

REGULATION OF COMPOUNDING PHARMACIES: A State or Federal Matter?

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When is a pharmacy a pharmacy, and when is it a drug manufacturer? That is the core issue facing regulators in this post-NECC world of drug regulation. This paper will explore the issues of regulation of compounding pharmacies and will focus on the incredible lack of attention paid by the Massachusetts Board of Pharmacies and the repeated dereliction of that Board's duties in the regulation of NECC. These lapses have led to termination of employment of several high officials at the Mass Department of Public Health.

In anticipation of this becoming a wider spread issue, we will explore the actions of other states in conjunction with compounding regulations.

The recent outbreak of viral meningitis which was attributed to three lots of methylprednisolone acetate (MPA) manufactured by New England Compounding Center has catapulted the compounding pharmacy industry into the public eye. While as of this time the death toll is over 30 and the infection rate is over 425, by the time of the webinar, it is likely that these numbers will increase.

Let us begin by examining what a compounding center *is*, what it *is not*, and what it sometimes *is but shouldn't be*. A compounding pharmacy is a business where a pharmacist "combines, mixes, or alters various drug ingredients to create a medication for an individual patient in response to a practitioner's prescription."¹ Thus, the compounding pharmacy does not manufacture one-size-fits-all drug preparations, which is the province of the drug manufacturer, but rather it prepares a custom dose of a given medication, for unique administration.

One factor unique to the pharmacy profession is that of drug counseling. When you go to your local CVS or Walgreen's, you are offered the opportunity to discuss your medicine with the pharmacist. In the compounding pharmacy setting, the patient has no contact whatsoever with the pharmacist. The compounder is, in theory, making a drug that is similar to other commercially prepared drugs, but with a unique aspect. Perhaps a particular patient is allergic to a dye that is found in a yellow pill, or a particular patient needs less of an inert ingredient, or a stronger dose of a drug than what is commercially available. That is where the compounding pharmacy does its magic.

¹ <http://www.crs.gov/Products/R/PDF/R40503.pdf>

The problem is that as we get into a drug that is made available by a compounding pharmacy, and that drug is safer, more effective, or otherwise more desirable than Pfizer's commercially available drug, then demand for the compounder's product increases, and the compounding pharmacy begins mass production of a "custom compound" drug. At what point does the compounding pharmacy become a competitor for Pfizer, Bayer or Merck? The compounding pharmacy preparation may not materially differ at all from the commercial drug. But, at some point, the commercial manufacturer is put at a disadvantage, as it must clear larger regulatory hurdles than the compounding pharmacy.

The heart of all drug regulation is the FDA. All new drugs must endure the NDA process and all the phase 1, 2, 3, etc. trial protocols, all at great expense in terms of time as well as money. Because the FDA has left pharmacy regulation to the states we see great disparities in quality control, manufacturing process, and sales and marketing of the compounding pharmacy products.

Compounding the compounding problem is the fact that the compounding pharmacy industry has tied itself to a strong lobby and has thwarted all regulatory schemes and attempts throughout time. There have been noble attempts by congress to tie down the compounding pharmacy operators – all to no avail. The FDA's first foray into regulating this industry was in 1992, when it issued a Compliance Policy Guide declaring that it would treat compounders like drug manufacturers if they were acting like them. Industry ignored this as a minor irrelevance. The FDA Modernization Act of 1997 was the centerpiece of this attempt at regulating the wild industry. This Act would have exempted compounders if they were really compounding and not manufacturing on a grand scale, or making already available products to compete with the FDA regulated manufacturers. The only way around this would be for the state to enter an agreement with the FDA that it would regulate with the same fervor, or if the compounders distributed less than 5% on an interstate basis. There were advertising provisions that were struck down by the 9th Circuit in 2002. The Supreme Court upheld the 9th Circuit.² According to an FDA Guidance,

The Supreme Court affirmed the 9th Circuit Court of Appeals decision that found section 503A of the Act invalid in its entirety because it contained unconstitutional restrictions on commercial speech (i.e., prohibitions on soliciting prescriptions for and advertising specific compounded drugs). The Court did not rule on, and therefore left in place, the 9th Circuit's holding that the unconstitutional restrictions on commercial speech could not be severed from the rest of section 503A. Accordingly, all of section 503A is now invalid.³

The Supreme Court did not totally gut the FDA regulations, however. Only the advertising portion of the 9th Circuit decision was upheld. Thus the FDA continued to regulate in 9 areas:

² *Thompson v. Western States Medical Ctr.*, 535 US 357 (2002)

³ <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM118050.pdf>

1. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions.
2. Compounding drugs that were withdrawn or removed from the market for safety reasons.
3. Compounding finished drugs from bulk active ingredients that are not components of FDA approved drugs without an FDA sanctioned investigational new drug application (IND) in accordance with 21 U.S.C. § 355(i) and 21 CFR 312.
4. Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA registered facility.
5. Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.
6. Using commercial scale manufacturing or testing equipment for compounding drug products.
7. Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.
8. Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products. In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA-approved drug that is commercially available. In these circumstances, FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient.
9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.⁴

The compounders have spared no expense when it comes to flooding the courts with attempts to block any and all federal regulation. Through their trade organization, the International Academy of Compounding Pharmacists (IACP), they were able to thwart the new regulations by continually resorting to the courts.

In September of 2011, the MD FL held⁵ that in the veterinary application of compounding, the FDA does not have jurisdictional authority over the compounding of medications by a licensed pharmacy so long as the pharmacy's activities are not manufacturing. That rests with individual state Boards of Pharmacy. Judge Corrigan also ruled that Congress did not give FDA jurisdictional authority when it enacted the FDCA in 1938 to take enforcement action against a pharmacy that is engaged in the traditional practice of compounding. He also ruled that size and scope of compounding does not mean a pharmacy is a manufacturer. He also said that the bulk use of active pharmaceutical ingredients (APIs) in compounding for humans and the

⁴ Report of Rep. Ed Markey, *Compounding Pharmacies, Compounding Risk*, 10/29/12

⁵ *US v. Franck's Lab, Inc.*, 816 F.Supp. 2d 1209 (Appeal Pending)

prohibition of bulk APIs for compounding for non-food producing animals is an illogical position for the FDA to take and contraindicated by its own actions over the past 50+ years.⁶

Most crucial of all, however was Corrigan's pronouncement that the FDA does not have jurisdiction over the traditional practice of pharmacy compounding. "That is the sole authority of the state Boards of Pharmacy."

The problem of compounding pharmacies is by no means limited to the New England Compounding Center. There are countless incidents arising from pharmacies in about 35 states. The FDA has been challenged repeatedly by the industry. Prior to the most recent NECC debacle, there had been at least 23 reported deaths and over 86 serious illnesses associated with compounding practices from compounding centers across the nation.

The common theme for FDA violations is that the compounders act like drug manufacturers. They sell copies of drugs available through the FDA regulated manufacturers, use non FDA-approved components, lack sterility in the manufacture, and dispense without prescription.

On top of this, there is wide variation amongst the state pharmacy boards in their regulation of their compounders. These issues give rise to instances of falsification of records, lack of oversight of manufacturing by a licensed pharmacist, and when Rep. Markey's staff went looking for answers, they were thwarted by poorly designed web pages that made it nearly impossible to find quick facts. Some boards, including Massachusetts, do not list voluntarily resolved or dismissed complaints, making them "go away" for all practical purposes. So it is clear that the FDA will meet with tremendous resistance, even if its oversight is legislated as a result of this series of incidents involving NECC.

Staff for Rep. Markey has done an initial survey of media and FDA reports involving compounders and his staff has found that there are problems found in the following states: AL, AR, AZ, CA, CT, DC, DE, FL, ID, IL, IN, KY, LA, MA, MD, MI, MN, MO, MS, NC, ND, NE, NH, NJ, NY, OH, OK, PA, PR, SC, TX, UT, VA, and WY.⁷

The FDA has, itself, noted that the compounders have violated several of *its* regulations also. These violations include failure to customize various doses and drugs, the use of unapproved and/or recalled unsafe or ineffective components, failure to follow Good Manufacturing Practices, such as manufacturing in unclean environments and acting more like drug manufacturers than pharmacies.

⁶ See Press release, http://iacompoundingpharmacyrx.affiniscape.com/associations/13421/files/U.S._District_Court_Rules_Favorably_for_Pharmacy_Compoun.pdf

⁷ Markey report at 10

Of course, as noted above, much of the FDA concern is irrelevant and without effect, as the true regulators of compounding pharmacies are the states. Let us now turn our attention to the state regulators.

The first premise in our failure analysis is that the State Pharmacy Board in any state is not the FDA. No state pharmacy board has the same laboratory or scientific sophistication as the FDA. Many such boards are passive, awaiting and acting only upon complaints brought to their attention. The next premise is that compounders are local businessmen and women, and as such there is often a certain air of familiarity between the boards and the pharmacists. For this reason as well as several others, it is often hard to trace complaints and enforcement actions on line or in any easy public manner. The NECC issue is full of instances of conflict and nepotism. In fact, simultaneously with this teleseminar, the Massachusetts House of Representatives, as well as the US House of Representatives are both holding hearings, probing this issue. The first had to do with the typical purview of Pharmacy Boards activities, none of which approach the magnitude of the issue giving rise to this paper. Only six states, Arizona, California, Missouri, New York, North Carolina and Rhode Island include enforcement records on their public website. In most states, the websites do not include amenities that make it easy to locate information on specific pharmacies or compounds. The four states allowing keyword searches are Arizona, California, New Jersey and North Carolina. If one is successful in attaining online information on licensee specific information, there is no access to the documents that detail the substance of a particular complaint.

Most relevant to this case, is the fact that in Massachusetts, if a pharmacy or pharmacist enters into a voluntary resolution of the issue, that issue is never posted on the website, keeping the prior issue totally secret from the public, unless someone actually physically goes to the Board for that information. That is how prior issues with NECC have evaded public knowledge up to now.

If one were to go to the web pages of all Pharmacy Boards looking for cases involving errant compounders, they would only find information on line for the following states: Arizona⁸, California⁹, New York¹⁰, North Carolina¹¹, and Rhode Island¹².

Rep. Markey's staff was able to locate 60 instances of media reports and FDA enforcement actions on compounding pharmacies. The footnote below, details all of those actions. This is great historical information, so inasmuch as it is very long, I felt it was worth including in its

⁸ <http://www.azpharmacy.gov/default.asp>

⁹ <http://www.pharmacy.ca.gov/> Searchable footnotes back to 2005

¹⁰ <http://www.op.nysed.gov/prof/pharm/> Still need a written request for full documentation

¹¹ <http://www.ncbop.org/> All records and backup are available online

¹² <http://www.health.ri.gov/licenses/healthcare/index.php#pharmacy> Only searchable through the name of the pharmacist, but complete records are available.

entirety. I have left out footnotes in this footnote, but the letters are all able to be found in the footnotes in Rep. Markey's text.¹³

¹³ A timeline of media reports and FDA enforcement actions on compounding pharmacies. Appendix A of Markey6 Report, *supra*

1. **June 2001** – An outbreak of an hospital-acquired bacterial infection occurred at an ambulatory surgery center in California. The outbreak was determined to be caused by a contaminated batch of betamethasone, a steroid solution that was compounded at a community pharmacy and delivered as an injection into the spine of patients. There were a total of 11 cases of infection, five cases of meningitis (of which three died), five cases of epidural abscesses, and one hip infection.
2. **July 2001** – The FDA sent a warning letter to Professional Compounding Centers of America, Inc. in Texas because of violations of good manufacturing practices associated with the repackaging of bulk ingredients for use by compounding pharmacies. These violations included a failure to ensure that penicillin-free antibiotics were kept free of contamination with penicillin (and vice-versa), and selling ingredients that had been withdrawn from the market due to safety or efficacy reasons to pharmacies.
3. **September 2001** – The FDA sent a warning letter to IV Systems in Illinois because a 2000 inspection of its Texas facility revealed that the facility was repackaging and reselling drugs without the proper labels, its activities revealed deviations from good manufacturing practices, and it was not registered as a pharmacy in Texas.
4. **October 2001** – The FDA sent a warning letter²¹ to Unique Pharmaceuticals, Ltd. In Texas because the company was operating more like a manufacturer than as a pharmacy, was making copies of commercially available drugs, and its activities had numerous violations of good manufacturing practices.
5. **January 2002** – A link was discovered between two deaths of women using prescription strength numbing cream before laser hair removal. Blanca Bolanos (age 25) died November 1, 2004 after being hooked up to respirator for two years after using the cream, having a seizure, and falling into a coma. Shiri Berg (age 22) died January 25, 2002 under almost identical circumstances – she was headed to Premier Body, a laser hair-removal clinic in North Raleigh. Premier Body closed in February 2005 with plans to liquidate. The women were given the prescription-strength cream to use outside the clinic. Neither woman had prescriptions for the cream, which was given to them by nonmedical employees at the hair-removal clinics. North Carolina medical and pharmacy boards were investigating Berg's death, as was the the FDA. The creams were both found to have been compounded at a much greater potency than recommended, causing an overdose of the medication.
6. **April 2002** – The FDA sent a warning letter to the Compounding Pharmacy in Illinois because it was manufacturing nicotine lollipops and other products that had ingredients that were not FDA-approved, without patient prescriptions, without registering as a manufacturer and without adequate labeling.
7. **September 2002** – The FDA sent a warning letter to Med-Mart Pulmonary Services in California because its investigation determined that the company's activities exceeded the scope of the regular course of the practice of pharmacy, and that the company's processes did not conform to good manufacturing processes, including evidence of microbial contamination of its products.
8. **October 2002** – An investigation into the meningitis death of a 77-year-old woman who died ten weeks after getting spinal injection at hospital pain clinic implicated Urgent Care Pharmacy, a compounding pharmacy in South Carolina. The pharmacy produced an injectable steroid pain reliever known as methylprednisolone that was contaminated with fungus. Shipments of the infected medicine were traced

to North Carolina, South Carolina, Illinois, Indiana, Kentucky, Louisiana, Mississippi, New Hampshire, *Massachusetts*, Virginia, and Connecticut. North Carolina officials later confirmed three other cases.

9. **April 2003** – After receiving several complaints, the FDA investigated and inspected Lee Pharmacy, Inc. of Fort Smith, Arkansas. This pharmacy was responsible for compounding undisclosed amounts of contaminated injectable methylprednisolone acetate. The medication is used to treat joint pain. The pharmacy issued a voluntary recall of the drug in question as well as other medications from the pharmacy amid questions from the FDA regarding the products sterility and potency. Neither federal nor state officials had reported illnesses from the recalled drugs.
10. **April 2003** – Kansas City pharmacy (Med 4 Home), owned by Lincare Holdings, Inc. of Clearwater, mishandled the recall of contaminated drugs, blocked a state inspector from entering its facility, and destroyed records. On March 10, 2003, the Missouri board of health received a temporary restraining order against Med 4 Home, its chief pharmacist, and Lincare’s president John P. Byrnes. The injunction barred the pharmacy from compounding and dispensing drugs. Trouble began when a quality assurance test in January 2003 showed bacterial contamination in at least two batches of Albuterol/Ipratropium (compounded inhalant solution for chronic lung diseases). More than 19,000 patients nationwide were estimated to have received the contaminated drug before contamination was discovered.
11. **May 2003** – The FDA sent a warning letter to Carneys Drugs in New Hampshire because the company compounded Fentanyl oral lozenges, which the FDA considered to be copies of commercially available drugs.
12. **October 2003** – The FDA sent a warning letter to Plum Creek Pharmaceuticals, Inc. in Texas because of the public health risks associated with the compounding of lollipops that contain Fentanyl, Naloxone and Midazolam for use as pain medication to cancer patients. According to the letter, “there have been reports of serious adverse effects, including death, due to accidental pediatric exposure to the commercially available Fentanyl lollipop product in doses comparable to the doses being made available” by the company, but the company did not provide for proper directions of use and childproofing.
13. **December 2003** – The FDA sent a warning letter to Custom Compounding Centers in Arkansas because its activities were found to exceed the scope of typical pharmacy activities.
14. **January 2004** – The FDA sent a warning letter to Monserrat Pharmaceuticals, Inc. in Puerto Rico because its investigation has determined that its activities exceeded the scope of the regular course of the practice of pharmacy, that it was making copies of commercially available drugs, and because the FDA found numerous violations of good manufacturing practices
15. **January 2004** – The FDA sent a warning letter to White Lake Pharmacy in Michigan because it was selling nicotine lollipops without prescriptions in a facility not licensed as a manufacturing facility, and was using advertising that made medical claims about the products’ use.
16. **June 2004** – The FDA issued a warning letter related to California’s Spectrum Chemicals and Laboratory Products’ New Jersey manufacturing facility because inspections revealed that the facility was providing to compounding pharmacies the drug domperidone, about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries. The FDA also sent warning letters to several compounding pharmacies known to have been compounding the substance as well as other substances that FDA warned them to cease compounding (Peoples Pharmacy, Inc. in Texas Drugs Are Us in New Jersey, Axiom Healthcare Pharmacy in Florida). At the same time, the FDA warned breastfeeding women not to use domperidone to increase their milk supply.

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17. **July 2004** – The FDA sent a warning letter to Gentere, Inc. in Ohio because the company, which was not registered with the FDA, manufactured large quantities of injectable drugs without valid prescriptions, and inspections additionally found significant deviations from good manufacturing practices related to its sterile compounding activities.
 18. **September 2004** – The FDA sent a warning letter to Delta Pharma Inc. in Mississippi because it was found to be more consistent in size and production volume with a drug manufacturer.
 19. **October 2004**– An outbreak of hepatitis C in Maryland was linked to blood contamination of radiopharmaceutical agent used for myocardial perfusion studies. The original contamination was traced to breaches in aseptic technique at a nuclear pharmacy. In total, 16 patients developed acute hepatitis C infection after undergoing myocardial perfusion studies on the same day at three unaffiliated outpatient clinics. The 16 patients were the only ones injected with the compounded tracer drawn from a single vial prepared at one pharmacy and delivered to the three clinics.
 20. **December 2004** – The FDA sent a warning letter to Lincare, Inc., and Reliant Pharmacy Services, Inc. in Florida because it determined that its activities were akin to that of a drug manufacturer and not a pharmacy.
 21. **December 2004** – The FDA sent a warning letter to Respi Care Group of Puerto Rico because the FDA’s investigation found the company’s activities were more akin to that of a drug manufacturer, it produced copies of commercially-available drugs, and it was manufacturing with “virtually no regard to the current good manufacturing practice,” including the identification of major problems related to sterile compounding such as operating in a visibly dirty facility.
 22. **March 2005** – The FDA issued a nationwide alert concerning contaminated, compounded magnesium sulfate solution used in an IV bag that caused five cases of sepsis in a New Jersey hospital. The medicine was manufactured by PharMEDium Services of Houston, Texas. A South Dakota patient treated with the drug died of sepsis. The product is frequently administered intravenously to patients undergoing cardiac surgery. On April 8, 2005, PharMEDium Services recalled all strengths of its 50 ml admixtures of Magnesium Sulfate solution. The company also voluntarily ceased production and distribution of the product until it could determine and correct the source of the problem. In April 2007, the FDA sent a warning letter⁴⁶ to PharMEDium regarding activities at its TX and MS facilities that was in part related to this alert.
 23. **March 2005** – The FDA sent a warning letter to Palace Pharmacy in Wyoming because of the company’s compounding of drugs containing domperidone (about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries).
 24. **June 2005** – The FDA sent a warning letter to Pragmatic Materials, Inc. in Ohio because of violations in good manufacturing practices when it repackaged bulk ingredients for use by compounding pharmacies, including providing non-prescription grade ingredients that the company labeled as prescription grade.
 25. **July 2005** – The FDA sent a letter to Cape Drugs in Maryland because of the company’s compounding of drugs containing domperidone (about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries).
 26. **August 2005** – Custom Rx Compounding Pharmacy in Richfield, Minnesota initiated a nationwide recall of Trypan Blue Ophthalmic Solution because it was contaminated with bacteria that could lead to serious

injury – potentially blindness – if applied to the eyes. The drug was distributed to hospitals and clinics in MD, MN, IL, NE, ND, MI, DC, and PA and was intended for use during cataract surgery. The pharmacy voluntarily recalled the product based on two reports of lost vision associated with use of the product as reported by Centers for Disease Control.

27. **September 2005** – The FDA notified healthcare professionals and hospitals of a product recall involving all injectable compounded products made by Central Admixture Pharmacy Service (CAPS) of Lanham, Maryland. The products were recalled because of sterility concerns that were discovered after several patients that received the CAPS medication developed a severe systemic inflammatory response. Four deaths and eleven other severe reactions were suspected to have resulted from these problems. CAPS distributed the affected injectable products to hospitals in MD, DE, DC, and VA. The FDA sent a warning letter to the company in February 2006 telling it to remedy deficiencies related to its sterile compounding activities in its facilities in AL, MD, PA, and MO as well as other deficiencies in its CA facility.
28. **November 2005** – The FDA sent a warning letter⁵⁴ to Spectrum Chemicals and Laboratory Products, Inc in Arizona because its New Jersey facility was repackaging bulk domperidone (about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries) and polidocanol (with reported adverse events including infections at the treated site and reversible cardiac arrest after polidocanol sclerotherapy) and reselling it to pharmacies for compounding. This was the second such letter to this company (see June 2004).
29. **December 2005** – The FDA sent a warning letter to Samson Medical Technologies, Inc. in New Jersey because its inspection found that the company was marketing antibiotics labeled as being usable in compounding by pharmacies even though that was not their intended use. The products were supposed to be reconstituted and then dispensed to patients in a hospital setting.
30. **February 2006** – Following a 2005 inspection, the FDA sent a warning letter to Southern Meds Joint Venture, LLC in Mississippi, telling it to cease its actions which included compounding of drugs in volumes that was not “consistent with traditional pharmacy compounding operation” and actions which included significant violations of good manufacturing practices related to the prevention of contamination of sterile products.
31. **August 2006** – The FDA notified consumers and healthcare professionals that RoTech Healthcare, Inc. in Florida, CCS Medical in Florida, and Reliant Pharmacy Services in Florida were manufacturing and distributing unapproved compounded inhalation drugs nationwide for use in patients with asthma, emphysema, bronchitis, and cystic fibrosis. The FDA warned the company that they were mass-producing unapproved drugs and were operating outside of the scope of a typical pharmacy.
32. **September 2006** – The FDA sent a warning letter to Hawkins, Inc. in Minnesota because it was found to be repackaging bulk ingredients and re-selling them to compounding pharmacies, and the FDA found significant deviations from good manufacturing practices.
33. **October 2006** – The FDA sent a warning letter to Wedgwood Village Pharmacy in New Jersey because the pharmacy was found to have been compounding copies of commercially-available drugs and compounding drugs in volumes that were in excess of traditional compounding pharmacy practices.
34. **October 2006** – The FDA sent a warning letter to Pharmacy Creations in New Jersey because it was compounding domperidone (about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries) and polidocanol, neither of which were FDA-approved active ingredients, as well as adenosine-5-

monophosphate, which had been withdrawn from the market because it was neither safe nor effective, and was also compounding copies of commercially available products.

35. **November 2006** – The FDA sent a warning letter to Health Dimensions Inc. in Michigan because it was compounding domperidone, (which was not FDA-approved and about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries). A second (name redacted but possibly polidocanol) drug, also not FDA-approved and known to have adverse events including deep venous thromboses, necrosis, and ulceration at the treated site and reversible cardiac arrest, was found to be compounded by the pharmacy.
36. **December 2006** – The FDA sent a warning letter to Spoonamore Drug Co in Kentucky because it was producing domperidone capsules (which was not FDA-approved, and about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries), progesterone capsules (which FDA believed was a copy of a commercially available product), testosterone five percent gel which FDA believed was a copy of a commercially-available product), and nicotine lollipops (which the FDA said lacked the required warning labels and may have been compounded using ingredients that were not FDA-approved).
37. **December 2006** – The FDA sent warnings to five pharmacies that were compounding topical anesthetic creams that were marketed to the general public rather than in response to specific patient prescriptions. The FDA noted that these creams “can cause grave reactions including seizures and irregular heartbeats. Two deaths have been connected to compounded topical anesthetic creams made by Triangle Compounding Pharmacy (North Carolina) and University Pharmacy (Utah), two of the five pharmacies receiving warning letters.” ***Other non-fatal reactions to the creams had also been documented. The three other pharmacies included New England Compounding Center (Massachusetts), Custom Scripts Pharmacy (Florida), and Hal’s Compounding Pharmacy (California).*** The FDA found additional problems with other drugs that were being compounded by these pharmacies.
38. **January 2007** – The FDA sent a warning letter to Kalchem, International, an Oklahoma company that was found to be distributing domperidone (which was not FDA approved, and about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries) to pharmacies for compounding.
39. **March 2007** – The FDA sent a warning letter to ComputeRx/Broncho-Dose, Ltd in Connecticut because it was found to have been compounding inhalation drugs in quantities that exceed traditional pharmacy practices and across 12 states. Additionally, the pharmacy ended up recalling one of its formulations because it was found to be less potent than the label advertised.
40. **April 2007** – The FDA sent a warning letter to PharMEDium Services regarding its facilities in Texas and Mississippi. The letter related to 2005 problems with the sterility of its compounded magnesium sulfate solution, some of which caused five cases of sepsis in a New Jersey hospital and a death of a patient in South Dakota. On April 8, 2005, PharMEDium Services recalled all strengths of its 50 ml admixtures of Magnesium Sulfate solution. The letter also related to an adverse event reportedly associated with an epidural injection made in the company’s Mississippi facility that was supposed to contain Fentanyl/Bupivacaine but actually contained Morphine Sulfate. The patient in question showed signs and symptoms of decreased consciousness, hypoxia, and hypotension. The FDA found additional labeling and manufacturing problems associated with the facilities.
41. **April 2007** – A measuring error at ApotheCure, a Texas compounding pharmacy, shipped 31 vials of mislabeled Colchicine into Oregon that was eight times more concentrated than the recognized standard level. Colchicine, which has not been approved by the FDA, has been used since the 1950s to treat gout.

More recently, it has been used by alternative medicine clinics to treat chronic back pain. In April 2007, at the request of the Texas State Board of Pharmacy, the company issued an immediate recall for all strengths, sizes and lots of this compounded drug that had been sold within the previous year.

42. **September 2007** – The FDA sent a warning letter to Med-South Pharmacy Inc. in Alabama following reports of injuries relating to betamethasone acetate/betamethasone sodium phosphate multi-dose injectable drug product. “The complaints included redness, large swollen areas, bruising at the injection site, rash, fever, and cellulitis, with some patients requiring intravenous antibiotics.” The FDA also noted that the company’s activities exceeded the scope of activities typically conducted by a pharmacy, identified problems with the company’s sterile compounding practices, and found the company was making copies of commercially available drugs.
43. **January 2008** – The FDA warned that pharmacies that were making claims about the safety and effectiveness of their bio-identical hormone replacement therapy, or BHRT products were unsupported by medical evidence and were considered false and misleading by the agency. The drugs contain hormones such as estrogen, progesterone and estriol, which is an FDA unapproved drug. The pharmacies that received the letters included Panorama Compounding Company in California, Saint John’s Medical Plaza Pharmacy in California, Murray Avenue Apothecary in Pennsylvania, Village Compounding Pharmacy⁸⁰ in Texas, Pharmacy Compounding Specialties in Texas, Reed’s Compounding Pharmacy in Arizona, and Pacifica Pharmacy in California. The FDA also sent warning letters to American Hormones Inc. in New York and Bellevue Pharmacy Solutions in Missouri that included some of the same concerns, and the FDA also noted that these companies were engaging in activities that exceeded the scope of typical pharmacies’ manufacturing practices, and were making copies of commercially-available drugs, and found that other drugs being compounded by the pharmacies were not FDA approved or were known to be associated with adverse reactions.
44. **March 2008** – The FDA sent a warning letter to Farmacia La Salud in Puerto Rico, because it was manufacturing, in scales inconsistent with traditional pharmacies, copies of commercially-available inhalation drugs, and that the company’s sterility practices were problematic.
45. **June 2008** – The FDA sent a warning letter to Newman Inc. in Alabama because the firm was found to have been compounding drugs in quantities that exceed traditional pharmacy practice, and that the health claims the company made about the drugs were false and misleading.
46. **October 2008** – The FDA sent a warning letter to Aerosol Science Laboratories Inc. in California because of false and misleading claims made about the company’s nasal aerosol drugs.
47. **November 2008** – The FDA sent a warning letter to Steven’s Pharmacy in California because the firm was found to have been compounding drugs in quantities that exceeded traditional pharmacy practice, as well as drugs that were copies of commercially available products. The FDA additionally noted that the topical anesthetics that the company was compounding contained high doses of drugs that were not approved for topical use and which had been associated with serious cases of systemic toxicity, and that the labels associated with the products did not contain necessary warnings. The company was also found to be compounding drugs that were not FDA-approved.
48. **December 2008** – The FDA sent a warning letter to Civic Center Pharmacy in Arizona because the company was found to compound a hormone therapy drug containing estriol, which was not FDA-approved, and that it also compounded copies of commercially available drugs.
49. **December 2008** – FDA sent a warning letter to Kreitchman PET Center in New York because of deviations from good manufacturing practices associated with the compounding of PET drugs.

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50. **January 2009** – The FDA sent a warning letter to Cyclotron Center of NE Florida because its activities were found to deviate from good manufacturing practices for PET drugs, including repeat violations related to the sterility of their processes that were also found in 2005.
 51. **September 2009** – The FDA sent a warning letter to Hopewell Pharmacy and Compounding Center in New Jersey because it was found to be compounding Sodium Tetradecyl Sulfate (STS) Injection, which was found to have been contaminated.
 52. **April 2010** – The FDA sent a warning letter to J & F International Inc., dba Alexandria Medical Arts Pharmacy & Compounding Laboratory in Virginia because it was found to be making domperidone (which was not FDA-approved, and about which there had been reports of cardiac problems and sudden deaths in patients receiving some intravenous forms that had been withdrawn in several countries).
 53. **April 2010** – The FDA issued a warning to six U.S. based medical spas and a company in Brazil for making false or misleading statements about drugs they claimed would eliminate fat in a procedure called “lipodissolve,” or for otherwise misbranding lipodissolve products. The letters were sent to Pure Med Spa in Florida, All About You Medspa in Indiana, Ininhealth in Minnesota, Spa 35 in Idaho, Monarch Med Spa in Pennsylvania, Medical Cosmetic in Maryland, and Ziomed and Mesoone in Brazil.
 54. **July 2010** – The FDA sent a warning letter to Med Prep Consulting, Inc. in New Jersey, a company that repackaged sterile drug products for other entities without a patient prescription and in a manner that was more consistent with a manufacturer than a pharmacist.
 55. **November 2010** – The FDA sent a warning letter to VanderVeer Center in Oregon because it was making false or misleading claims about the safety and effectiveness of its Lipodissolve products, which were claimed to eliminate fat.
 56. **March 2011** – The FDA sent a warning letter to Proportional Technologies, Inc. in Texas because of significant violations related to the manufacturing of PET drugs, including practices related to assuring the sterility of the drugs.
 57. **April 2011** – The Alabama Department of Public Health confirmed that bacteria from a Birmingham, Alabama pharmacy sickened 19 people and killed nine others, when patients in a hospital were given an intravenous nutritional supplement. Samples gathered from the Meds IV's Oxmoor Road compounding facility tested positive for lethal bacteria introduced to the pharmacy's nutritional supplement when tap water used to clean a container was used for mixing the drug. A number of other cases of illness in the preceding months were believed to have been linked to the compounding facility.
 58. **August 2011** – *The New York Times* reported that four patients in a Tennessee Veterans hospital suffered complications, including brain damage, and blindness from eye injections of Avastin, which had been contaminated by bacteria when the drug was compounded by the pharmacy in the VA hospital in Nashville. Avastin was used to treat macular degeneration, the most common cause of blindness in older Americans. The FDA has not approved Avastin for eye injections. Lucentis, the drug approved by the FDA for macular degeneration, costs about \$2,000 for a single-dose vial. Avastin only costs around \$50 a dose, and according to a study published by the New England Journal of Medicine, it is equally effective in fighting the disease. Hospitals turn to Avastin as a cheaper alternative to Lucentis. However, Avastin does not come in single-dose vials for eye injections, so hospital pharmacies have to compound Avastin for eye injections from packaging intended for intravenous use. A similar situation in the Miami, Florida area where a compounding pharmacy repacked Avastin and shipped to eye clinics in the area left 12 people

Finally, there are a few postscripts that need to be mentioned in this paper. These include the doubtful viability of the insurance pool, combined with other assets of the Conigliaro and Cadden families, the owners of NECC, for fulfillment of the financial obligations to the many victim of this tragedy; the possibility of piercing the corporate veil in this case; and the inclusion of other entities as defendants.

The law in Massachusetts on piercing the corporate veil is very similar to that of other jurisdictions. Our seminal case is, *My Bread Baking Co. v. Cumberland Farms, Inc.*, 353 Mass. 614 (1968), which looked at the conduct of George Haseotes, the owner of Cumberland Farms, Inc., in his dealings with a bread distributor. In that case, the Supreme Judicial Court of Massachusetts held,

“1. ...Where there is common control of a group of separate corporations engaged in a single enterprise, failure (a) to make clear which corporation is taking action in a particular situation and the nature and extent of that action, or (b) to observe with care the formal barriers between the corporations with a proper segregation of their separate businesses (see *Acton Plumbing & Heating Co. v. Jared Builders, Inc.* 368 Mich. 626, 628-630), records, and finances, may warrant some disregard of the separate entities in rare particular situations in order to prevent gross inequity.

2. On the evidence the jury could reasonably have reached the following conclusions. ... (b) Although no one of the codefendant operating store corporations was a subsidiary of C.F. Inc. (in the sense that C.F. Inc. owned the whole or a part of its stock), all the defendant corporations (including C.F. Inc.) were under the full stock control of the Haseotes family and were operated as a closely coordinated single enterprise. Haseotes himself could be found to have been a dominant figure in the whole "Cumberland Farms" enterprise. ... (d) Because all the corporations were operated ambiguously from the same headquarters as part of a single enterprise, the jury could reasonably infer that Haseotes, in furtherance of the interests of C.F. Inc. in the distribution of its

with loss of severely impaired vision. The FDA issued a warning to health care professionals warning of the problem.

59. **July 2012** – The FDA sent a warning letter to Franck's Lab, Inc. dba Franck's Compounding Lab in Florida because some of its injectable products were found to be contaminated, following reports of patients who developed eye infections. Inspections revealed unsanitary conditions and multiple bacterial and fungal species at various locations in the facility.

60. **July 2012** – The FDA sent a warning letter to Infupharma in Florida because it identified significant violations of Current Good Manufacturing Practice including those related to sterile compounding, its activities went beyond the scope of traditional pharmacy activities, and because inspections found bacterial contamination in samples of Avastin the company was repackaging.

products, 621*621 was intervening actively in the conduct of the satellite corporations. (e) Haseotes without (so far as this record shows) clear indication of the capacity in which (and the corporation for which) he was acting, dealt in 1960 with Duchaine of My Bread for "Cumberland Farms" in a very confused manner. ...

So it really comes down to 5 steps to pierce the veil. Owners of corporations must take steps to show that the business is a separate entity from the owners. An owner must

1. Respect the formalities of business ownership. Draft bylaws, and adjust them as situations arise. Issue stocks and enter them in a ledger, file all needed certifications and pay all fees in a timely manner. Discovery will show us if the Caddens and Conigliaros respected these steps.
2. Document all business activities and shareholder meetings, etc. Keep minutes of all such meetings.
3. Segregate all assets of the corporation from personal assets. Separate business accounts, credit cards, etc. Look for comingling of funds and assets such as business machinery. Did Ameridose do scanning at NECC? Did NECC sales force sell Ameridose product?
4. Was all the NECC capital designated as NECC's and was the company adequately capitalized, or did it need Ameridose to survive?
5. Were the NECC employees and officers also working for Ameridose or for Conigliaro Industries? Did one company buy equipment, cars, or insurance for the benefit of the other? Were there any contracts or leases or other agreements made by one company for all?

Of course, the real test is what the Judge thinks. If a judge cannot distinguish between what belongs to the business and what belongs to the owner—and the owners cannot provide proof that all formalities have been followed—it may be deemed that the owners are acting more like a sole proprietorship or general partnership than a corporation and the judge would then "pierce the corporate veil" and award the officers and directors' personal assets to the plaintiffs.

The final chapter in this litigation will likely be defined by the financial wherewithal of the defendants. To that end, we need to explore the potential liability of the Commonwealth of Massachusetts, which did a particularly unimpressive job of regulating, and which ignored many – too many – sure-fire warning shots, and which actually allowed this whole tragedy to occur; the doctors and hospitals that supplied the product to the plaintiff as the end user; and anyone else that participated in the sales, marketing or distribution of the defective product. There is liability for all distributors of all products if there is a product defect.

The regulation of the compounding industry is about to see all new participants. The congressional concern, together with the electoral results and the particularly heinous combination of events giving rise to these cases has created a perfect storm for the compounding pharmaceutical business. It is our duty to assure that justice be carried out, and

that any industry and any regulators that are dealing with such high potential for harm, not be allowed to repeat this tragic combination of circumstance and indifference.