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Joyce Ingrid Crawford

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Drug Manufacturer Masquerade: Compounding Manufacturers Use a Wide Gap of State and Federal Oversight Authority to Evade Mandatory Safety Controls

By Joyce Crawford

Abstract:

Compounding pharmacies mix, combine, or alter drugs that are not otherwise available in the commercial market. This paper discusses the development of the compounding industry, and the various state and federal oversight authorities surrounding it. These entities are a necessary part of the healthcare delivery system, especially in hospitals and clinics where compounded drugs are needed in greater volume and cannot be produced on-site. Recently, however, the compounding industry has grown rapidly, and the industry controls that preserve safety and quality controls are no longer sufficient.

In order for the industry to remain a viable option for safe medication to healthcare providers, changes need to be made to ensure the quality of the products. This objective could be made from within the industry through management or technology; however, this paper discusses how federal and state regulatory agencies can better ensure that no matter what the source, the public is supplied only with safe medication. As discussed later, it became clear that regulatory responsibility over this industry between state and federal agencies was not clear. A thorough investigation by Congress has determined that lack of definition and clarification of Federal oversight created confusion and agency liability exposure in the compounding manufacturer industry.

The most recent and extreme case occurred in late 2012, when an outbreak of fungal meningitis was caused by contaminated vials of methylprednisolone acetate, produced by the New England Compounding Center in Framingham, Massachusetts. The contaminated solution was injected into patient' joints and spine to treat pain, but instead caused 751 infections and 64 deaths. In light of this horrific tragedy, the state and federal agencies, along with Congress, have investigated and discussed how to prevent this from happening again.

The result of this investigation was the exposure of a gap in regulatory authority between the state boards of pharmacy that license pharmacies within their state, and the FDA which oversees the mass production and distribution of drugs nationally. This gap allowed facilities to operate under a state license, and hide behind state authority, even when there was evidence that they were operating more like a manufacturer.

To close this gap, ensure compliance with safety controls, and prevent another outbreak of adverse events, Congress has enacted legislation, the Drug Quality and Security Act, to clarify jurisdictional definition, and require specific registration and reporting from compounding manufacturers. This paper discusses the strengths and weaknesses of the Drug Quality and Security Act, and what issues remain.

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I. Introduction

Compounding manufacturing is the mixing or altering of medications to produce a drug not readily available in the commercial market.¹ It is distinguished from large-scale drug manufacturing because, under certain circumstances, compounded drugs are not required to comply with the New Drug application process, and other labeling and advertising requirements through the U.S. Food and Drug Administration (FDA).² Compound drug production is also separate from retail pharmacies because these drugs are generally produced before an individual prescription is given to a patient, and are produced in large quantities rather than one at a time.³

The FDA regulates large-scale drug manufactures.⁴ States regulate retail pharmacy production of drugs.⁵ Compounding facilities fall in the middle ground, and require oversight by both the FDA and the State regulatory authorities. The Drug Quality and Security Act was passed on November 27, 2013 and attempts to clarify regulatory authority over drug compounding facilities, by allowing those that meet specific criteria to register with the FDA and avoid being required to comply with the New Drug application process.⁶ Part II of this paper gives details on the horrific 2012 outbreak of fungal meningitis infections that spurred the enactment of new legislation relating to compounding manufacturers. Part III will discuss the

¹ *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360-361 (2002).

² Drug Quality and Security Act, Pub. L. No. 113-54, § 503B, available at <http://beta.congress.gov/113/bills/hr3204/BILLS-113hr3204enr.pdf>.

³ Ernest Anderson, et al., *Outsource Hosp. Sterile Compounding: A New and Safer Era To Come*, PHARMACY PRACTICE NEWS, Sept. 2013, at 1.

⁴ *The Fungal Meningitis Outbreak: Could it have been prevented?: Hearing Before the H. Subcomm. On Oversight and Investigations of the H. Comm. on Energy & Com.*, 112th Cong. (2012) [hereinafter *House Nov. 2012 Hearing*], available at <http://energycommerce.house.gov/hearing/fungal-meningitis-outbreak-could-it-have-been-prevented>, (last visited Dec. 5, 2013).

⁵ *Id.*

⁶ THE WHITE HOUSE, Statement by the Press Sec’y on H.R. 1848, H.R. 3204, S. 252 (Nov. 27, 2013) available at <http://www.whitehouse.gov/the-press-office/2013/11/27/statement-press-secretary-hr-1848-hr-3204-s-252> (last visited 12/5/2013), Drug Quality and Security Act, Pub. L. No. 113-54, § 503B, available at <http://beta.congress.gov/113/bills/hr3204/BILLS-113hr3204enr.pdf>.

compounding industry, its history as well as a brief comparison with large-scale pharmaceutical manufacturing. Part IV will explain the statutory and regulatory framework for this industry. Part IV will then discuss the judicial interpretations relevant to federal authority, and the state role in pharmacy licensing. Part V will present the position that expanded federal authority is needed to properly oversee this industry and prevent future public safety risks, and the current legislation, its strengths and weaknesses, and concerns that must be addressed to ensure it will have the desired effect.

II. Background on the 2012 NECC Outbreak

In late September 2012, reports spread across the United States about patients falling ill and dying from a terrible disease, which was later identified as fungal meningitis.⁷ This avoidable tragedy was one of the worst public health crises this nation has ever experienced.⁸ The disease was caused by microbial growth inside what was supposed to be a sterile syringe, the result of unsterile conditions at the production facility and contamination.⁹ This particular drug was a steroid injection, preservative-free methylprednisolone acetate (MPA), which was administered to approximately 14,000 patients in 20 states to treat pain.¹⁰ These shots were given to patients with joint and back pain, often associated with arthritis.¹¹ Some of these shots contained a common mold called *Exserohilum rostratum*, a human pathogen usually found in soil and on

⁷ CENTERS FOR DISEASE CONTROL & PREVENTION, MULTISTATE FUNGAL MENINGITIS OUTBREAK INVESTIGATION, <http://www.cdc.gov/hai/outbreaks/meningitis.html> (last updated Oct. 23, 2013) [hereinafter CDC INVESTIGATION].

⁸ Sabrina Tavernise & Andrew Pollack, *FDA Details Contamination at Pharmacy*, N.Y. TIMES (Oct. 16, 2012), available at http://www.nytimes.com/2012/10/27/health/fda-finds-unsanitary-conditions-at-new-england-compounding-center.html?_r=0 (last visited Dec. 6, 2013).

⁹ CDC INVESTIGATION, *supra* note 7.

¹⁰ *Id.*

¹¹ CENTERS FOR DISEASE CONTROL & PREVENTION, MORBIDITY AND MORTALITY WEEKLY REPORT: *Multistate Outbreak of Fungal Infection Associated with Injection of Methylprednisolone Acetate Solution from a Single Compounding Pharmacy*, (Oct. 19, 2012) http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6141a4.htm?s_cid=mm6141a4_w.

plants.¹² This fungus rarely causes disease in humans, but a combination of factors made it deadly, including the fact that it was a preservative free vial, and in many of these deadly cases was injected directly into the spine, which has limited protection from the body's immune system.¹³ After injection, the infection multiplied and spread through the epidural space, through the spinal fluid and eventually damage to the brain caused bleeding and stroke.¹⁴

This compounding pharmacy that produced the drugs, the New England Compounding Center (or NECC) located in Framingham, Massachusetts, made 17,000 potentially contaminated vials of the steroid injection. The 3,000 remaining unused lots were voluntarily recalled by NECC after the link was made to the outbreak.¹⁵ To date, there are 751 reported cases, and 64 Americans have died.¹⁶

This was not the first time unsafe drugs from compounding pharmacies have injured people, though it was by far the worst and most widespread harm.¹⁷ Even before the NECC outbreak, compounding pharmacies have been linked to at least 23 deaths,¹⁸ and nine major adverse events including infections, hospitalizations, loss of eyesight, and death.¹⁹ The increased use of

¹² CDC INVESTIGATION, *supra* note 7.

¹³ *House Nov. 2012 Hearing*, *supra* note 4, (exchange between Dr. Hamburg and Congressman Burgess occurring at 1:30 on the video).

¹⁴ Tom M. Chiller, et al., *Clinical Findings for Fungal Infections Caused by Methylprednisolone Injections*, NEW ENG. J. MED. (Oct. 24, 2013), available at <http://www.nejm.org/doi/full/10.1056/NEJMoa1304879#t=articleTop>.

¹⁵ U.S. FOOD AND DRUG ADMIN., MULTISTATE OUTBREAK OF FUNGAL MENINGITIS AND OTHER INFECTIONS: CDC AND FDA LABORATORY-CONFIRMED ORGANISMS FROM PRODUCT SAMPLES, (Dec. 12, 2012) available at <http://www.fda.gov/%20Drugs/DrugSafety/FungalMeningitis/default.htm>.

¹⁶ CDC INVESTIGATION, *supra* note 7.

¹⁷ OFFICE OF CONGRESSMAN EDWARD J. MARKEY, STATE OF DISARRAY: HOW STATES' INABILITY TO OVERSEE COMPOUNDING PHARMACIES PUTS PUBLIC HEALTH AT RISK, (2013) [hereinafter STATE OF DISARRAY], available at <http://www.scribd.com/doc/136535463/State-of-Disarray-Compounding-4-15-2013> (last visited Dec. 5, 2013).

¹⁸ *Id.*

¹⁹ *Pharm. Compounding: Proposed Legislative Solution: Hearing Before the S. Comm. on Health, Educ., Labor & Pensions*, 113th Cong. (2013) [hereinafter *Senate May 2013 Hearing*], available at <http://www.help.senate.gov/hearings/hearing/?id=f9b68c5e-5056-a032-52b6-4e632afd726a> (last visited

compounded drugs has developed a robust industry that provides a necessary supply of drugs that are not readily available on the retail market.²⁰ The compounding industry has grown faster than the laws that regulate it, and gaps in the regulatory system have surfaced.²¹ This lack of uniform nationwide oversight has only added to the inability of state and federal authorities to perform inspections and monitor these laboratories for safety.²² Drug manufacturers are required by the Federal Food, Drug, and Cosmetic Act to provide sufficient proof of safety and efficacy for their products.²³ However, compounding pharmacies are not required to submit a New Drug Application (NDA) before making drugs, so there is no similar approval and oversight process.²⁴

Since the deadly fungal meningitis outbreak, the problem of inconsistent and confusing regulatory authority persists. With a combination of poor communication between state and federal agencies, and bad actors like NECC, the likelihood of another similar public health crisis is almost certain.²⁵ The solution to prevent this from happening again is to expand federal authority over certain types of compounding pharmacies to bridge the regulatory gaps, together with vigorous enforcement of the authority state and federal agencies already possess.

III. The Compounding Industry & Oversight Mechanisms

A. Compounding distinguished from traditional drug manufacturing

Dec. 5, 2013), STATEMENT OF JANET WOODCOCK, DIR. OF THE FDA CENTER FOR DRUG EVAL. AND RESEARCH, 2-3 (May 9, 2013) *available at* <http://www.help.senate.gov/imo/media/doc/Woodcock2.pdf>.

²⁰ *House Nov. 2012 Hearing, supra* note 4 (testimony of Hon. Margaret Hamburg, Comm’r of Food and Drugs).

²¹ *Senate May 2013 Hearing, supra* note 19.

²² *Id.* (statement of Dr. Lauren Smith Interim Comm’r of the MA Dep’t of Health).

²³ 21 U.S.C. § 355 (2012).

²⁴ 21 U.S.C. § 353a (2012).

²⁵ *House Nov. 2012 Hearing, supra* note 4 (testimony of Dr. Hamburg “it’s not a question of if but when”).

If you place the two entities, large manufacturers and local pharmacists, on a spectrum of drug producing businesses, compounding pharmacies would fall somewhere in the middle. It is important to distinguish large-scale commercial drug manufacturing, from compounding, and discuss their respective roles in the provision of drugs to the healthcare system. Traditional compounding is the transformation by combining, altering, grinding, or mixing a custom medication that is not otherwise widely available.²⁶ This is often necessary for pediatric and geriatric care, where dosage needs to be adjusted, or for a patient who is allergic to a component of the drug.²⁷ Traditional compounding also includes suspending a drug in liquid, or adding a more appealing flavor to orally administered solutions.²⁸

Traditional compounding is generally performed by, or under the supervision of, a pharmacist, and historically at either a local retail pharmacy or on-site at a hospital or clinic.²⁹ Compounding is an integral part of delivering quality healthcare, and the traditional type of one-person one-prescription drug production has traditionally been regulated by state licensing and oversight authorities.³⁰ Compounding can be done for non-sterile medications, such as creams, ointments or gels applied to skin, or pills and capsules taken by mouth.³¹ Non-sterile drugs have a lower-risk of complications or adverse reactions and generally are subject to less regulatory scrutiny.³² Sterile preparations are usually drugs injected or infused, such as a shot or an IV drip

²⁶ *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360-361 (2002).

²⁷ *Id.* at 361.

²⁸ *Id.*

²⁹ U.S. FOOD & DRUG ADMIN., COMPLIANCE POLICY GUIDE § 460.200 (2002) *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm>.

³⁰ *Id.*, U.S. FOOD & DRUG ADMIN., COMPLIANCE POLICY GUIDE 7132.16, MANUFACTURE DISTRIBUTION AND PROMOTION OF ADULTERATED MISBRANDED, OR UNAPPROVED NEW DRUGS FOR HUMAN USE BY STATE-LICENSED PHARMACIES, MAR. 16, 1992.

³¹ U.S. PHARMACOPEIA, USP 36-NF 31: THE OFFICIAL COMPENDIA OF STANDARDS, Section 795, Pharm. Compounding: Nonsterile preparations, (2013-2014 ed. 2012).

³² *Id.* (There are still significant risks associated with non-sterile preparations, especially potency and purity.)

that carry a much higher risk for the spread of infection.³³ According to proper formulary guidelines, the MPA steroid drugs that caused the fungal meningitis, from NECC were supposed to be a sterile preparation.³⁴

For certain drugs, for example the electrolytes used in IVs, manufacturers do not distribute them in one-dose units.³⁵ They are shipped in bulk concentrated form and need to be diluted and repackaged for use.³⁶ Historically, the doctor, nurse or pharmacist would make the compound sterile products (CSPs) on-site, even bedside, before administering the drug to the patient.³⁷ As hospitals and health systems have grown, the demand for compounded drugs grew; it became more efficient for the hospital or clinic to outsource the production of these drugs, rather than producing them on-site.³⁸ These compounding facilities located off-site, are also known as “outsource compounders”, or “outsource facilities”, and are also useful for hospitals when drugs are in short supply.³⁹

This should be contrasted against the large-scale drug manufacturing that big pharmaceutical companies perform. This type of manufacturing has been highly regulated because it presents more potential safety risks to patients.⁴⁰ Drugs that are mass-produced are not for a specific patient who already has a prescription; they are shipped all over the country, and often stored for

³³ U.S. PHARMACOPEIA, USP 36-NF 31: THE OFFICIAL COMPENDIA OF STANDARDS, Section 797, 795: Pharm. Compounding: Sterile preparations, (2013-2014 ed. 2012).

³⁴ *Id.*

³⁵ Jaimy Lee & Paul Barr, *Taking the risk: Despite meningitis outbreak, some hosp. have little choice but to rely on compounding pharmacies*, MODERN HEALTHCARE (Oct. 13, 2012) www.modernhealthcare.com/article/20121013/MAGAZINE/310139991.

³⁶ *Id.*

³⁷ Ernest Anderson, et al., *Outsource Hosp. Sterile Compounding: A New and Safer Era To Come*, PHARMACY PRACTICE NEWS, Sept. 2013, at 1.

³⁸ *Id.*

³⁹ *Senate May 2013 Hearing*, *supra* note 19.

⁴⁰ U.S. FOOD AND DRUG ADMIN., FACTS ABOUT CURRENT GOOD MFG. PRACTICES (CGMPs), (May 2, 2013) *available at* <http://www.fda.gov/drugs/developmentapprovalprocess/manufacturing/ucm169105.htm> (last visited Dec. 5, 2013).

a period of time before being sold. This distribution across state lines and with a longer shelf life, warrants heightened scrutiny, and is overseen by the federal government to ensure that companies follow what the FDA calls “Current Good Manufacturing Practices.”⁴¹

B. Federal Authority

a. Federal Statutory Authority

The Food and Drug Administration (FDA), is the United States’ national agency that regulates, among other things, drugs, vaccines and biologics.⁴² The FDA is governed by the Food Drug & Cosmetic Act (FDCA), and its subsequent amendments, as well as Title 21 of the Code of Federal Regulations. The FDA is responsible for ensuring the safety and efficacy of drugs, through its pre- and post-market review and approval process.⁴³

The FDCA itself was born out of the political response to a deadly high-volume compound drug. In 1937, Sulfanilamide was widely used as a safe treatment for streptococcal infections, and when the need for a liquid form arose, a pharmacy in Tennessee compounded 633 shipments and sent them out for use.⁴⁴ The mixture proved deadly for over 100 people, and the resulting public outcry bolstered the political support for the 1938 Federal Food, Drug, and Cosmetic Act

⁴¹ See generally FDA Current Good Mfg. Practices Rule, 21 C.F.R. § 210.1, 211.1-211.208 (2013).

⁴² U.S. FOOD AND DRUG ADMIN., FDA FUNDAMENTALS, (May 6, 2013) <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm192695.htm>. (last visited Dec. 5, 2013).

⁴³ 21 U.S.C. §§ 301-450 (2012), (“no person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed [with the FDA] . . . is effective with respect to such drug.” 21 U.S.C. § 355(a)).

⁴⁴ CAROL BALLENTINE, FDA CONSUMER MAGAZINE, TASTE OF RASPBERRIES, TASTE OF DEATH: THE 1937 ELIXER SULFANILAMIDE INCIDENT (June 1981 Issue), *available at* <http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SulfanilamideDisaster/> (last updated Oct. 7, 2010).

(1938 FDCA).⁴⁵ The 1938 FDCA and subsequent amendments in 1962, have refined the FDA authority over manufacturers and “new drugs”.⁴⁶

Pharmaceutical companies that research and develop compounds, must seek approval for testing from the FDA, and subsequently submit the results of these extensive trials to the FDA for New Drug approval.⁴⁷ The FDA, in the interest of drug integrity and quality, has continued authority to monitor these registered manufacturers to inspect facilities, and review documents and records.⁴⁸ The FDA defines a “new drug” as;

“Any drug, the composition of which...is not generally recognized, among experts qualified by scientific training and experience to evaluate...the drug, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except [older drugs designated to be “grandfathered” in].⁴⁹

Under this broad definition, arguably, each individual compounded drug is a “new drug”. As such, each would require a NDA, or an Abbreviated New Drug Application (ANDA) with the FDA before sale and marketing in the United States.⁵⁰ This literal interpretation of “new drug” would require each compounded drug to prove with sufficient evidence that it is safe and effective for use; this process would be a huge burden to the compounding industry.⁵¹ The

⁴⁵ Wallace F. Janssen, FDA Consumer Magazine, The Story of the Laws Behind the Labels (June 1981 Issue), available at <http://www.fda.gov/AboutFDA/WhatWeDo/History/Overviews/ucm056044.htm> (last updated Dec. 14, 2011).

⁴⁶ 21 U.S.C. § 321(p)(1) (2012).

⁴⁷ U.S. FOOD AND DRUG ADMIN., NEW DRUG APPLICATION (NDA), available at <http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/newdrugapplicationnda/default.htm> (last updated Feb. 21, 2013).

⁴⁸ 21 U.S.C. § 321(p) (2012), (The FDCA authorizes the FDA with the power to enforce its requirements in 21 U.S.C. § 371(a)).

⁴⁹ Med. Ctr. Pharmacy v. Mukasey, 536 F.3d 383, 395 (5th Cir. 2008)

⁵⁰ Jesse M. Boodoo, *Compounding Problems and Compounding Confusion: Fed. Regulation of Compounded Drug Products and the THE FDAMA Circuit Split*, 36 AM. J.L. & MED. 220, 230-31 (2010)

⁵¹ *Id.* (“It would be neither practical nor plausible for pharmacists to study individualized compounds in clinical trials or prepare NDAs for the near infinite variety of possible compounds that might be prescribed.” *Id.*).

FDCA grants the FDA discretionary authority, not to prosecute for “minor violations” of the Act.⁵²

The FDA has defined “manufacturer” as; “a person who manufactures a drug...or who is licensed by such person to distribute or market the drug...”⁵³, and as “the person who performs the...operations required to produce the product: (1) mixing, ...(9) sterilizing, and (10) filling sterile...drugs into dispensing containers.”⁵⁴ However, within the statutes and regulations, there is no line defining or distinguishing a retail manufacturer from a compounding pharmacy. There is no clear language that states that pharmacies are exempt from jurisdiction under the FDA’s authority. It is conceivable that these two types of businesses could overlap, where a pharmacy operates in a manner that qualifies them as a manufacturer. The laws do make clear that, if the moniker “manufacturer” applies, many requirements attach. These requirements include the NDA or ANDA, particular labeling, Good Manufacturing Practices (GMPs), advertising restrictions, etc.⁵⁵

Over a decade ago, in 1992, the FDA raised concerns that state-licensed pharmacists were using compounding as a shield to avoid the FDA process for manufacturing.⁵⁶ In response, the FDA issued its first compounding Compliance Policy Guide (1992 CPG), which stated that compounding pharmacies were not explicitly exempt from FDA authority, but that the FDA would generally defer to state authorities and not target traditional retail pharmacies for compounding.⁵⁷ In 1997, Congress passed the Food and Drug Administration Modernization

⁵² 21 U.S.C. § 336 (2012).

⁵³ 21 C.F.R. § 99.3(f) (2013).

⁵⁴ 21 C.F.R. § 201.1(d) (2013).

⁵⁵ 21 U.S.C. § 321 (2012).

⁵⁶ U.S. FOOD & DRUG ADMIN., COMPLIANCE POLICY GUIDE § 460.200 (2002) *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm> (last updated Jan. 20, 2010).

⁵⁷ *Id.*

Act (FDAMA), which incorporated many of the policies laid out in the 1992 CPG, and brought compounding pharmacies within the scope of FDA authority.⁵⁸

The FDAMA exempted traditional compounding at retail pharmacies from the NDA requirements, so long as the drugs were for individual patients with a valid prescription, made using only approved ingredients, under endorsed standard manufacturing processes, and not “essentially copies” of a commercially available drug.⁵⁹ This exemption from federal regulation would only apply in states that entered a Memorandum of Understanding (MOU) with the Department of Health and Human Services.⁶⁰ This MOU gave specific procedures for the way state regulators were expected to conduct investigations and respond to complaints about compounding pharmacies that were shipping products outside the state.⁶¹ In states that did not enter the MOU, the exemption would only apply to small compounding pharmacies that shipped less than 5% of sales across state lines.⁶² FDAMA Section 503A forbade compounders from compounding drugs that have been withdrawn from the market for safety reasons.⁶³

The FDAMA’s most controversial provision, 503A(b)(3)(c), forbade compounders from advertising or promoting their drugs.⁶⁴ Drug compounding companies quickly challenged the FDAMA in court. This paper will discuss this challenge more fully in the next section, but from the start, the line between state and federal jurisdiction to regulate compounding pharmacies was unclear. The FDA updated its guidance document on compounding pharmacies in 2002 (2002 CPG), which stated the FDA will exercise enforcement discretion if a compounding pharmacy

⁵⁸ Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 127, 111 Stat. 2296 (1997) (codified at 21 U.S.C. § 353a (2012)).

⁵⁹ 21 U.S.C. § 353a (2012).

⁶⁰ *Id.*

⁶¹ *Id.*

⁶² 21 U.S.C. § 353a(b)(3) (2012).

⁶³ 21 C.F.R. § 216.24 (2013).

⁶⁴ 21 U.S.C. §353a(c) (2012).

was found to have engaged in any of nine explicit activities, but would otherwise defer to state regulatory authorities.⁶⁵ These nine activities relate to the scale of operations and the safety of the drugs the pharmacy works with, specifically;

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)...
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... (except where “appropriate”, or if there is a drug shortage)
9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.⁶⁶

Unfortunately, without bright, clear and defined lines of *binding* jurisdiction of authority and a strategy for state and federal communication about violations, investigation procedures and safeguards broke down.

b. Judicial Interpretations of Federal Statutes

In 1999, a group of compounding pharmacies, supported by their trade association the International Academy of Compounding Pharmacists (IACP)⁶⁷, challenged the FDAMA Section

⁶⁵ U.S. FOOD & DRUG ADMIN., COMPLIANCE POLICY GUIDE § 460.200 (2002) *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm> (last updated Jan. 20, 2010).

⁶⁶ *Id.*

⁶⁷ OFFICE OF CONGRESSMAN EDWARD J. MARKEY, COMPOUNDING PHARMACIES COMPOUNDING RISK 2 (2012), *available at* <http://interactive.snm.org/docs/Compounding%20Pharmacies%20->

503A on First Amendment free speech grounds in the Federal District Court in Nevada.⁶⁸ This case was later appealed to the Ninth Circuit.⁶⁹ The pharmacies argued that it was unconstitutional for the government to prevent these companies from advertising and promoting their products, because it restricted their right to commercial free speech.⁷⁰ The District Court and Federal Appeals Court held that the restriction was not permissible.⁷¹ Since this regulation was only one of many in the FDAMA amendments pertaining to compounding pharmacies, the court also had to determine whether this provision was severable, or whether the whole Section 503A of the FDAMA had to be struck down.⁷² The Ninth Circuit ultimately determined that Congress would not have passed this law without the advertising language, therefore it was not severable, and all of the FDAMA §503A was invalid.⁷³ However, this holding is only binding in the Ninth Circuit.⁷⁴

The Supreme Court granted review of that decision.⁷⁵ Neither party appealed the issue of severability, so the Supreme Court only addressed the constitutionality of the commercial speech restriction.⁷⁶ In *Thompson v. Western States Medical Center*, the Supreme Court upheld the Ninth Circuits holding that the FDAMA Section 503A provision prohibiting compounding

[%20Compounding%20Risk%20FINAL_0.pdf](#), Int'l Assoc. of Compounding Pharmacies (IACP) is the largest trade Assoc. for the compounding industry, and has continuously challenged the FDA's authority to regulate these companies, arguing that they lie under the sole jurisdiction of the state boards of pharmacy.

⁶⁸ *W. States Med. Ctr. v. Shalala*, 69 F. Supp. 2d 1288, 1291-92 (D. Nev. 1999).

⁶⁹ *W. States Med. Ctr. v. Shalala*, 238 F.3d 1090 (9th Cir. 2001). The Ninth Circuit covers a large part of the United States, including Nevada, Arizona, California, Oregon, Idaho, Montana, Washington, Alaska and Hawaii. It also includes the Northern Mariana Islands and Guam. Ninth Circuit Court of Appeals, Circuit Court Map, http://www.ca9.uscourts.gov/content/view.php?pk_id=0000000135 (last visited Oct. 18, 2013)

⁷⁰ *W. States Med. Ctr. v. Shalala*, 238 F.3d 1090, 1093-94 (9th Cir. 2001).

⁷¹ *Id.*

⁷² *Id.* at 1096.

⁷³ *Id.* at 1097-98.

⁷⁴ 28 U.S.C. §§1291, 1292, 1294 (2012).

⁷⁵ *Thompson v. W. States Med. Ctr. et al.*, 535 U.S. 357, 360 (2002).

⁷⁶ *Id.* at 366.

pharmacies from advertising was an unconstitutional restriction on commercial speech.⁷⁷

Unfortunately for the FDA, this left the agency and its legal team unclear of what authority they had outside of the Ninth Circuit over compounding pharmacies. In response, the FDA revised the 1992 CGP and published the updated Compliance Policy Guide (2002 CPG), as discussed earlier in Part II B.

In 2008, the Fifth Circuit held the opposite of the Ninth Circuit on the severability issue.⁷⁸ The Fifth Circuit found that though the restriction on commercial speech was unconstitutional, the provision was severable and therefore the rest of §503A stands.⁷⁹ In light of this patchwork of applicable legal framework, the FDA reaffirmed its previous statement from the 2002 CPG, that the FDA would treat all of Section 503A as invalid, except in the Fifth Circuit. Outside of the Fifth Circuit the FDA would continue to operate under its Compliance Policy Guide to regulate compounding pharmacies.⁸⁰ This Guidance document however, in its first sentence acknowledges that it is not binding; it is not law.⁸¹ Though it will not have the effect of law in court, courts will grant the agency *deference* to its policy and interpretations.⁸²

⁷⁷ *Id.* at 376-77.

⁷⁸ *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 387 (5th Cir. 2008). The Fifth Circuit includes Texas, Louisiana, and Mississippi. U.S. Courts, Court Locator, http://www.uscourts.gov/court_locator.aspx (last visited Oct. 18, 2013).

⁷⁹ *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 405 (5th Cir. 2008).

⁸⁰ *House Nov. 2012 Hearing*, *supra* note 4 (testimony of Hon. Margaret Hamburg, Comm'r of Food and Drugs).

⁸¹ U.S. FOOD & DRUG ADMIN., COMPLIANCE POLICY GUIDE § 460.200 (2002) *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm> (last updated Jan. 20, 2010).

⁸² *Chevron, U.S.A., Inc. v. Nat'l Res. Def. Council, Inc.* 467 U.S. 837, 842 (1984), "One can loosely define deference as the willingness of a court to accept an agency's interpretations of a statute or policy over competing interpretations offered by regulated persons or public interest groups. Once the agency decides the issue, a rigorous "hard look" by a federal court might overrule the agency's interpretation of the statute, but a deferential review will likely accept the agency's interpretation--and with it, the agency's decision regarding issuing the license or rule." James T. O'Reilly, *Losing Deference in the FDA's Second Century: Judicial Review, Politics, and a Diminished Legacy of Expertise*, 93 CORNELL L. REV. 939, 941-42 (2008).

A 2004 case helps further demonstrate the line between compounding at a retail pharmacy and a compounding manufacturer, and is an example of where a court granted the FDA 2002 CPG guidelines deference. The FDA was brought to court in 2004 after it tried to inspect Wedgewood Pharmacy, a compounding pharmacy in New Jersey.⁸³ The FDA had evidence that Wedgewood was acting more like a manufacturer, so the FDA agent in charge applied for an administrative warrant, which was granted by a magistrate giving access to the facility and distribution records.⁸⁴ In the application for the administrative warrant, the FDA pointed to specific evidence that Wedgewood was operating as a manufacturer. The evidence included:

“in early 1998, Wedgewood had shipped over 1,000 vials of Poison Ivy Extract without receiving the requisite prescriptions for specific patients; in May 2002, Wedgewood had acquired an encapsulation machine which could be used for large-scale drug manufacturing; in 2001 and 2002, it had purchased bulk quantities of substances in excess of the amounts normally associated with a retail pharmacy, including enough diazepam (the active ingredient in Valium) to manufacture over one million 10 mg doses during a six-month period, an amount "typical of a commercial drug manufacturer"; and it routinely produced veterinary drugs in bulk, without receiving specific veterinary prescriptions.”⁸⁵

This provides an example of what tangible and real actions the FDA considers in defining how a retail manufacturer operates. The administrative warrant would allow the FDA to assess whether Wedgewood’s production was consistent with the actions of a manufacturer, and if so determine if there were violations of the FDCA.⁸⁶

Wedgewood argued that it was exempt from authority 21 USCS § 374(a)(2)(A), which grants FDA authority general inspection rights. The Third Circuit Court of Appeals held that the 2002 CPG should be granted deference, and because there was evidence that Wedgewood was acting as a manufacturer, the FDA was therefore not only entitled to inspection of facilities, but also to

⁸³ *Wedgewood Village Pharmacy v. United States*, 421 F.3d 263 (3rd Cir. 2005).

⁸⁴ *Id.* at 265.

⁸⁵ *Id.*

⁸⁶ *Id.*

inspect records and distribution documents.⁸⁷ This holding was a win for the FDA. However, the FDA was cognizant that moving forward, short of having evidence to support probable cause for an administrative warrant, there would be continued push-back from compound pharmacies to allow entry for inspection or access to records. The FDA wanted to avoid further litigation over what authority it had over compounding pharmacies and became extremely risk averse.⁸⁸ At this point, the FDA precariously relied on the states to strictly regulate within their borders, and identify those pharmacies that were operating outside the scope of their state pharmacy license.⁸⁹

C. State Authority

Historically, States have had jurisdiction to license and regulate pharmacies that distribute drugs to individuals based on prescriptions from physicians.⁹⁰ Each state has their own pharmacy regulations, generally administered by a board of pharmacy, which vary in registration, fee and oversight requirements.⁹¹ Typically state boards of pharmacy (hereinafter “SBOP”) investigate local pharmacies for offences such as billing violations, or failure to have a licensed pharmacist on site, or the unlawful distribution of controlled substances.⁹²

⁸⁷ *Id.* at 272-73.

⁸⁸ *A Continuing Investigation into the Fungal Meningitis Outbreak and Whether it Could Have Been Prevented: Hearing Before the H. Subcomm. On Oversight and Investigations of the H. Comm. on Energy & Com.*, 113th Cong. (2013) [hereinafter *House Apr. 2013 Hearing*], available at <http://energycommerce.house.gov/hearing/continuing-investigation-fungal-meningitis-outbreak-and-whether-it-could-have-been-prevented#video> (last visited Dec. 5, 2013).

⁸⁹ *House Apr. 2012 Hearing*, *supra* note 88.

⁹⁰ *See House Nov. 2012 Hearing*, *supra* note 4 (testimony of Hon. Margaret Hamburg, Comm’r of Food and Drugs), U.S. FOOD & DRUG ADMIN., COMPLIANCE POLICY GUIDE § 460.200 (2002) available at <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm> (last updated Jan. 20, 2010), THE NAT’L CONFERENCE OF STATE LEGISLATURES, STATE REGULATION OF COMPOUNDING PHARMACIES, available at <http://www.ncsl.org/research/health/regulating-compounding-pharmacies.aspx> (last updated Nov. 27, 2013) [hereinafter NCSL REPORT].

⁹¹ NCSL REPORT, *supra* note 90.

⁹² OFFICE OF CONGRESSMAN EDWARD J. MARKEY, COMPOUNDING PHARMACIES COMPOUNDING RISK 3 (2012), available at http://interactive.snm.org/docs/Compounding%20Pharmacies%20-%20Compounding%20Risk%20FINAL_0.pdf

Under the current laws, compounding pharmacies are primarily governed by the SBOP of the state they operate in, and at the state level there is inconsistency of industry standards.⁹³ Each state grants the SBOP authority to license and regulate the pharmacies operating within that state. The SBOPs determine the frequency of facility investigations and how they are conducted.⁹⁴ Some states conduct routine in-person inspections, some are announced, other states rely on pharmacy self-inspections, or only inspect in response to complaints about the pharmacy.⁹⁵ Some states have adopted standards developed by the United States Pharmacopoeia (USP), an independent non-profit that sets quality, purity, and strength standards for foods and medicines.⁹⁶ Twenty-seven states have incorporated USP Section 795, which addresses Non-Sterile Compounding, and Section 797 for Sterile Compounding Preparation into their pharmacy regulations.⁹⁷ The remaining states have developed their own standards, which may not be as stringent. Some states permit non patient-specific compounding in certain narrow situations.⁹⁸

SBOP are responsible for the pharmacists operating within their jurisdiction, however if drugs are compounded and shipped over state lines, the compounding pharmacy is required to be licensed in multiple states.⁹⁹ Again, these states may have different levels of safety requirements, and inspection standards, and the pharmacy's home state must ensure that quality and process controls are in effect.¹⁰⁰

IV. Political Aftermath of the NECC Outbreak

⁹³ STATE OF DISARRAY, *supra* note 17, at 10.

⁹⁴ NCSL REPORT, *supra* note 90.

⁹⁵ STATE OF DISARRAY, *supra* note 17, at 10.

⁹⁶ U.S. PHARMACOPEIA, ABOUT U.S.P., available at <http://www.usp.org/about-usp> (last visited Nov. 17, 2013).

⁹⁷ NCSL REPORT, *supra* note 90.

⁹⁸ *Id.*

⁹⁹ Ernest Anderson, et al., *Outsource Hosp. Sterile Compounding: A New and Safer Era To Come*, PHARMACY PRACTICE NEWS, Sept. 2013, at 1.

¹⁰⁰ *Id.*

A. NECC violations through the regulatory lens

Now, that a tragedy has occurred and been widely publicized, the FDA and the state of Massachusetts have expressed deep regret for not acting sooner on the warning signs for NECC, and for a failure to provide regulatory clarity.¹⁰¹ The problem is that even with solid and unambiguous rules, there may still be bad actors like NECC.

The NECC was allegedly using generated patient lists from clinics regardless if those patients had prescriptions, as their record of “individual patients” for whom their drugs were being produced.¹⁰² The Massachusetts Dept. of Public Health noted that NECC had shipped out two of the later-recalled lots of contaminated MPA before the results of sterility testing had been received.¹⁰³ The FDA investigation inspection following the outbreak found there was mold growing on surfaces that were supposed to be sterile, and an air conditioning unit intended to stabilize air temperature and humidity was turned off at night, though it was supposed to run continuously.¹⁰⁴ The FDA form 483 issued following the facility inspection stated that vials of MPA from one of the suspect lots had “greenish black foreign matter” in the solution.¹⁰⁵

The NECC was a licensed pharmacy by the Commonwealth of Massachusetts, but had been flagged by the state and federal authorities multiple times in the past before the meningitis

¹⁰¹ See *House Nov. 2012 Hearing, supra* note 4, *Reforming the Drug Compounding Regulatory Framework: Hearing Before the H. Subcomm. On Health of the H. Comm. on Energy & Com.*, 113th Cong. (2013) [hereinafter *House July 2013 Hearing*] available at <http://energycommerce.house.gov/hearing/reforming-drug-compounding-regulatory-framework> (last visited Dec. 5, 2013).

¹⁰² Sabrina Tavernise & Andrew Pollack, *FDA Details Contamination at Pharmacy*, N.Y. TIMES (Oct. 16, 2012), available at http://www.nytimes.com/2012/10/27/health/fda-finds-unsanitary-conditions-at-new-england-compounding-center.html?_r=0 (last visited Dec. 6, 2013).

¹⁰³ STAFF OF H. SUBCOMM. ON OVERSIGHT AND INVESTIGATIONS OF THE H. COMM. ON ENERGY & COM., MAJORITY MEMORANDUM 5 (Nov. 12, 2012).

¹⁰⁴ Tavernise, *supra* note 102.

¹⁰⁵ U.S. FOOD & DRUG ADMIN., FORM 483 (Oct. 26, 2012) available at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM325980.pdf>

outbreak for violations.¹⁰⁶ In 2002, the FDA was alerted to two cases of symptoms of bacterial meningitis linked to NECC for the same drug, MPA, which led to FDA and state facility investigations.¹⁰⁷ The Massachusetts SBOP issued three “non-disciplinary private advisory letters” to the NECC in 2004, after complaints came from South Dakota, Texas and Wisconsin that the NECC was soliciting bulk orders rather than patient specific prescriptions.¹⁰⁸ In 2006, as part of a consent decree for past violations, the NECC submitted to an FDA and SBOP inspection, which turned up 189 vials of a commercially available product “Trypan Blue.”¹⁰⁹ This discovery led to an FDA Warning Letter sent to the NECC, generally the last step before enforcement action, but further action was never taken.¹¹⁰

The state failed to take action, and subsequently the state agency’s administration has been placed under new management.¹¹¹ The FDA was tentative to take enforcement action because of a “patchwork quilt”¹¹² of jurisdiction that arose out of the court challenges to the FDAMA amendments. The Circuit Court split led to two different legal frameworks being applied in certain states, and other states left guessing what law applied to them. If the compounding

¹⁰⁶ STAFF OF H. SUBCOMM. ON OVERSIGHT AND INVESTIGATIONS OF THE H. COMM. ON ENERGY & COM., MAJ. MEMO. 6-7 (2012). (This section describes how the FDA had conducted three prior series of inspections of NECC, each based on separate allegations or events that amounted to violations. In 2002 and 2003 the FDA issued NECC two form 483s detailing a list of violations they observed during inspection, and in 2006 sent NECC a Warning Letter. The state board of pharmacy had investigated at least twelve separate complains concerning NECC or the CEO Mr. Cadden who was connected to NECCs sister-company Ameridose. Id.).

¹⁰⁷ STAFF OF S. COMM. ON HEALTH, EDUC., LABOR, & PENSIONS, 112TH CONG., REP. ON THE NEW ENGLAND COMPOUNDING CENTER AND THE MENINGITIS OUTBREAK OF 2012: A FAILURE TO ADDRESS RISK TO THE PUB. HEALTH 1 (2012) *available at* http://www.help.senate.gov/imo/media/doc/11_15_12%20HELP%20Staff%20Report%20on%20Meningitis%20Outbreak.pdf.

¹⁰⁸ *Id.* at 7.

¹⁰⁹ *Id.* at 8.

¹¹⁰ *Id.*

¹¹¹ *DPH Fires Mass. Pharmacy Board Dir. As Part Of NECC Investigation*, CBS BOSTON, Nov. 7, 2012, <http://boston.cbslocal.com/2012/11/07/dph-fires-mass-pharmacy-board-director-as-part-of-necc-investigation/>.

¹¹² *House Nov. 2012 Hearing*, *supra* note 4.

pharmacy followed the requirements of the state and federal government, or even their own standard operating procedures to keep their laboratory and clean room up to code, this likely would never have happened.¹¹³ This was not just the failure of NECC to maintain high quality and safety standards, but also a failure of the federal and state authorities from taking more aggressive action after repeated reports of violations and unsafe products.¹¹⁴

B. Federal and state investigation on how to address the regulatory gap.

In April 2013, the FDA issued a report that it had amplified its enforcement and regulation of sterile drug compounding pharmacies.¹¹⁵ Though still asserting that it lacks sufficient authority, the FDA conducted 31 total inspections, three with additional administrative warrants because of refusal to cooperate by the compounding pharmacy.¹¹⁶ The FDA identified these compounding pharmacies based on a risk assessment, considering the type of drugs being compounded, distribution, as well as previous reports from states on allegations of violations.¹¹⁷ Almost all of these inspections were conducted in coordination with the respective SBOP regulators.¹¹⁸ The FDA found violations and subsequently issued Form 483s, an official document detailing the violations observed, for 29 out of the 31 pharmacies.¹¹⁹ The FDA shared the inspection results

¹¹³ *House Nov. 2012 Hearing, supra* note 4.

¹¹⁴ U.S. FOOD AND DRUG ADMIN., WARNING LETTER TO NEW ENGLAND COMPOUNDING CTR. (Dec. 4, 2006), *available at* <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm076196.htm> (last updated July 8, 2009), STAFF OF SUBCOMM. ON OVERSIGHT AND INVESTIGATIONS OF THE H. COMM. ON ENERGY & COM., MAJ. MEMO., 16-20 (2012), *available at* <http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/Hearings/OI/20121114/HMTG-112-HHRG-IF02-20121114-SD001.pdf>.

¹¹⁵ U.S. FOOD AND DRUG ADMIN., SUMMARY: 2013 FDA PHARMACY INSPECTION ASSIGNMENT, *available at* <http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm347722.htm> (last updated Dec. 2, 2013).

¹¹⁶ *Id.*

¹¹⁷ *Id.*

¹¹⁸ *Id.*

¹¹⁹ *Id.*

with the states, and 11 facilities were subsequently shut down after the April inspections, by their respective states.¹²⁰

Since the 2012 fungal meningitis outbreak, the somber urgent tone of discussions in both state and federal legislative chambers has been a catalyst for statutory action. Since the outbreak, ten states have introduced or passed new legislation, or implemented new regulations placing additional restriction on compounding pharmacies.¹²¹ On the federal level, committee hearings have been held in both the House and the Senate, and a compromise bill was passed and recently signed into law to address the regulatory gaps.

Then Representative, now Senator Edward Markey of Massachusetts, teamed up with Representatives Henry Waxman (D-CA), John Dingell (D-MI), Frank Pallone (D-NJ) and ranking member of the House Committee on Energy and Commerce Diana DeGette (D-CO) to launch an investigation on compounding pharmacies.¹²² The legislative offices sent out questionnaires to the SBOP, and from the responses (from all but Rhode Island), put together a report published on April 15, 2013.¹²³ The report indicated that only thirteen of the states could identify which pharmacies were performing sterile compounding.¹²⁴ The report also concludes that there is no formal mechanism for SBOP to know about adverse events or other issues that arise from out-of-state pharmacies.¹²⁵ States where issues with drugs arise or are discovered, do not consistently contact the state of origin of the drug, nor the FDA.¹²⁶

¹²⁰ *Examining Drug Compounding: Hearing before the H. Subcomm. On Health of the Comm. on Energy & Com.* 113th Cong. (2013) [hereinafter *House May 2013 Hearing*] available at <http://energycommerce.house.gov/hearing/examining-drug-compounding> (last visited Dec. 6, 2013).

¹²¹ STATE OF DISARRAY, *supra* note 17, at 12. (States include: NJ, MN, CA, MD, MA, OK, SC, UT and VA. Id.).

¹²² *Id.*

¹²³ STATE OF DISARRAY, *supra* note 17.

¹²⁴ *Id.* at 17

¹²⁵ *Id.* at 21

¹²⁶ *Id.*

In addition, the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor and Pensions held multiple hearings, including subcommittee hearings, to gather investigational testimony from the Commissioner of the FDA, and the Director of the FDA Center for Drug Evaluation, the Interim Commissioner of the Massachusetts Department of Public Health, family members of patients who died from fungal meningitis, researchers from the Pew Charitable Trusts, Industry Trade Association representatives, and many others.¹²⁷ The many hours of questions and answers helped guide the legislators in crafting legislation, the result of which was passed and signed into law on November 27, 2013.¹²⁸

Within these hearings and discussions, there was dispute over whether the FDA actually required expanded authority to regulate compounding manufacturers, or whether the agency was too relaxed on enforcement. The compounding industry and political conservatives argued that the FDA already has the requisite authority to regulate these compounding manufacturers, and that it is now “back-peddling” on its perceived authority in the shadow of the meningitis outbreak.¹²⁹ The conservative side argues that the FDA, based on 503A in the Fifth Circuit, and the 2002 Compliance Policy Guide in the other states, is adequate authority to regulate compounding pharmacies.¹³⁰ In addition, they argue that if the compounding manufacturer

¹²⁷ See *House Nov. 2012 Hearing*, *supra* note 4, *House May 2013 Hearing*, *supra* note 120, *House July 2013 Hearing*, *supra* note 101, *House Apr. 2012 Hearing*, *supra* note 88, *Senate May 2013 Hearing*, *supra* note 19.

¹²⁸ THE WHITE HOUSE, Statement by the Press Sec’y on H.R. 1848, H.R. 3204, S. 252 (Nov. 27, 2013) available at <http://www.whitehouse.gov/the-press-office/2013/11/27/statement-press-secretary-hr-1848-hr-3204-s-252> (last visited 12/5/2013).

¹²⁹ *House July 2013 Hearing*, *supra* note 101, (exchange between Congressman Pitts and Dr. Woodcock).

¹³⁰ *House Apr. 2012 Hearing*, *supra* note 88, *Senate May 2013 Hearing*, *supra* note 19.

resists and asserts that they are operating within their state license, the FDA can still apply for and obtain an administrative warrant to gain access.¹³¹

The FDA and many Democrats disagreed. The FDA requested clarity and definition of authority, and the registration of certain compounding manufacturers.¹³² The FDA Commissioner, Dr. Margaret Hamburg, repeatedly stated in the Congressional hearings, and in written testimony, that the FDA does not want unlimited authority over all compounders, and that it does not want to be in the business of regulating any pharmacy that is incidentally licensed to compound.¹³³ Dr. Hamburg asserted that authority should remain with the states.¹³⁴ The FDA Commissioner and Dr. Janet Woodcock, Director of the FDA Center for Drug evaluation and research, also expressed that this current process is reactionary, that it responds to problems but does not prevent them.¹³⁵ Through the hours of questioning, the legislators specifically asked what authority the FDA thought it needed to properly prevent this type of health crisis from happening again.¹³⁶

The FDA requested clarity from Congress of the definition of non-traditional manufacturer or compounding manufacturer, emphasizing that this was the most central issue.¹³⁷ Ambiguity will only perpetuate the pushback from facilities for ability to inspect, and result in continued litigation challenging FDA actions. The FDA requested that the line between traditional

¹³¹ 21 U.S.C. § 374 (2012). (21 U.S.C. § 374 grants inspection rights to the FDA for warrantless searches, however if the FDA is met with resistance, the Dep't of Justice: Civil Division will assist in obtaining a warrant. 28 C.F.R. § 0.45(j) Consumer litigation.)

¹³² *House Apr. 2012 Hearing, supra* note 88, STATEMENT OF HON. MARGARET HAMBURG, COMM'R OF FOOD AND DRUG at 7-8 (Apr. 16, 2013), available at <http://docs.house.gov/meetings/IF/IF02/20130416/100668/HHRG-113-IF02-Wstate-HamburgM-20130416.pdf>.

¹³³ See *House Nov. 2012 Hearing, supra* note 4, *House May 2013 Hearing, supra* note 120, *House July 2013 Hearing, supra* note 101, *House Apr. 2012 Hearing, supra* note 88, *Senate May 2013 Hearing, supra* note 19.

¹³⁴ *House May 2013 Hearing, supra* note 120.

¹³⁵ *House Nov. 2012 Hearing, supra* note 4.

¹³⁶ *Id.* (Congressman Dingell repeatedly asked for Comm'r Hamburg to "Submit to us what you need.").

¹³⁷ *House May 2013 Hearing, supra* note 120.

compounding pharmacies, and manufacturers be articulated. Both the FDA, the industry and the legislators used many terms to describe these entities, calling them anything from compounding pharmacies, compounding manufacturers, and outsourcing facilities, which adds to the definitional confusion.¹³⁸ The FDCA and FDAMA draw the line that a compounding pharmacy will not be subject to New Drug Application requirements if they produce a limited amount of the compounded drug, but the FDA asked Congress to specify whether that means “10 units, 1,000 units or 10,000 units” etc.¹³⁹ This is vital because even if these companies are operating outside the scope of their state compounding license, the FDA authority over traditional manufacturers has different scope and applicability than what is needed for compounding manufacturers.¹⁴⁰

Another concern repeatedly expressed by the FDA was that if a doctor, clinic or pharmacy discovers a problem in one state with a drug that came from out-of-state, the SBOP where the problem was found cannot go out and investigate and regulate the pharmacy in a foreign state.¹⁴¹ They must contact the home SBOP and hope that they respond.¹⁴² To remedy this potential area for problems, the FDA expressed a desire for a formal communication procedure both between states and between the states and the FDA.¹⁴³

Another issue expressed by the FDA is that the agency has no metrics on how many of these compounding manufacturers exist across the United States, with estimates varying between 7,500¹⁴⁴ and 23,000.¹⁴⁵ The FDA asked for legislation to either require that pharmacies that

¹³⁸ *House May 2013 Hearing, supra* note 120.

¹³⁹ *Id.*

¹⁴⁰ *Id.*

¹⁴¹ *House Apr. 2012 Hearing, supra* note 88.

¹⁴² *Id.*

¹⁴³ *Id.*

¹⁴⁴ INT'L ACAD. OF COMPOUNDING PHARMACISTS, MEMBER ALERT, *available at* <http://www.iacprx.org/displaycommon.cfm?an=1&subarticlenbr=277> (last visited Dec. 5, 2013)

compound high volumes of sterile products for shipment to other states, register with the FDA, or instruct the FDA to promulgate a rule regarding registration.¹⁴⁶ This way the FDA would know where these facilities are located, what they are producing, and to what locations they are distributing.¹⁴⁷ This registration process was suggested to require the companies to pay a fee, to help cover the additional administrative costs to the FDA.¹⁴⁸ Adding a penalty, or monetary fine, for not registering would also provide an incentive for companies to comply. This knowledge of where these entities are operating, would be followed-up by FDA ability to inspect facilities, as well as documents and records (to be able to determine where they were shipping and when, which batches to inspect), the ability to take and test samples from the facilities, the ability to seize adulterated drugs, to issue penalties and even close down facilities found in violation of the FDCA.

V. Crafting New Legislation to Prevent Another Outbreak

After hours of hearings, pages of testimony, and requests for comments and input from both the government agencies and the compounding industry, Congress decided that legislation was necessary to prevent another outbreak. Though several bills were drafted in both the House and Senate, one bill emerged from Committee as the compromise between the House and the Senate. This bill H.R.3204/S.8027, was recently signed into law, titled the “Drug Quality and Security Act.”¹⁴⁹

A. Proposed Federal statutory changes

¹⁴⁵ *House May 2013 Hearing, supra* note 120. This wide range of numbers is likely exaggerated by the lack of definition of “compounding pharmacy.”

¹⁴⁶ *House May 2013 Hearing, supra* note 120.

¹⁴⁷ *Id.*

¹⁴⁸ *Id.* Many Legislators when questioning Comm’r Hamburg emphasized that the federal government is still under sequester, and were skeptical whether the FDA could financially, or based on its current resources, take on more inspection and enforcement obligations. *Id.*

¹⁴⁹ Drug Quality and Security Act, Pub. L. No. 113-54, *available at* <http://beta.congress.gov/113/bills/hr3204/BILLS-113hr3204enr.pdf>.

A flurry of federal legislation has been introduced in response to the meningitis outbreak, and the subsequent congressional hearings. There were several proposals in the House, and one from the Senate Committee on Health, Education, Labor and Pensions.¹⁵⁰ On September 28, 2013, on the eve of the shutdown of the Federal Government, the House, after a short, and mostly one-sided debate passed H.R. 3204 on a voice vote.¹⁵¹ This bill was sponsored by the Chair of the House Committee on Energy and Commerce, Republican Representative Fred Upton of Michigan, and was cosponsored by six Democrats and four Republicans.¹⁵² This bill was a compromise bill between the House and Senate Committees that were working on similar drafts, and passed in the Senate by a voice vote on November 18, 2013.¹⁵³ It was signed into law by the President on November 27, 2013.¹⁵⁴ It is also worth noting that this bill was supported by many relevant organizations, including PhRMA, PharMEDium¹⁵⁵, and the National Community Pharmacists Association.¹⁵⁶

¹⁵⁰ VALID Act, H.R. 2186, 112th Cong. (2012). Comm’r Margaret A. Hamburg, MD, and MDPH Interim Comm’r Lauren Smith, MD, MPH, indicated that they supported Markey’s bill during the Nov. 14, 2012 hearing. *House Nov. 2012 Hearing*, supra note 4, Pharm. Quality, Security, and Accountability Act, S. 959 113th Cong. (2013).

¹⁵¹ Drug Quality and Security Act, Pub. L. No. 113-54, available at <http://beta.congress.gov/113/bills/hr3204/BILLS-113hr3204enr.pdf>. There was about 45 minutes of discussion on the bill, without any real dispute. The fact that it was a voice vote means that there was no roll call before the vote was taken, there was no majority needed. This was a bill sponsored by both Democrats and Republicans so it was presumed to have overwhelming support. RULES OF THE H.R., RULE XX 1(a)-(c), available at <http://clerk.house.gov/legislative/house-rules.pdf>.

¹⁵² *Id.*, Congress, Cosponsors: H.R. 3204 - 113th Cong. (2013-2014), available at <http://beta.congress.gov/bill/113th/house-bill/3204/cosponsors> (last visited Dec. 6, 2013). Cosponsors include: Congress(wo)men Upton (R-MI), Degette (D-CO), Dingell (D-MI), Matheson (D-UT), Pallone (D-NJ), Waxman (D-CA), Griffith (R-VA), Latta (R-OH), Murphy (R-PA), Pitts (R-PA).

¹⁵³ S. 959, 113th Cong. (2013), available at <http://www.gpo.gov/fdsys/pkg/BILLS-113s959rs/pdf/BILLS-113s959rs.pdf>.

¹⁵⁴ THE WHITE HOUSE, STATEMENT BY THE PRESS SEC’Y ON H.R. 1848, H.R. 3204, S. 252 (Nov. 27, 2013) available at <http://www.whitehouse.gov/the-press-office/2013/11/27/statement-press-secretary-hr-1848-hr-3204-s-252> (last visited 12/5/2013)

¹⁵⁵ Letter from PharMEDium to the H. Comm. on Energy & Com. letter expressing support for H.R. 3204 (Sept. 27, 2013) available at <http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/letters/DQSA/20130>

The Drug Quality and Security Act (hereinafter “the Act”), began as two bills with different agendas and so, has two parts. The first section, Title I, amends the FDAMA Section 503, and creates an exception to certain FDA regulations for those entities, which it labels “outsourcing facilities”, that comply with eleven requirements and voluntarily register with the FDA.¹⁵⁷ Title II of the Act makes changes to drug distribution and supply chain tracing laws, and is not pertinent to the change in regulatory authority over outsourcing facilities, therefore, will not be discussed in this analysis.¹⁵⁸

This Act eliminates the controversial advertising provision in section 503A of the FDAMA, and amends the section intended to apply to traditional compounding or retail pharmacies. The bill re-names the current 503B, to be 503C, and inserts a new section 503B, intended to encompass compounding manufacturers or “outsource facilities”.¹⁵⁹ The new 503B acknowledges that outsourcing facilities are manufacturers, and will be regulated as such under the FDCA, but carves out an exemption for those facilities that operate in accordance with 503B.¹⁶⁰ The eleven requirements for exempt outsource facilities laid forth in 503B are:

- 1) Voluntary registration with FDA as an “outsourcing facility”.
- 2) The drug compounded does not use “bulk drug substances”, unless done in compliance with the USP monograph, or there is a shortage for the drug.
- 3) Any other ingredients, besides bulk substances, are compounded in compliance with the USP.
- 4) The outsource facility does not compound drugs or components withdrawn from the market because it is unsafe or not effective.
- 5) The outsource facility cannot compound what are “essentially copies” of an FDA approved drug.

[927PhaMEDium.pdf](#). PharMEDium is “the nation’s leading provider of hospital pharmacy-outsourced sterile admixture services”. *Id.*

¹⁵⁶ OFFICE OF CONGRESSMAN FRED UPTON, H.R. 3204, THE DRUG QUALITY AND SECURITY ACT, (Sept. 27, 2013), available at <http://energycommerce.house.gov/fact-sheet/hr-3204-drug-quality-and-security-act> (last visited Dec. 6, 2013).

¹⁵⁷ Drug Quality and Security Act, Pub. L. No. 113-54, [hereinafter Drug Quality and Security Act] § 503B, available at <http://beta.congress.gov/113/bills/hr3204/BILLS-113hr3204enr.pdf>.

¹⁵⁸ Drug Quality and Security Act, *supra* note 157 at Title II.

¹⁵⁹ Drug Quality and Security Act, *supra* note 157 at § 503B.

¹⁶⁰ *Id.*

- 6) If outsource facility compound drugs that are “demonstrably difficult” to produce, as identified by the FDA, they must follow additional safeguards during production.
- 7) If the drug has been compounded from a drug that is subject to a risk evaluation and mitigation strategy (identified as more dangerous in some respect), then it must follow specific safety controls determined by the FDA.
- 8) The outsourcing facility is prohibited from wholesaling.
- 9) The outsourcing must pay fees to the FDA.
- 10) It must label the drug with contact information of the outsourcing facility, specific information about the batch and lot number of the drug, the drug name, and “this is a compounded drug”, and “not for resale”, among other things.
- 11) In addition to registering with the FDA, the outsourcing facility must make its facility and records “available” for regular risk-based inspections by the FDA, report all adverse events.¹⁶¹

If the eleven requirements of 503B are met, outsourcing facilities are expressly exempted from the NDA application process, and certain labeling requirements.¹⁶²

The Act requires outsourcing facilities to pay a \$15,000 annual fee to register with the FDA, adjusted for inflation and for small businesses (to be defined by the FDA).¹⁶³ Outsourcing facilities would be subject to current good manufacturing practice requirements of the FDCA, and those registered facilities would not be required to be a licensed pharmacy within the state they operate.¹⁶⁴ There is careful attention to try to prevent the mistakes of the past; including adding a provision specifically stating that if any section of this law is found unconstitutional, it is severable and the rest will stand.¹⁶⁵ The FDA is required to establish a risk-based inspection system for outsourcing facilities, taking into account various factors including, the compliance history of the facility, any recalls linked to the facility, whether it has registered (implying that unregistered facilities are still subject to inspection authority).¹⁶⁶ In Section 105 of the Act, “Enhanced Communication”, SBOPs are required to alert the FDA when they take action against compounding pharmacies operating outside of 503A, with warning letters, suspension of license,

¹⁶¹ *Id.*

¹⁶² *Id.*

¹⁶³ Drug Quality and Security Act, *supra* note 157 at § 744K.

¹⁶⁴ Drug Quality and Security Act, *supra* note 157 at § 503B.

¹⁶⁵ Drug Quality and Security Act, *supra* note 157 at § 106.

¹⁶⁶ Drug Quality and Security Act, *supra* note 157 at § 503B(b)(4).

or recall of drugs.¹⁶⁷ The FDA would be required to contact SBOP if they receive an alert from a state, or if the FDA itself makes a determination based on a risk-based inspection that a pharmacy is operating outside of 503A.¹⁶⁸

B. Analyzing the strengths and weaknesses of the Act

Some argue, regardless of whether they are called “compounding manufacturers” or “outsourcing facilities”, that the FDA and the States currently have the adequate authority to regulate non-traditional compounding facilities.¹⁶⁹ This argument is unconvincing, as the legal framework of the past was insufficient. The new legislation shows promise to address many of the concerns raised by the FDA, however it leaves some questions to be answered.

The first obvious disconnect from what the FDA requested, and the language of the Act, is that 503A is amended only to eliminate the unconstitutional advertising provision. Sec. 503A(a)(2)(A) defines that a licensed pharmacist or licensed physician can compound without a valid prescription “in limited quantities”, without defining “limited quantity”.¹⁷⁰ This leaves the same definitional loophole open for facilities to claim that they are exempt from the FDCA new drug approval and labeling requirements, operating under a state pharmacy license, and not subject to FDA authority. The same lawsuits and industry resistance to inspections are very likely to continue. In addition, though the new 503B includes a definition of “compounding”, 503A does not. The Act’s silence may give the FDA the ability to adopt a reasonable, but perhaps different definition that applies to traditional compounding.¹⁷¹

The next important difference is that registration as an “outsourcing facility” is voluntary and left to the discretion of the compounding facility. This seemingly puts the onus on the hospitals,

¹⁶⁷ Drug Quality and Security Act, *supra* note 157 at § 105(a)(1)-(b)(3).

¹⁶⁸ Drug Quality and Security Act, *supra* note 157 at § 105(d)(1)-(2).

¹⁶⁹ *House May 2013 Hearing*, *supra* note 120.

¹⁷⁰ 21 U.S.C. § 353a(2)(A).

¹⁷¹ *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.* 467 U.S. 837, 842 (1984).

clinics, and healthcare providers to only purchase drugs from registered outsourcing facilities, or those properly licensed by the state. Registered outsourcing facilities with higher operating costs, including FDA fees, will have to compete with unregistered facilities. Rather than leaving it up to the outsourcing facility, legislators should have written in specific criteria, such as sterile drug production, across state lines, and above a certain number of units, i.e. 1,000 units per month or more, in volume. In Sec. 503B(d)(4)(a) of the Act, an “outsourcing facility” is defined as: “(i) is engaged in the compounding of sterile drugs; (ii) has elected to register as an outsourcing facility; and (iii) complies with all of the requirements of this section.”¹⁷² This leaves open the question as to whether the Act applies to facilities who produce non-sterile products, and if not, whether the FDA should leave regulation of non-sterile facilities entirely to the state. The Act does not address the compounding or repackaging of biological drugs, or biologics, and whether they also may be outsourcing facilities. The FDA regulates both human and veterinary drug manufacturing, but H.R. 3204 does not address the compounding of medicines for animal use, so it is unclear how those facilities may be affected.

The FDA is required by the Act to establish a list of those bulk drugs “for which there is a clinical need”, or are in a drug shortage.¹⁷³ The drugs included on this list are not exempt from regulation, but are subject to different restrictions, due to the emergency need to create more supply.¹⁷⁴ The Act does not address how outsourcing facilities, hospitals or clinics may request that drugs are added to that list, or how the FDA might process a request of such nature.¹⁷⁵ The

¹⁷² Drug Quality and Security Act, *supra* note 157 at § 503B(a)(2)(A).

¹⁷³ *Id.*

¹⁷⁴ Drug Quality and Security Act, *supra* note 157 at § 503B.

¹⁷⁵ Under *Chevron*, the first question is “whether Congress has directly spoken to the precise question at issue.” *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.* 467 U.S. 837, 842(1984). If Congress has done so, its “unambiguously expressed intent” must be followed by the agency in its application. *Id.* at 842-43. If Congress has not done so, or remained silent on the question at issue, a reviewing court must respect the FDA’s interpretation and issuance of regulations thereof so long as it passes the relatively low

Act did not set forth how these requirements will be initiated or phased in, which means that it would take effect immediately upon its passage. This may have the effect of halting compound drug production at facilities that are attempting to get into compliance.

Commissioner Hamburg released a statement of mild disappointment after the Act became law.¹⁷⁶ The Commissioner acknowledged that she was “pleased” with its passage, and that it is a “good step” toward “stronger drug quality and safety laws”, but that all of authority and clarity she asked for was not included.¹⁷⁷

Almost immediately after the Act was signed into law, the FDA issued two draft guidance documents on how the FDA interprets each section of the Act.¹⁷⁸ The FDA also issued three Notice of Proposed Rules for the list of bulk substances to apply to each section, and requested nominations for additions to those lists.¹⁷⁹ The draft guidance for Sec. 503B gives outsource facilities instruction on how to register with the FDA if they meet the requirements, when they must register, what information is required and what fees will be assessed.¹⁸⁰ The draft guidance

"arbitrary, capricious, or manifestly contrary to the statute" standard. *Id.* at 843-44. The issue goes to the FDA's construction of a statute that it administers, the necessary lens for the argument is *Chevron*. *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.* 467 U.S. 837 (1984).

¹⁷⁶ Margaret A. Hamburg, *New Law Enhances Safety of Compounded Drugs and Protection of the Drug Supply Chain*, FDA VOICE (Dec. 2, 2013) <http://blogs.fda.gov/fdavoices/index.php/2013/12/new-law-enhances-safety-of-compounded-drugs-and-protection-of-the-drug-supply-chain/> (last visited Dec. 9, 2013).

¹⁷⁷ *Id.*

¹⁷⁸ U.S. FOOD AND DRUG ADMIN., REGULATORY POLICY INFO. (Dec. 2, 2013) <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm166743.htm> (last visited Dec. 5, 2013).

¹⁷⁹ Bulk Drug Substances That May Be Used to Compound Drug Products in Accordance With Section 503A of the Fed. Food, Drug, and Cosmetic Act; Request for Nominations, 78 Fed. Reg. 72841 (proposed Dec. 4, 2013) (to be codified at 21 C.F.R. undef). Bulk Drug Substances That May Be Used to Compound Drug Products in Accordance With Section 503B of the Federal Food, Drug, and Cosmetic Act, Concerning Outsourcing Facilities; Request for Nominations, 78 Fed. Reg. 72838 (proposed Dec. 4, 2013) (to be codified at 21 C.F.R. undef). Drug Products That Present Demonstrable Difficulties for Compounding Under Sections 503A and 503B of the Fed. Food, Drug, and Cosmetic Act; Request for Nominations, 78 Fed. Reg. 72840 (proposed Dec. 4, 2013) (to be codified at 21 C.F.R. undef).

¹⁸⁰ U.S. FOOD AND DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY: INTERIM PRODUCT REPORTING FOR HUMAN DRUG COMPOUNDING OUTSOURCING FACILITIES UNDER SECTION 503B OF THE FEDERAL FOOD,

for pharmacy compounding under the new Sec. 503A restates the requirements for exemption from enhanced FDA reporting and advertising restrictions, and emphasizes that the FDA will exercise enforcement authority over those entities that operate outside that exemption.¹⁸¹ The guidance states that the FDA will use a risk-based approach to discovering and investigating compounding pharmacies or outsource facilities to catch violations.¹⁸² However, these guidance documents leave the same loophole open for compounding facilities to decline registration with the FDA, claim compliance with state pharmacy laws, and potentially avoid heightened regulatory scrutiny. If compounding manufacturers, or outsource facilities, collectively decide not to register with the FDA, the Act leaves open many of the same concerns addressed above in Part IV (B).

Under the new law, forces beyond government regulation could also drive patient safety. With the new Act responsibility for ensuring safe drugs are administered to patients also falls to the clinics and hospitals that purchase these compound medications. If these vendors all decide to only purchase from outsource facilities that are registered with the FDA, then it may be seen as an indication of quality and become the industry standard.

The intended effect of the Act is to ensure more uniform nationwide compliance with safety procedures in outsourcing facilities, especially those that compound sterile preparations.

Consistent and rigorous compliance will lead to greater patient safety. The FDA is able to ensure

DRUG, AND COSMETIC ACT, (Dec. 4, 2013) *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-1428-0002> (last visited Dec. 9, 2013) (this has only been assigned a docket number as of yet, and has not been published in the Federal Register).

¹⁸¹ Guidance: Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act; Request for Comments, 78 Fed. Reg. 72901, 72901-2 (proposed Dec. 4, 2013) *available at* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM377051.pdf>.

¹⁸² *Id.*

compliance in the big pharmaceutical manufacturing facilities, with a proverbial carrot and stick approach. The Department of Justice offers an incentive to whistleblowers (relators) who report violations under the False Claims Act.¹⁸³ In those cases, if a relator reports information that results in a judgment the relator can receive up to thirty percent of the penalty assessed.¹⁸⁴ The big pharmaceutical companies do business in the millions or billions of dollars, and therefore have a lot to lose if they get hit with large civil and criminal monetary penalties for violations. The FDA should ensure that it uses these same incentives and penalties against outsource facilities, or compounding manufacturers who operate outside the law. This type of cash incentive should also be applied to whistleblowers that report compounding safety and quality violations, and hand out heavy monetary penalties to bad actors. The FDA should not hesitate to use individual exclusion from the Medicare/Medicaid reimbursement system, to prevent people like Barry Cadden, the CEO at NECC, or his partners, from reorganizing under a different company name after one has its license revoked for violations.

B. Conclusion

As this paper has presented, the former status quo ensuring the safety and quality of compounded drugs, especially sterile products, creates enforcement confusion and has resulted in contaminated drugs. The combination of FDAMA §503A in the Fifth Circuit, and the 2002 CPG everywhere else promoted a reactionary enforcement environment rather than a proactive regulation environment. The states and the FDA need a proactive and aggressive approach to ensure sterile products are produced in facilities that follow current GMPs, tailored to these businesses and their safety issues. Congress has acted to clarify the responsibilities and duties of both the FDA and the states, but it remains to be seen if this law will be adequate. In addition to

¹⁸³ 31 U.S.C. § 3729 et seq. (2012).

¹⁸⁴ 31 U.S.C. § 3730(d)(2)-(3) (2012).

the jurisdictional clarity, both state and federal enforcement authorities must take action and continue to keep the pressure on compounding facilities with risk-based inspections. The FDA currently oversees approximately 5,600 manufacturers,¹⁸⁵ and with the fiscal financial limits under sequestration it may be difficult, but it is necessary to prevent future public health crises.

¹⁸⁵ *House July 2013 Hearing, supra* note 101.