential contaminants from entering the clean room, that were "visibly soiled with assorted debris"; and a leaking boiler that "created an environment susceptible to contaminant growth" adjacent to the clean room.[30]

The New England Compounding Center and the co-owned compounding company, Ameridose, both have lengthy track records of producing drugs of questionable sterility and potency, and both were the subject of repeated adverse event reports and consumer complaints.

Ameridose

Although regulators had already documented extensive problems concerning NECC's compounding practices, the Massachusetts Board of Registration in Pharmacy approved a license for the owners of NECC, the Conigliaro family, to open a second compounding company called Ameridose in 2006.[31] While NECC primarily manufactured drugs for purchase by pain clinics and physicians, Ameridose focused on compounding IV mixtures for use by hospitals across the country.

Between 2006 and 2012, Ameridose grew rapidly and, by the time of the NECC-caused meningitis crisis, Ameridose-compounded drugs were available to the 3,000 hospital members of Novation, the largest group purchasing organization in the country, in addition to 22,000 other providers and facilities.[32]

Ameridose engaged in many of the same unsafe compounding practices as did NECC. Between 2007 and 2012, Ameridose was the subject of at least 18 adverse event reports, in addition to a report from an employee-informant, and investigations by both federal and state authorities.[33] Findings established that Ameridose products posed considerable risks arising from issues of sterility, potency, mislabeling, adulteration, and illegal manufacturing.[34] For example, in August 2008, FDA investigators found that Ameridose products were shipped immediately without waiting for the results of sterility testing; testing for potency and dose uniformity was not routinely performed; and Ameridose failed to comply with the requirements of USP <797> in violation of Massachusetts law.[35]

A subsequent follow-up inspection resulted in sampling of Fentanyl, a drug opioid analgesic that FDA inspectors noted was already "very potent" at "80x" the potency of morphine in its standard form.[36] Testing demonstrated that Ameridose-compounded Fentanyl was concentrated at 118.4 percent the standard level, leading to a recall of that particular batch of that particular drug.[37] Following the 2008 inspections, a Warning Letter was drafted for Ameridose that enumerated many instances of illegal manufacturing of unapproved, misbranded, and adulterated drug products.[38] While the Warning Letter was tentatively cleared by the FDA's Office of the Chief Counsel in early March 2009, concerns over a single sentence delayed final approval for months.[39] In September 2009, the Warning Letter was deemed stale because it had been over a year since the initial inspections, and the letter was never sent.[40]

In 2010, an employee-informant of Ameridose described concerns such as the elimination of several product safety checks and the presence of particulate matter in a batch of Succinylcholine that was deemed acceptable for distribution.[41] The informant also related that untrained sales force personnel had assisted in labeling operations in a clean room, one of the three clean rooms was used despite a positive test result for mold growth, and employees sanitized areas before taking environmental samples.[42]

Following the 2012 meningitis outbreak, FDA investigators documented concerns at the larger-scale Ameridose that were virtually identical to those they found at the co-owned NECC facility. Among the issues discovered were failures to guarantee the sterility of drugs and the uniformity of doses, including findings that batches of drugs were not subjected to sterility testing, and that procedures to prevent microbiological contamination of sterile drugs were inadequate.[43] Further, FDA investigators found that Ameridose failed to clean or maintain equipment and utensils sufficiently to prevent contamination, lacked equipment for adequate control over air pressure, and was infested with vermin.[44]

The Scope of the Public Health Risk: Beyond NECC and Ameridose

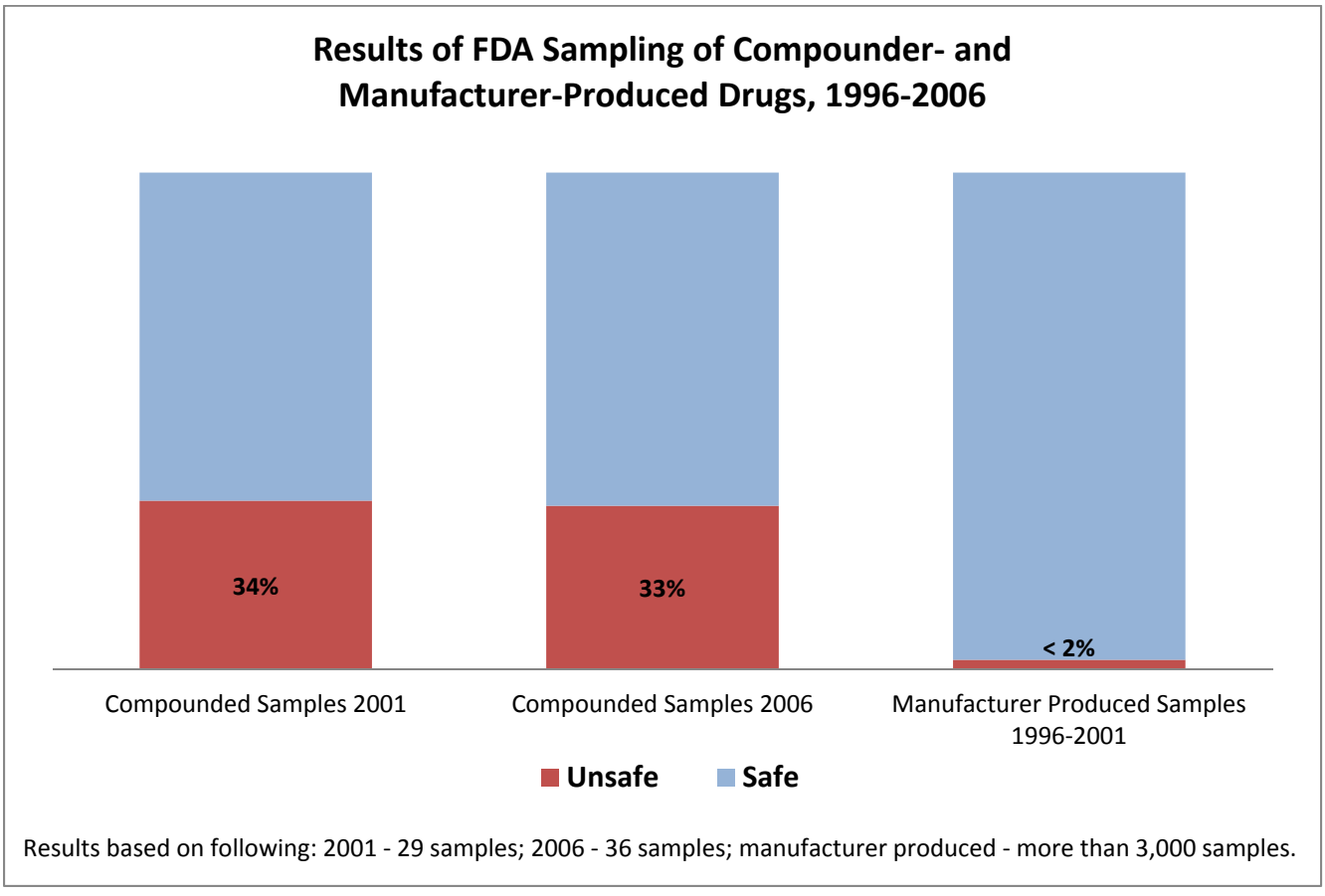
NECC and Ameridose were hardly the only companies engaged in practices that were of serious concern to the FDA. Between 2004 and 2010, the agency issued at least 46 Warning Letters to compounders documenting concerns ranging from failure to test drugs for contaminants and potency, to the use of unjustifiable beyond use dates[45] Additionally, between 2001 and 2011, an FDA document compiling

some of the most serious adverse events related to drug compounding details at least 25 deaths and 36 serious injuries, including hospitalizations, that were linked to large-scale drug compounding companies, including 13 deaths in 2011 alone.[46]

In addition, since the NECC outbreak, state boards of pharmacy, the National Association of Boards of Pharmacy, and the FDA have taken steps to understand and inspect companies engaged in large-scale drug compounding more effectively. As a result of those efforts, at least 10 companies have issued recalls for sterile drug products, many in response to documented contamination; at least 11 companies have been the subject of cease-and-desist orders by state authorities; and Iowa has initiated license revocations against at least five companies.[47]

FDA Sampling Documented Risks of Compounding

In an effort to understand better the risks posed by increasingly large drug compounding companies, the FDA undertook surveys of compounded drugs in 2001 and 2006. In 2001, the FDA purchased products from 12 companies offering products for sale online, and, in 2006, it collected samples in unannounced visits to 36 compounding pharmacies.[48] The FDA also tested the active ingredients used to compound the drugs and determined that no underlying active ingredient failed quality testing.[49]



The 2001 survey was based on standard quality testing conducted on compounded drugs, including sterile injectables, pellet implants, and ophthalmic products.[50] Ultimately, the agency was able to

complete testing on a total of 29 samples.[51] Of those, 10 of the samples, or 34 percent, *failed* one or more standard quality tests.[52] By contrast, in routine FDA samples of drug products from commercial manufacturers, the analytical testing failure for those drugs has been less than 2 percent.[53] When compared to this failure rate, the failure rate of 34 percent for compounded drugs indicates the need for better quality controls in most compounding companies. Specifically, the survey found that most of the samples that failed quality testing contained improper amounts of the active ingredient, and thus were either super-potent or sub-potent.[54] In addition, one sterile injectable was found to have an unacceptably high level of bacterial endotoxins.[55] The failed products included sterile injectable betamethasone, a drug which has resulted in meningitis infections on several occasions, and commonly used fertility drugs, including estradiol.[56]

Similarly, the 2006 survey collected samples from unannounced visits to compounding pharmacies from around the United States.[57] Quality testing was completed on 36 samples, all of which were sterile injectable drugs.[58] Of the 36 samples tested, 12, or 33 percent, failed one or more standard quality tests.[59] As in 2001, the survey found that the samples that failed quality testing were either super-potent or sub-potent.[60] Moreover, the test results were not off by small margins; in fact, the samples ranged from having 67.5 percent to 268.4 percent of the drug potency declared on the product labeling.[61] All tested drug products with the active ingredient of lidocaine and estradiol failed the analysis.[62] Since none of the active pharmaceutical ingredients that went into the final product failed testing, the FDA concluded that "the analytical failures of the finished drug products were likely related to the compounding processes at the pharmacies."[63] As the FDA concluded, "the fact that nearly one-third failed analytical testing raises public health concerns."[64]

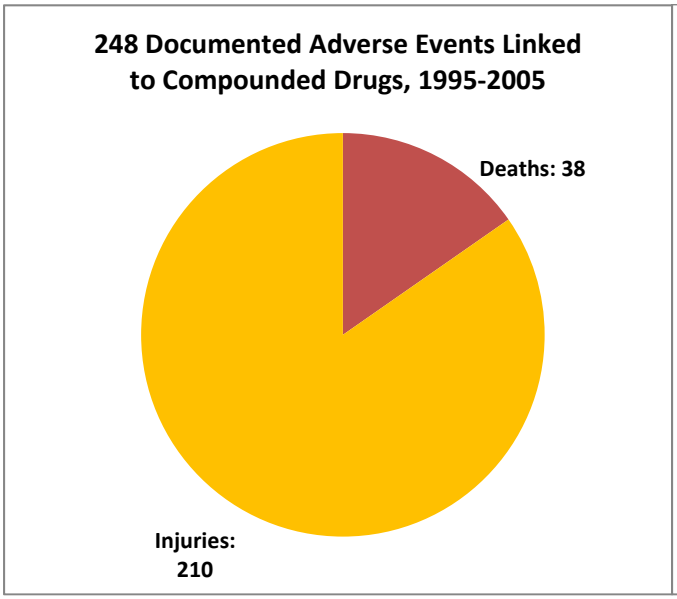
Adverse Events

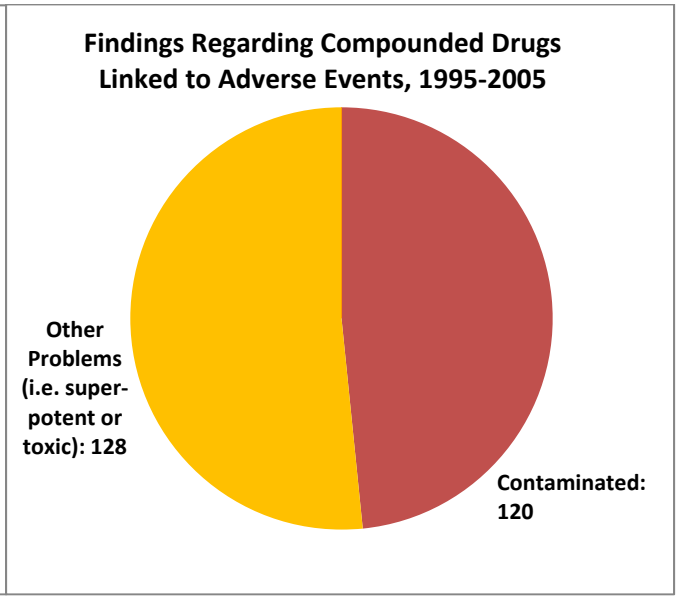
The gravity of the public health threat posed by large-scale drug compounders can be better understood by examining some of the documented adverse events. Between 2001 and 2011, an FDA document compiling some of the most serious adverse events related to drug compounding details at least 25 deaths and 36 serious injuries, including hospitalizations, that were linked to large-scale drug compounding companies, including 13 deaths in 2011 alone.[65] As the FDA stated in the memo, "Based on the information presented…, we feel that there are significant public health concerns with the compounding of sterile drug products."[66]

Between 1988 and 2005, at least 38 deaths and 210 injuries were linked to compounding company drugs that were contaminated, mislabeled or caused lethal overdoses

A separate accounting of adverse events and complaints linked to drug compounding companies between 1988 and 2005 documents at least 38 deaths and 210 injuries from drugs that were contaminated, mislabeled, or caused lethal overdoses because they contained more of the active pharmaceutical ingredient than indicated.[67] These 248 tragedies included the deaths of six infants and children, and at least 18 other children paralyzed, burned, hospitalized, and suffering from other severe reactions.[68] The FDA said that these reports represented only a small percentage of total adverse events

from compounded drugs.[69] There is currently no system in place that requires adverse event reporting or accurately tracks adverse events to compounded products.





The adverse events detailed by the FDA include three 2007 deaths that were associated with compounded Colchicine from a pharmacy in Texas.[70] Colchicine, which can be very toxic when given in high doses, is used to prevent gout attacks (sudden, severe pain in one or more joints) in adults, and to relieve the pain accompanying gout attacks when they occur. Three patients died after being administered the drug by injection for back pain.[71] Within hours of receiving the injections, the patients became seriously ill and were taken to local hospitals.[72] When the FDA investigated and tested samples of the compounded product, sample potency varied from 640 percent to 62 percent of the level of Colchicine declared.[73]

Last month, on April 15, 2013, the same pharmacy announced a total recall of all lots of all sterile compounded products.[74] The company continues to operate under current law as a pharmacy not subject to good manufacturing practices, and currently manufactures numerous drug products, including hormones, thyroid and adrenal drugs, and eye drops.

Numerous other examples exist of compounding pharmacies repeatedly failing to meet high-quality safe and sterile manufacturing practices, including a California pharmacy selling contaminated compounded cardioplegia solution (used in open-heart surgery) that resulted in severe infections, sepsis, and three deaths in 2005.[75] The same compounding pharmacy produced super-potent hydromorphone in 2009, causing patients to overdose.[76] The company continues to operate under current law as a pharmacy not subject to good manufacturing practices, and it currently operates 25 locations nationwide. During recent inspections of six of these 25 locations, the FDA found such disturbing problems as potential potency issues, microorganism contamination, and pests.[77]

Similarly in 2002, several people developed fungal infections and two died after being injected with methylprednisolone made by a South Carolina pharmacy.[78] The South Carolina Board of Pharmacy found the pharmacy unsanitary and its sterilization practices inadequate.[79] It suspended the pharmacist's license for four years and fined him $10,000. Ultimately, the pharmacy closed.[80]

Findings of Recent Investigations and Inspections

In the eight months since the NECC-caused meningitis crisis, it has become clear that public health risks from large-scale drug compounding persist. As a result of increased oversight from state and federal regulators, at least 48 compounding companies have been found to be producing and selling drugs that are contaminated, were created in unsafe conditions, or otherwise violate state licensing requirements.[81] Ten companies have issued nationwide recalls of drugs compounded at their facilities.[82] In at least four cases, the recall was issued in response to documentation of actual contamination.[83] Further, 11 compounding pharmacies have been ordered to cease and desist operations, including two of those that had issued nationwide recalls.[84]

In Massachusetts, one compounding pharmacy recalled all of its sterile products after unidentified particulates were observed in five vials of drugs.[85] After producing a super-potent painkiller that caused two people to be hospitalized last year, the company was already under investigation by state authorities.[86] In November 2012, the state ordered the company to stop making a generic form of Viagra because it was found to be using "improper components."[87]

Adverse events and complaints linked to drug compounding companies between 1988 and 2005 account for at least 38 deaths and 210 injuries.

A second Massachusetts specialty pharmacy recalled allegedly sterile fertility drugs after a patient discovered an unknown substance floating in a vial of medication that had been shipped to 2,100 patients in 39 states.[88] In February 2013, state health officials issued a cease-and-desist order prohibiting the company from producing sterile compounded drugs.[89]

Similarly, in March 2013, a hospital nurse spotted debris floating in a vial of intravenous drugs.[90] Tests confirmed that the debris was a fungus and, consequently, prompted a massive recall by the New Jersey compounding pharmacy that produced the drugs.[91] Although the New Jersey Board of Pharmacy has restricted the company from compounding intravenous drugs, and the state Attorney General is seeking the revocation of the pharmacy's license, the company previously manufactured a wide variety of other sterile drugs, including antibiotics, anesthetics, and pain management medications.[92]

More recently, in April 2013, a Florida pharmacy recalled all lots of its sterile drug products after an FDA inspection revealed "black particles of unknown origin" in seven vials of an injectable steroid.[93] FDA investigators also found "a cloth-like filament of unknown origin" in one vial of chromium-chloride injections, an additive used for intravenous nutritional supplements.[94] Tests confirmed the presence of bacteria.[95]

Six additional companies also have recalled potentially contaminated drugs over the past few months, spurred by FDA inspections that identified serious quality control deficiencies resulting in the high

potential for contaminated products.[96] In addition, the FDA issued "inspectional observations" to 20 other compounding pharmacies that contained findings including inappropriate and/or inadequate clothing for sterile processing, lack of appropriate air filtration systems, insufficient microbiological testing, failure to conduct potency testing, and problems related to expiration and beyond use dates.[97]

Finally, the Iowa Board of Pharmacy has filed charges against at least five companies for violations including incorrect labeling, noncompliant sterile areas, and improper distribution of drugs.[98] These actions are the result of an ongoing series of inspections of all out-of-state pharmacies licensed in Iowa, conducted in partnership with the National Association of Boards of Pharmacy.[99] Tennessee and Florida are both surveying state compounding pharmacies in an effort to regulate these companies more effectively.[100] Other states have also been re-examining their oversight of these entities.

Conclusion

The NECC-linked meningitis crisis occurred against a backdrop of a significant increase in the number of companies that manufacture large batches of high-risk compounded drugs and market and ship them nationally. Investigations and sampling studies conducted by the FDA plainly demonstrate that many of these companies were and are not following good manufacturing standards or meeting other practice standards. At the same time, the FDA struggled to develop a clear and enforceable policy for these types of large-scale drug compounders. The agency faced numerous challenges in developing this policy, including repeated legal challenges to the agency's attempted enforcement actions against high-risk compounders, but the agency ultimately never released a workable policy.

Today, eight months after quick work by the Tennessee Department of Health and the CDCP isolated NECC-produced steroids as the source of the infections, the public health risk from compounded drugs persists. Some states have engaged in an effort to understand and inspect large-scale compounders operating in or licensed within their borders more effectively, and the FDA has similarly inspected a number of large compounders closely. That scrutiny has demonstrated the scope of the public health risk posed by large-scale compounding manufacturers and the need for well-defined lines that differentiate these companies from traditional pharmacy compounders, providing medicine for individual patients. To reduce the risk to the public health from compounded drug products, it is essential that a clear statutory framework be enacted that requires compounding manufacturers to follow the appropriate good manufacturing practices that will better ensure that the drugs produced are sterile and contain the correct amount of the active pharmaceutical ingredient.

Endnotes

[1] CDC, *Multi-State Meningitis Outbreak - Current Case Count*, May 6, 2013, http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html, (accessed May 17, 2013).
[2] Id.
[3] CDC Testimony before the Senate HELP Committee, Re: *The CDC and Public Health Response to the 2012 Fungal Meningitis and Other Infections Outbreak*, November 15, 2012 ("Their [local infectious disease officials, including state epidemiologists, healthcare associated infection (HAI) prevention coordinators, and others whose positions are directly supported through CDC's Epidemiology and Laboratory Capacity (ELC) cooperative agreement and CDC's Emerging Infections Program (EIP)] efforts at the state and local level have been extraordinary and in many cases undoubtedly contributed directly to saving the lives of exposed patients.").
[4] CDC, *Multi-State Meningitis Outbreak - Current Case Count*, May 6, 2013, http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html, (accessed May 17, 2013).
[5] *E.g.*, 60 Minutes, *"Lethal Medicine Linked to Meningitis Outbreak*," March 10, 2013, http://www.cbsnews.com/video/watch/?id=50142537n (accessed May 15, 2013); 60 Minutes, *"A Painful Road to Recovery,"* March 10, 2013, http://www.cbsnews.com/video/watch/?id=50142543n (accessed May 15, 2013).
[6] 60 Minutes, *"Lethal Medicine Linked to Meningitis Outbreak*," March 10, 2013, http://www.cbsnews.com/video/watch/?id=50142537n (accessed May 15, 2013).
[7] Jodie Tillman, *Infection adds mystery to meningitis outbreak*, TAMPA BAY TIMES, January 19, 2013, *available at* http://www.tampabay.com/news/health/infection-adds-mystery-to-meningitis-outbreak/1271439 (accessed May 20, 2013).
[8] CDC, *Multi-State Meningitis Outbreak - Current Case Count*, May 6, 2013, http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html, (accessed May 17, 2013).
[9] CDC Testimony before the Senate HELP Committee, Re: *The CDC and Public Health Response to the 2012 Fungal Meningitis and Other Infections Outbreak*, November 15, 2012 ("My remarks today will focus specifically on the identification of, and subsequent public health response to, the outbreak associated with injections of contaminated preservative-free methylprednisolone acetate (MPA), an injectable steroid produced by the New England Compounding Center (NECC).").
[10] *See, e.g.*, Iowa Board of Pharmacy, *Re: Iowa nonresident Pharmacy License of Med Quest Pharmacy, License No 3399, Statement of Charges & Notice of Hearing*, January 16, 2012; Iowa Board of Pharmacy, *Re: Iowa nonresident Pharmacy License of PharMedium Services LLC, License No 5759, Statement of Charges & Notice of Hearing*, January 16, 2012; Iowa Board of Pharmacy, *Re: Wholesale Drug License of PharMedium Services LLC, License No 3763, Statement of Charges & Notice of Hearing*, January 16, 2012; Iowa Board of Pharmacy, *Re: Iowa nonresident Pharmacy License of Talon Compounding Pharmacy, License No 4027, Statement of Charges & Notice of Hearing*, January 16, 2012; Iowa Board of Pharmacy, *Re: Iowa nonresident Pharmacy License of Unique Pharmaceuticals, LTD, License No 3265, Statement of Charges & Notice of Hearing*, January 16, 2012; Iowa Board of Pharmacy, *Re: Iowa nonresident Pharmacy License of Wedgewood Pharmacy, License No 3577, Statement of Charges & Notice of Hearing*, January 16, 2012; Massachusetts Department of Health and Human Services Press Release, *Department of Public Health Announces Update on Unannounced Pharmacy Inspections*, February 05, 2013, *available at*: http://www.mass.gov/eohhs/gov/newsroom/press-releases/dph/update-on-unannounced-pharmacy-inspections-announced.html (accessed May 21, 2013); FDA News Release, *FDA alerts health care providers of recall of all sterile drug products by Med Prep Consulting in New Jersey*, March 18, 2013, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm344314.htm (accessed May 17, 2013); FDA Recall Firm Press Release, *Clinical Specialties Compounding Pharmacy Announces Voluntary Nationwide Recall of All lots of Sterile Products Repackaged and Distributed by Clinical Specialties Compounding Due to Lack of Sterility Assurance,* March 20, 2013, *available at:* http://www.fda.gov/Safety/Recalls/ucm344786.htm (accessed May 21, 2013); FDA Recall Firm Press Release, *Green Valley Drugs Announces Voluntary Nationwide Recall of All Lots of All Sterile Products Compounded, Repackaged, and Distributed by Green Valley Drugs Due to Quality Control Concerns,* April 5, 2013, *available at:* http://www.fda.gov/Safety/Recalls/ucm347559.htm (accessed May 21, 2013; FDA News Release, *FDA issues alert about lack of sterility assurance of drug products from ApotheCure, Inc. and NuVision Pharmacy and of forthcoming recall*, April 15, 2013, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm348093.htm (accessed May 17, 2013); Lena Sun, *Balanced Solutions Compounding Pharmacy Recalls Sterile Drug Products*, THE WASHINGTON POST, April 21, 2013, *available at* http://articles.washingtonpost.com/2013-04-21/national/38717632_1_fda-new-england-compounding-center-products (accessed May 20, 2013); FDA Recall Firm Press Release, *Nora Apothecary & Alternative Therapies*

Announces a Voluntary Multi-State Recall of All Sterile Compounded Products Due to a Lack of Sterility Assurance, April 22, 2013, *available at:* http://www.fda.gov/Safety/Recalls/ucm349040.htm (accessed May 21, 2013); FDA Recall Firm Press Release, *In Cooperation with FDA, The Compounding Shop, LLC Declares a Voluntary Recall of All Lots of Sterile Compounded Products Due to a Lack of Sterility Assurance Distributed Within its Local Market Area*, May 6, 2013, *available at:* http://www.fda.gov/Safety/Recalls/ucm351841.htm (accessed May 21, 2013); Letter from FDA to PharMEDium Services, LLC, Lake Forest Illinois, February 5, 2013; Letter from Foundation Care LLC to FDA, Re: *Foundation Care LLC, Earth City, Missouri (FEIN #3005364771) Response to FDA Form 483 Issued March 19, 2013*, April 9, 2013; Letter from IVSolutions of Lubbock to FDA, Re: *FDA 483, IVSolutions of Lubbock*, April 2, 2013; Kay Lazar, *Lab Results Expected Soon on Recalled Waltham Pharmacy Fertility Drugs*, THE BOSTON GLOBE, February 27, 2013, *available at* http://www.bostonglobe.com/lifestyle/health-wellness/2013/02/26/test-results-expected-soon-recalled-fertility-drugs-from-waltham-pharmacy/6atDVwnAbNrLSr1E0dHSFJ/story.html (accessed May 16, 2013); Chelsea Conaboy, *Recalled Woburn Compounding Pharmacy Products Were Shipped to 21 States*, BOSTON.COM, March 27, 2013, *available at* http://www.boston.com/whitecoatnotes/2013/03/27/recalled-woburn-compounding-pharmacy-products-were-shipped-states/hOenagPUFpnVzthgA3PeDO/story.html (accessed May 20, 2013); FDA *Inspectional Observations*, Form FDA483, issued to: Custom Compounding Centers, LLC, Los Alamitos, California, December 13, 2012; PharMEDium Services LLC, Chester, Virginia, December 14, 2012; Central Admixture Pharmacy Services, Inc., Woburn, Massachusetts, January 29, 2013; PharMEDium Services LLC, Poland, Ohio, February 7, 2013; Wedgewood Village Pharmacy, Inc., Swedesboro, New Jersey, February 11, 2013; Central Admixture Pharmacy Services, Inc., Wallingford, Connecticut, February 19, 2013; Lee and Company, d/b/a Lee Pharmacy, Inc., Fort Smith, Arkansas, February 21, 2013; Central Admixture Pharmacy Services, Inc., Chicago, Illinois, February 22, 2013; PharMEDium Services LLC, Cleveland, Mississippi, February 22, 2013; Avella of Deer Valley, Inc., Phoenix, Arizona, February 25, 2013FDA *Inspectional Observations*, Form FDA483, issued University Pharmacy, Inc., Salt Lake City, Utah, February 26, 2013; PharMEDium Services LLC, Sugar Land, Texas, February 27, 2013; JCB Labs LLC, Wichita, Kansas, February 27, 2013; Central Admixture Pharmacy Services, Inc., Kansas City, Missouri, February 28, 2013; Central Admixture Pharmacy Services, Inc., Livonia, Michigan, February 28, 2013; PharMEDium Services LLC, Edison, New Jersey, February 28, 2013; Oakdell Pharmacy, Inc., San Antonio, Texas, March 1, 2013; Triangle Compounding, Cary, North Carolina, March 1, 2013; Home Intensive Care Pharmacy, Inc., San Antonio, Texas, March 1, 2013; PharMEDium Services LLC, Portage, Michigan, March 6, 2013; Central Admixture Pharmacy Services, Inc., Homewood, Alabama, March 7, 2013; Lowlyn Pharmacies, Inc., Blanchard, Oklahoma, March 8, 2013; College Pharmacy Incorporated, Colorado Springs, Colorado, March 15, 2013; FVS Holdings, Inc., d/b/a Green Valley Drugs, Henderson, Nevada, March 15, 2013; Foundation Care LLC, Earth City, Missouri, March 19, 2013; IV Solutions of Lubbock [sic], Lubbock, Texas, March 20, 2013; Drugs Are Us, Inc., d/b/a Hopewell Pharmacy, Hopewell, New Jersey, March 21, 2013; Lowlite Investments, Inc., d/b/a Olympia Pharmacy, Orlando, Florida, March 21, 2013; Medaus, Inc., Birmingham, Alabama, March 22, 2013; PharMEDium Services LLC, Memphis, Tennessee, March 22, 2013; Stewart Compounding Pharmacy, Fayetteville, North Carolina, March 25, 2013; Pentec Health, Inc., Boothwyn, Pennsylvania, April 1, 2013 (*hereinafter* "Recent Regulatory Actions").

[11] Recent Regulatory Actions, *supra* 10.

[12] Among other requirements, drug manufacturers are subject to a preapproval process that generally requires clinical testing. Manufacturers must also register with the agency and identify their drug products.

[13] Food and Drug Administration Modernization Act of 1997 (FDAMA); *Western States Medical Center v. Shalala*, 238 F.3d 1090 (9th Cir. 2001); *Medical Center Pharmacy v. Mukasey*, 536 F.3d 383 (5th Cir. 2008).

[14] FDA, *Guidance for FDA Staff and Industry, Compliance Policy Guides Manual, Se. 460.200, Pharmacy Compounding*, May 2002.

[15] *Medical Center Pharmacy v. Mukasey*, 536 F.3d 383 (5th Cir. 2008); *Wedgewood Village Pharmacy Inc. v. United States*, 421 F.3d 263 (3d Cir. 2005); *United States v. Franck's Lab, Inc.*, 816 F. Supp. 2d 1209 (M.D. Fla. 2011); *Medical Center Pharmacy v. Gonzales*, 451 F. Supp. 2d 854 (W.D. Tex. 2006).

[16] FDA Internal Document, Re: *Procedures for Clearing FDA Warning Letters and Untitled Letters*, July 2012, *available at* http://www.fda.gov/downloads/ICECI/ComplianceManuals/RegulatoryProceduresManual/UCM176965.pdf (accessed May 16, 2013). In 2001, a policy was implemented that required all Warning Letters and untitled letters to be reviewed by the FDA Chief Counsel's Office. The policy was revised in 2009, but it continues to require review for a wide range of letters, including any letter implicating compounding or other controversial legal issues.

[17] *E.g.*, FDA Internal Email, Re: *CMS Quality Control Check*, September 1, 2009 ("Ameridose's Warning Letter (Case ID 40318) was put on hold due to conflicting court rulings related to Pharmacy Compounding. We are currently not proceeding

with issuance of this warning letter because it has now been 1 [sic] year since the district's inspection of the firm. We may in the future conduct an inspection of this firm, but for now this case is closed.").

[18] *See* FDA Warning Letter, Re: *NWE-06-07W*, December 4, 2006.

[19] FDA Internal Memorandum, Re: *Draft Guidance on Compounding of Human Drugs Under Section 503A of the Federal Food, Drug, and Cosmetic Act – Compliance Policy Guide*, November 1, 2010.

[20] FDA Internal Document, Re: *Draft Revised Compliance Policy Guide Sec. 460.200*, August 15, 2012; FDA Internal Memorandum, Re: *Rationale for 503A Policy and Regulatory Strategy*, October 4, 2011.

[21] FDA Internal Document, *Draft Compounding CPG Announcing Enforcement of Section 503A of the FDCA*, October 2, 2012.

[22] Untitled Letters from Food and Drug Administration to Chairman Harkin and Ranking Member Enzi, December 6, 2012.

[23] *E.g.*, Colorado State Board of Pharmacy, *Special Report*, Re: *New England Compounding Pharmacy, Inc. (WHO 7832)*, July 20, 2012; FDA Warning Letter to NECC, December 4, 2006; Massachusetts Board of Registration in Pharmacy, *Consent Agreement* re: *Docket No. DS-03-055, PH-03-066*.

[24] Id.

[25] Id.

[26] Untitled Letters from Food and Drug Administration to Chairman Harkin and Ranking Member Enzi, December 6, 2012.

[27] FDA Warning Letter to NECC, December 4, 2006; Massachusetts Board of Registration in Pharmacy, *Consent Agreement* re: *Docket No. DS-03-055, PH-03-066*; Massachusetts Board of Registration in Pharmacy, *Consent Agreement* re: *Docket No. DS-03-055, PH-03-066*.

[28] FDA *Inspectional Observations*, Form FDA483, issued to Barry Cadden, Owner, New England Compounding Pharmacy, Inc., d/b/a New England Compounding Center, October 26, 2012; Massachusetts Board of Registration in Pharmacy Report, *NECC Preliminary Investigation Findings*, October 23, 2012, at 4.

[29] FDA *Inspectional Observations*, Form FDA483, issued to Barry Cadden, Owner, New England Compounding Pharmacy, Inc., d/b/a New England Compounding Center, October 26, 2012.

[30] Id.

[31] Ameridose, LLC, *Application for a New Store – 50 Fountain Street*, 2006.

[32] *See* Todd Wallack, *Ameridose faced previous safety questions*, BOSTON GLOBE, October 10, 2012, *available at* http://www.boston.com/news/local/massachusetts/2012/10/11/ameridose-faced-previous-safety-questions/9kI81p8FOEuOKG5X9rnZoM/story.html (accessed May 17, 2013). In June 2012, prior to the NECC outbreak, Novation announced that it would sever its agreement with Ameridose after the company failed an audit. During that audit, Novation found that Ameridose neglected to separate sterile products from non-sterile objects and lacked sufficient quality controls, though the agreement was not officially severed at the time of the NECC-triggered outbreak.

[33] Untitled Letters from Food and Drug Administration to Chairman Harkin and Ranking Member Enzi, December 6, 2012; FDA Consumer Complaint/Injury Report, Re: *Complaint #115569*, July 13, 2010.

[34] FDA *Inspectional Observations*, Form FDA483, issued to Gary Conigliaro, General Manager, Ameridose, LLC, August 6, 2008.

[35] FDA Internal Memorandum, Re: *Warning Letter Recommendation*, October 6, 2008; FDA *Establishment Inspection Report, Ameridose, LLC*, August 22, 2008; FDA *Inspectional Observations*, Form FDA483, issued to Gary Conigliaro, General Manager, Ameridose, LLC, August 6, 2008.

[36] FDA Internal Email, Re: *Ameridose spl 366491*, September 10, 2008.

[37] Id.

[38] FDA Internal Memorandum, Re: *Warning Letter Recommendation*, October 6, 2008.

[39] FDA Internal Email, Re: *Ameridose LLC, Framingham, MA (FEI 2005881167)*, December 8, 2009 ("What has happened is CDER approved the WL. Its [sic] been in OCC for over a year. Its [sic] stuck there.").

[40] FDA Internal Email, Re: *CMS Quality Control Check*, September 1, 2009 ("Ameridose's Warning Letter (Case ID 40318) was put on hold due to conflicting court rulings related to Pharmacy Compounding. We are currently not proceeding with issuance of this warning letter because it has now been 1 [sic] year since the district's inspection of the firm. We may in the future conduct an inspection of this firm, but for now this case is closed."). *See also* FDA Internal Email, Re: *Compounding Pharmacy*, September 2, 2009 ("…NWE-DO spent a lot of time developing this case last year and having it 'closed' for nebulous reasons is troubling. If you look this up in CMS CDER actually concurred with our rec [sic] back in Feb. [sic]. So, I'm not sure what happened. This is quite frustrating since I thought we had a good WL. I've told our IB [sic] not to bother inspecting compounding pharmacies if we aren't going to act on the violations.").

[41] FDA Internal Memorandum, Re: *Memorandum of Telecon, Between [Redacted] at Ameridose and Karen Archdeacon, CO, NWE-DO, re: GMP Allegations at Ameridose, Westboro, MA*, August 13, 2010.
[42] FDA Internal Memorandum, Re: *Memorandum of Telecon, Between [Redacted] at Ameridose and Karen Archdeacon, CO, NWE-DO, re: GMP Allegations at Ameridose, Westboro, MA*, July 16, 2010 ("He indicated that personnel from their sales force were assisting in labeling operations in a clean room. He indicated that they had not been trained to perform such an operation. … He indicated that their firm was behind in orders and that this is why they needed additional personnel to assist in the manufacturing."; "On 8/5/10, he was aware that one of the 3 clean rooms had a positive result for mold growth. … He indicated that the room was used that day and that the managers performed a cleaning of the room in the event. He indicated that this cleaning was not documented."; "He also indicated that when they take environmental samples, they clean the area first before taking the sample.").
[43] FDA *Inspectional Observations*, Form FDA483, issued to Gary Conigliaro, Vice President and General Manager, Ameridose, LLC, November 9, 2012.
[44] Id.
[45] FDA Internal Memorandum, Re: *Compounding Pharmacies – Enforcement Issues*, August 28, 2012.
[46] FDA Internal Memorandum, Re: *Rationale for 503A Policy and Regulatory Strategy*, October 4, 2011.
[47] Recent Regulatory Actions, *supra* 10.
[48] FDA Report, *Report: Limited FDA Survey of Compounded Drug Products*, last updated June 18, 2009, *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm155725.htm (accessed May 17, 2013); FDA Report, *2006 Limited FDA Survey of Compounded Drug Products*, last updated March 22, 2010, *available at* http://www.fda.gov/drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm (accessed May 17, 2013). The FDA collected samples of finished compounded product from 36 companies in 2006, though it visited others that year and collected API samples from some of them.
[49] FDA Report, *2006 Limited FDA Survey of Compounded Drug Products*, last updated March 22, 2010, *available at* http://www.fda.gov/drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm (accessed May 17, 2013).
[50] FDA Report, *Report: Limited FDA Survey of Compounded Drug Products*, last updated June 18, 2009, *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm155725.htm (accessed May 17, 2013).
[51] Id.
[52] Id.
[53] Id.
[54] Id.
[55] Id.
[56] Id.; FDA Internal Document, *Adverse Events Associated With Pharmacy Compounding*, September 9, 2005**.**
[57] FDA Report, *2006 Limited FDA Survey of Compounded Drug Products*, last updated March 22, 2010, *available at* http://www.fda.gov/drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm (accessed May 17, 2013).
[58] Id.
[59] Id.
[60] Id.
[61] Id.
[62] Id.
[63] Id.
[64] Id.
[65] FDA Internal Memorandum, Re: *Rationale for 503A Policy and Regulatory Strategy*, October 4, 2011.
[66] Id.
[67] FDA Internal Document, *Adverse Events Associated With Pharmacy Compounding*, September 9, 2005.
[68] Id.
[69] Id.
[70] FDA Internal Document, *Appendix I: Compounding Adverse Events from 2001 to 2011*; CDC, *Deaths from Intravenous Colchicine Resulting from a Compounding Pharmacy Error --- Oregon and Washington, 2007*, October 12, 2007, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5640a3.htm (accessed May 17, 2013).
[71] Id.

[72] Id.
[73] U.S. Department of Justice, *U.S. Files Criminal Charges Against Dallas Company in Connection with Misbranded Drug Shipment That Led to Three Deaths*, Feb. 10, 2012, http://www.justice.gov/opa/pr/2012/February/12-civ-199.html (accessed May 17, 2013).
[74] FDA News Release, *FDA issues alert about lack of sterility assurance of drug products from ApotheCure, Inc. and NuVision Pharmacy and of forthcoming recall*, April 15, 2013, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm348093.htm (accessed May 17, 2013).
[75] FDA Internal Document, *Appendix I: Compounding Adverse Events from 2001 to 2011*.
[76] Id.
[77] Recent Regulatory Actions, *supra* 10.
[78] FDA Internal Document, *Appendix I: Compounding Adverse Events from 2001 to* 2011; David Brown, *Previous Fungal Meningitis Outbreak A Decade Ago Resulted in No Oversight Changes*, The Washington Post, November 5, 2012, *available at* http://articles.washingtonpost.com/2012-11-05/national/35505699_1_fungal-meningitis-outbreak-patient-specific (accessed May 20, 2013).
[79] David Brown, *Previous Fungal Meningitis Outbreak A Decade Ago Resulted in No Oversight Changes*, The Washington Post, November 5, 2012, *available at* http://articles.washingtonpost.com/2012-11-05/national/35505699_1_fungal-meningitis-outbreak-patient-specific (accessed May 20, 2013).
[80] Id.
[81] Recent Regulatory Actions, *supra* 10.
[82] Id.
[83] Id.
[84] Id.
[85] Chelsea Conaboy, *Recalled Woburn Compounding Pharmacy Products Were Shipped to 21 States*, BOSTON.COM, March 27, 2013, *available at* http://www.boston.com/whitecoatnotes/2013/03/27/recalled-woburn-compounding-pharmacy-products-were-shipped-states/hOenagPUFpnVzthgA3PeDO/story.html (accessed May 20, 2013).
[86] Id.
[87] Id.
[88] Kay Lazar, *Lab Results Expected Soon on Recalled Waltham Pharmacy Fertility Drugs*, THE BOSTON GLOBE, February 27, 2013, *available at* http://www.bostonglobe.com/lifestyle/health-wellness/2013/02/26/test-results-expected-soon-recalled-fertility-drugs-from-waltham-pharmacy/6atDVwnAbNrLSr1E0dHSFJ/story.html (accessed May 16, 2013).
[89] Id.
[90] FDA Recall – Firm Press Release, *Medprep Consulting Inc. Announces Voluntary Nationwide Recall Of All Lots Of All Compounded Products Due To Potential Mold Contamination*, March 17, 2013, http://www.fda.gov/Safety/Recalls/ucm344229.htm (accessed May 17, 2013); JoNel Aleccia, *Nurse Spotted Mold-Tainted Drugs Right Away, Hospital Says*, NBC NEWS, March 19, 2013, *available at* http://vitals.nbcnews.com/_news/2013/03/19/17373700-nurse-spotted-mold-tainted-drugs-right-away-hospital-says?lite (accessed May 20, 2013).
[91] Id.
[92] Id.
[93] FDA *Inspectional Observations*, Form FDA483, issued to Axium Healthcare Pharmacy d/b/a Balanced Solutions Compounding, March 15, 2013, *available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM345694.pdf (accessed May 17, 2013).
[94] Id.
[95] Lena Sun, *Balanced Solutions Compounding Pharmacy Recalls Sterile Drug Products*, THE WASHINGTON POST, April 21, 2013, *available at* http://articles.washingtonpost.com/2013-04-21/national/38717632_1_fda-new-england-compounding-center-products (accessed May 20, 2013).
[96] Recent Regulatory Actions, *supra* 10.
[97] Id.
[98] Id.
[99] *See generally* Bruce and Joan Buckley, *Is Compounding Denial Coma Over*, PHARMACY PRACTICE NEWS, February 2013, *available at*

http://www.pharmacypracticenews.com/ViewArticle.aspx?d=Clinical&d_id=50&i=February+2013&i_id=927&a_id=22501 (accessed May 16, 2013).

[100] Florida Department of Health Report, *Florida Board of Pharmacy Compounding Survey Report*, January 23, 2013, *available at* http://www.doh.state.fl.us/mqa/pharmacy/info_MPCSR.pdf (accessed May 16, 2013); Nate Rau, TN PHARMACY BOARD LEARNING WIDE SCOPE OF LICENSED COMPOUNDING IN STATE, THE TENNESSEAN, January 17, 2013, *available at* http://www.tennessean.com/article/20130117/NEWS07/301170046/TN-pharmacy-board-learning-wide-scope-licensed-compounding-state (accessed May 16, 2013).