

ONE HUNDRED TWELFTH CONGRESS  
**Congress of the United States**  
**House of Representatives**  
COMMITTEE ON ENERGY AND COMMERCE  
2125 RAYBURN HOUSE OFFICE BUILDING  
WASHINGTON, DC 20515-6115

Majority (202) 225-2927  
Minority (202) 225-3641

**MEMORANDUM**

**November 13, 2012**

**To: Democratic Members of the Subcommittee on Oversight and Investigations**  
**Fr: Energy and Commerce Committee Democratic Staff**  
**Re: Hearing on “The Meningitis Outbreak: Could It Have Been Prevented?”**

On Wednesday, November 14, 2012, at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Oversight and Investigations will hold a hearing titled: “The Meningitis Outbreak: Could it Have Been Prevented?”

As of November 8, 2012, 438 people have contracted fungal meningitis and 32 people have died in 19 states after receiving injections of preservative-free (PF) methylprednisolone acetate (80mg/ml) compounded at the New England Compounding Center (NECC) in Framingham, Massachusetts.<sup>1</sup>

The Food and Drug Administration (FDA) and the Massachusetts Board of Registration in Pharmacy (the Board) have a significant history of inspection and enforcement activities related to NECC and associated companies Ameridose and Alaunus. The hearing provides an opportunity to examine these past interactions and understand what actions state and federal authorities could have taken to prevent the outbreak. The hearing is also an opportunity to discuss the patchwork of laws governing pharmacy compounding. Legal authority over pharmacy compounding has been complicated by court decisions that have cast doubt on FDA’s authority to regulate compounders. Compounders operate in a regulatory gap between state regulated pharmacies and federally regulated drug manufacturers.

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<sup>1</sup> Centers for Disease Control and Prevention, *Multistate Fungal Meningitis Outbreak investigation: Current Situation* (Nov. 12, 2012) (online at [www.cdc.gov/HAI/outbreaks/currentsituation/](http://www.cdc.gov/HAI/outbreaks/currentsituation/)).

## I. BACKGROUND

The first case of meningitis linked to steroid injections was reported to the Centers for Disease Control (CDC) by the Tennessee Department of Health on September 21, 2012; within a week, the first case and numerous other cases had been linked to injections from NECC. FDA, CDC, and Massachusetts officials have worked with NECC and state and local health departments across the nation to recall products potentially linked to the outbreak and to contact approximately 14,000 patients that may have received injections.<sup>2</sup>

Preliminary investigations by FDA and the Massachusetts Board of Health identified significant problems with sterilization processes and cleanliness at the NECC facility that produced the drugs.<sup>3</sup> NECC, along with Ameridose and Alaunus Pharmaceuticals - two related companies with which NECC shares common ownership - have temporarily ceased operations, recalled their products, and key company officials have voluntarily surrendered their licenses to practice pharmacy.<sup>4</sup> The Director of the Board has been terminated from his position. The Director of the Department of Health's Division of Health Professions Licensure and a Board attorney have been placed on administrative leave.<sup>5</sup> A Board member who is also a senior Ameridose official has been asked to resign her position on the Board.<sup>6</sup> FDA, the Department of Justice (DOJ), the Massachusetts Attorney General, and states across the country are conducting criminal investigations into the circumstances surrounding the outbreak.<sup>7</sup>

## II. REGULATION OF COMPOUNDING PHARMACIES

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<sup>2</sup> *Id.*

<sup>3</sup> Food and Drug Administration, *Form 483 Issued to Barry Cadden* (Oct. 26, 2012) and Massachusetts Department of Public Health, Board of Registration in Pharmacy Report, *New England Compounding Center: Preliminary Investigation Findings* (Oct. 23, 2012).

<sup>4</sup> See U.S. Food and Drug Administration, *FDA Reports Voluntary Recall of All Ameridose Drug Products* (Oct. 31, 2012) (online at [www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm326361.htm](http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm326361.htm)) and Massachusetts Department of Public Health, Board of Registration in Pharmacy Report, *New England Compounding Center: Preliminary Investigation Findings* (Oct. 23, 2012).

<sup>5</sup> Briefing by Dr. Lauren Smith, Interim Director, Massachusetts Department of Public Health to House Energy and Commerce Committee Majority and Minority Staff (Nov. 12, 2012) and Massachusetts Department of Public Health, *Statement of Interim Commissioner Dr. Lauren Smith on NECC Investigation* (Nov. 7, 2012) (online at [www.mass.gov/eohhs/docs/dph/quality/boards/pharmacy/121107-statement-from-lauren-smith.pdf](http://www.mass.gov/eohhs/docs/dph/quality/boards/pharmacy/121107-statement-from-lauren-smith.pdf)).

<sup>6</sup> *State Wants Pharmacist To Resign As A Regulator*, The Boston Globe (Oct. 28, 2012).

<sup>7</sup> See *Feds Open Criminal Inquiry Into Firm Linked to Deadly Meningitis Outbreak*, CNN (Oct. 23, 2012); *Mass. AG Enters Probe of Meningitis Outbreak*, Boston Globe (Oct. 11, 2012); *U.S. States Raise Heat on Company Linked to Deadly Meningitis Outbreak*, Reuters (Oct. 13, 2012).

Traditional drug compounding involves the mixing or altering of FDA-approved medications by pharmacists to fulfill the special needs of individual patients, such as individuals with specific allergies or young children who cannot tolerate FDA-approved dosage forms.<sup>8</sup> Because these pharmacies are creating a new drug product, they technically fall under FDA's regulatory authority.<sup>9</sup> However, according to FDA, the agency "has historically exercised enforcement discretion and generally has not taken enforcement action against pharmacies engaged in traditional compounding."<sup>10</sup> These traditional compounding pharmacies are regulated at the state level, typically by state pharmacy boards.<sup>11</sup>

However, numerous pharmacy compounders have gone beyond the traditional practice of pharmacy compounding, mixing bulk quantities of raw materials to make new drugs, copy FDA approved products, and sell large volumes of products at the wholesale level.<sup>12</sup> These compounders act more like drug manufacturers than traditional compounding pharmacies. The dual nature of these pharmacies raises questions about appropriate regulatory authority because pharmacies are traditionally regulated at the state level and drug manufacturers are regulated at the federal level by FDA.<sup>13</sup>

In 1997, Congress included several new provisions regulating the practice of pharmacy compounding in the Food and Drug Administration Modernization Act (FDAMA).<sup>14</sup> Section 503(A) of the law exempted compounded drugs from the other requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), so long as the pharmacy was licensed in a state, made the drug pursuant to a valid prescription for an individual patient, limited interstate shipments to no more than 5% of the its business, and did not engage in advertising or promotion.<sup>15</sup> Section 503(A) also states that compounders may not "compound regularly or in inordinate amounts ... any drug products that are essentially copies of a commercially available drug product."<sup>16</sup>

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<sup>8</sup> See American Pharmacists Association, *The Art, Science and Technology of Pharmaceutical Compounding, Chapter 1* (July 25, 2012).

<sup>9</sup> Food and Drug Administration, *2006 FDA Survey of Compounded Drugs* (online at [www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm](http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm)).

<sup>10</sup> *Id.*

<sup>11</sup> *Id.*

<sup>12</sup> Office of Representative Ed Markey, *Compounding Pharmacies, Compounding Risk* (Oct. 29, 2012).

<sup>13</sup> Congressional Research Service, *FDA's Authority to Regulate Drug Compounding: A Legal Analysis* (Oct. 17, 2012).

<sup>14</sup> Pub.L. No.105-115, (1997).

<sup>15</sup> Pub.L. No.105-115, §503(A) (1997).

<sup>16</sup> *Id.*

Before the law could take effect, compounding pharmacies challenged the advertising and promotion restrictions in Section 503(A) in federal court.<sup>17</sup> The Ninth Circuit Court found that Section 503(A)'s ban on advertising and promotion was an unconstitutional limit on free speech. It also found that the unconstitutional provisions could not be severed from Section 503(A) and that the entire section was therefore void.<sup>18</sup> Subsequently, the Supreme Court agreed that the advertising and promotion ban was unconstitutional, but did not comment on the 9th Circuit ruling that the unconstitutional provisions could not be severed from Section 503(A) and that the entire section was therefore void.<sup>19</sup>

Following the Supreme Court's ruling, there continued to be confusion over whether FDA retained authority to regulate compounded drugs under section 503(A). To resolve this confusion, FDA issued its 2002 Compliance Policy Guide, which outlined the agency's authority over compounders and how it planned to use its enforcement discretion.<sup>20</sup> FDA stated that it would rely heavily on state oversight of compounders and focus its enforcement on compounding pharmacies that were producing large quantities of drugs without valid prescriptions, producing commercially available products, selling drugs wholesale or to third parties for resale, or otherwise violating the new drug, adulteration, or misbranding provisions of the FDCA.<sup>21</sup>

In 2004, compounding pharmacies challenged FDA's authority more broadly, arguing that FDA could not regulate compounded drugs as "new drugs" under the FDCA.<sup>22</sup> In 2008, the Fifth Circuit Court of Appeals found that compounded drugs were "new drugs" and were subject to the FDCA's drug approval, adulteration, and misbranding requirements.<sup>23</sup> The Court went further still and disagreed with the Ninth Circuit's view on the severability of Section 503(A), effectively reinstating Section 503(A) within the Fifth Circuit's jurisdiction - Texas, Louisiana, and Mississippi. Throughout the rest of the country not covered by the Fifth or Ninth Circuit decisions, it remains unclear whether the constitutional components of Section 503(A) remain in force. FDA has therefore continued to exercise its authority under the FDCA in accordance with its 2002 Compliance Policy rather than Section 503(A).

Outside of the Fifth Circuit, the degree to which FDA's 2002 Compliance Policy sets binding legal standards on compounders is in dispute. Governed primarily by agency guidance

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<sup>17</sup> *Western States Medical Center, et al. v. Shalala*, 69 F. Supp. 2d 1288 (D. Nev. 1999).

<sup>18</sup> *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002).

<sup>19</sup> See Congressional Research Service, *FDA's Authority to Regulate Drug Compounding: A Legal Analysis* (Oct. 17, 2012).

<sup>20</sup> Food and Drug Administration, *Compliance Policy Guides Manual §460.200, Pharmacy Compounding* (May 2002) (online at [www.fda.gov/ora/compliance\\_ref/cpg/cpgdrg/cpg460-200.html#BACKGROUND](http://www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg460-200.html#BACKGROUND)).

<sup>21</sup> *Id.*

<sup>22</sup> *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383 (5th Cir. 2008).

<sup>23</sup> *Id.*

that lacks the force of agency rules, the current system has been criticized as “lack[ing] a clear description of the circumstances under which the agency will take action against pharmacies.”<sup>24</sup> The nonpartisan Congressional Research Service concluded that “the question of how FDA may regulate compounded drugs may not be settled unless Congress takes legislative action.”<sup>25</sup>

### III. HISTORY OF NECC, AMERIDOSE, AND ALANUS

The New England Compounding Center (NECC) was founded in 1998 by Barry Cadden and his brother-in-law, Greg Conigliaro. It was licensed as a pharmacy with the Commonwealth that same year.<sup>26</sup> By 2003, NECC was marketing and selling products in every state in the country.<sup>27</sup>

In 2006, Mr. Cadden and Mr. Conigliaro founded Ameridose. Initially located in the same office complex as NECC, Ameridose was licensed by the Commonwealth of Massachusetts as a specialty pharmacy and by FDA as a drug manufacturer.<sup>28</sup>

In 2009, Mr. Cadden and Mr. Congiliaro founded Alaunus Pharmaceuticals, a wholesale pharmaceutical distributor.<sup>29</sup> The corporate website states that Alaunus is an “emerging pharmaceutical company that identifies, develops, and markets generic pharmaceutical products to physicians and pharmacies throughout the United States” and says that the company “has several products under development.”<sup>30</sup>

Mr. Cadden, Mr. Conigliaro, and members of their families are the principal owners of NECC, Ameridose, and Alaunus.<sup>31</sup>

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<sup>24</sup> See Congressional Research Service, *FDA’s Authority to Regulate Drug Compounding: A Legal Analysis*, at 9 (Oct. 17, 2012) and Kevin Outterson, *Regulating Compounding Pharmacies after NECC*, *New England Journal of Medicine* (Nov. 7, 2012).

<sup>25</sup> Congressional Research Service, *FDA’s Authority to Regulate Drug Compounding: A Legal Analysis*, at 8 (Oct. 17, 2012).

<sup>26</sup> Massachusetts Board of Registration in Pharmacy, *Application for a New Store: New England Compounding Pharmacy, Inc.* (Feb. 9, 1998).

<sup>27</sup> Food and Drug Administration, *Establishment Inspection Report Attachment, New England Compounding Center*, at 5 (Feb. 10, 2003).

<sup>28</sup> *Merging of Families Fueled Businesses Linked to Meningitis Outbreak*, *The Boston Globe* (Oct. 18, 2012).

<sup>29</sup> *Id.*

<sup>30</sup> Alaunus Pharmaceuticals, *About Alaunus* (online at [www.alaunuspharma.com/about.html](http://www.alaunuspharma.com/about.html)) (accessed Nov. 11, 2012).

<sup>31</sup> Briefing from Counsel for NECC to House Energy and Commerce Committee Majority and Minority Staff (Nov. 2, 2012).

NECC and Ameridose have grown rapidly. In 2008, two years after its founding, Ameridose expanded to a new 76,000-square-foot location.<sup>32</sup> Since 2008, the firm's workforce has grown from 50 workers to close to 400.<sup>33</sup> NECC has doubled its workforce over the past three years to nearly 50 employees.<sup>34</sup>

#### IV. THE MASSACHUSETTS BOARD OF REGISTRATION IN PHARMACY

The Massachusetts Board of Registration in Pharmacy is authorized under Massachusetts law as a professional licensure board within the Department of Public Health.<sup>35</sup> The Board is comprised of 11 members who are appointed to five year terms by the Governor.<sup>36</sup> The Board is charged with licensing pharmacists and pharmacies, promulgating regulations, conducting inspections, and imposing discipline "to maintain pharmacists' professional competencies and to promote the highest standards of professional practice."<sup>37</sup>

At least seven members of the current Board have served since at least 2004, with some initially appointed as early as 1998.<sup>38</sup> One member of the Board, Sophia Pasedis, is a member of Ameridose's executive team, serving as Vice President of Regulatory Affairs and Compliance.<sup>39</sup> Ms. Pasedis has also been listed as the Manager of Record at an Ameridose facility in 2010 and

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<sup>32</sup> *Merging of Families Fueled Businesses Linked to Meningitis Outbreak*, The Boston Globe (Oct. 18, 2012).

<sup>33</sup> *Id.*

<sup>34</sup> *Id.*

<sup>35</sup> M.G.L. c. 13 §9.

<sup>36</sup> *See* M.G.L. c. 13 §22 and M.G.L. c. 13 §9.

<sup>37</sup> *See* M.G.L. c. 13 § 9; M.G.L. c. 112, §§ 24 - 42; 247 CMR 4.00.

<sup>38</sup> *See* Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 10, No. 11 (Oct. 2002); Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 11, No. 1 (Apr. 2004); Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 11, No. 2 (Aug. 2004); Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 11, No. 3 (Dec. 2004); Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 11, No. 4 (Apr. 2005); Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 12, No. 1 (July 2005); and Massachusetts Board of Registration in Pharmacy Newsletter, MA Vol. 12, No. 2 (Apr. 2006). Sophia Pasedis, Steven Budish, George A. Cayer, and Donald D. Accetta, appointed 2004; Kathy J. Fabiszewski, appointed 2005; James DeVita, appointed 1999; Karen Ryle, appointed 1998.

<sup>39</sup> *State Wants Pharmacist To Resign As A Regulator*, The Boston Globe (Oct. 28, 2012).

the pharmacist in charge at an Ameridose facility in 2012.<sup>40</sup> Ms. Pasedis also served as Director of Pharmacy Services at NECC in 2005.<sup>41</sup>

## V. FEDERAL AND STATE INSPECTIONS, OVERSIGHT AND ENFORCEMENT ACTIONS

NECC, Ameridose, and Alaunus have been the subject of state and federal inspections, oversight, and enforcement on numerous occasions. In the past, NECC has drawn state and federal scrutiny for producing products without a patient specific prescription, for failing to follow proper record keeping and compounding practices, and for instances in which products have been implicated in adverse drug events.<sup>42</sup> Prior to the current outbreak, NECC has recalled products on at least two occasions following adverse events and been the subject of numerous state and federal complaints and investigation actions.<sup>43</sup> Ameridose has been inspected by state and federal officials on at least five occasions but has never faced an enforcement action prior to this current outbreak.<sup>44</sup> The Majority Memorandum released on November 12, 2012, contains a detailed description of these interactions.

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<sup>40</sup> Ameridose LLC., *Application for Licensure as a Wholesale Distributor, List of Personnel with Power of Attorney for Controlled Substances* (May 9, 2012) and Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Investigative Report, PHA-201-0107 and PHS-2010-0108* (Feb. 10, 2011).

<sup>41</sup> E-mail from Sophia Pasedis, Member, Massachusetts Board of Registration in Pharmacy, to Steve Perry (Dec. 6, 2005).

<sup>42</sup> See, e.g. Food and Drug Administration, *Warning Letter to Barry J. Cadden, NEW-06-07W* (Dec. 4, 2006); Massachusetts Board of Registration in Pharmacy, *Consent Agreement, In the Matter of New England Compounding Center and Barry J. Cadden, Docket Numbers DS-03-055, PH 03-066, and DS 05-040* (Jan. 10, 2006); Massachusetts Department of Public Health, Division of Health Professions Licensure, *Investigation Report: Barry J. Cadden* (Nov. 23, 2004); Massachusetts Department of Public Health, Division of Health Professions Licensure, *Investigation Report: New England Compounding Center and Barry J. Cadden* (Mar. 4, 2004); Food and Drug Administration, *Establishment Inspection Report Attachment, New England Compounding Center* (Feb. 10, 2003); Food and Drug Administration, *Memorandum from Kristina Joyce, Consumer Safety Officer and Mark Lookabaugh, Compliance Officer to Central File* (Feb. 24, 2003).

<sup>43</sup> See, e.g. Food and Drug Administration, *Memorandum from Kristina Joyce, Consumer Safety Officer and Mark Lookabaugh, Compliance Officer to Central File* (Feb. 24, 2003); Food and Drug Administration, *Establishment Inspection Report Attachment, New England Compounding Center* (Feb. 10, 2003).

<sup>44</sup> Food and Drug Administration, *Form 483 Issued to Greg Conigliaro*, at 12 (Nov. 9, 2012); Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Investigative Report, PHA-201-0107 and PHS-2010-0108* (Feb. 10, 2011); Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Inspection Report: Ameridose, LLC* (Nov. 19, 2008); Food and Drug Administration, *Establishment Inspection Report: Ameridose LLC* (Dec.

The most recent inspections of NECC and Ameridose occurred in September and October 2012 after NECC was identified as the source of the meningitis outbreak. These inspections have found significant problems with sterility, cleanliness, record keeping, and overall quality control at both NECC and Ameridose.<sup>45</sup> Among other problems at NECC, FDA and Massachusetts investigators found “greenish black foreign matter” and “white filamentous material” in recalled lots, “visibly soiled” floor mats, and large batches of product that were distributed to facilities without patient specific prescriptions.<sup>46</sup> FDA also found that NECC’s own monitoring systems had identified unsafe levels of bacteria and mold but the company had taken no action.<sup>47</sup>

At Ameridose, FDA observed a similar set of problems to those identified at NECC. FDA found that “procedures designed to prevent microbiological contamination of products...are not established, written, and followed.”<sup>48</sup> FDA found that gowns and gloves were not sterile, and that environmental and personnel monitoring were not performed appropriately.<sup>49</sup> FDA found that equipment and utensils were not adequately cleaned, that insects were present within ten feet of where products are manufactured, and that a bird was present in building where sterile products are packaged and stored.<sup>50</sup> FDA also found that Ameridose failed to investigate contamination it observed at least 53 times during sterility testing of stock solutions and failed to investigate adequately complaints and to properly classify adverse events associated with products. Improperly classified adverse events included “increased cases of post-partum hemorrhaging,” “an over-sedated, unresponsive” patient, “respiratory distress”, and another unspecified life-threatening adverse event<sup>51</sup>

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7, 2007); Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Inspection Report: Ameridose, LLC* (July 13, 2006).

<sup>45</sup> Food and Drug Administration, *Form 483 Issued to Barry Cadden* (Oct. 26, 2012) and Food and Drug Administration, *Form 483 Issued to Greg Conigliaro* (Nov. 9, 2012).

<sup>46</sup> Food and Drug Administration, *Form 483 Issued to Barry Cadden* (Oct. 26, 2012) and Massachusetts Department of Public Health, Division of Health Professions Licensure, Board of Registration in Pharmacy, *Preliminary Investigation Findings: New England Compounding Center* (Oct. 23, 2012).

<sup>47</sup> Food and Drug Administration, *Form 483 Issued to Barry Cadden* (Oct. 26, 2012)

<sup>48</sup> Food and Drug Administration, *Form 483 Issued to Greg Conigliaro*, at 12 (Nov. 9, 2012).

<sup>49</sup> *Id.*

<sup>50</sup> *Id.* at 15, 18.

<sup>51</sup> *Id.* at 2, 4, 5.

**VI. WITNESESS**

The following witnesses have been invited to testify:

**Ms. Joyce Lovelace**  
Albany, KY

**Mr. Barry J. Cadden**  
Founder/Co-President  
New England Compounding Center  
Ameridose  
Alaunus Pharmaceuticals

**The Honorable Margaret Hamburg**  
Commissioner  
Food and Drug Administration

**Dr. Lauren Smith**  
Interim Commissioner  
Massachusetts Department of Public Health