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## **Compound Fracture**

**Bills Will Not Fix FDA's Broken Oversight of Drug Compounding**

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In September 2012, a 78-year old judge named Eddie Lovelace died in Nashville, Tennessee, from an apparent stroke.<sup>1</sup> His death was later revealed to be the first in an unprecedented outbreak of fungal meningitis and joint infections associated with a contaminated drug produced by the New England Compounding Center (NECC), in Framingham, Massachusetts. Drug compounding involves reformulating or repackaging approved medicines to better tailor their use to individual patients' needs. Compounded drugs are not subject to premarket approval like mass-produced medicines, but pharmacies that produce them are regulated by state governments and often by the U.S. Food and Drug Administration (FDA).

After additional cases of fungal meningitis began to appear, public health officials traced the problem to preservative-free doses of injectable methylprednisolone, sold by NECC to treat spine and joint problems. An estimated 14,000 patients in 76 hospitals, medical centers, and clinics in 23 states received injections from the batches of contaminated vials.<sup>2</sup> At least 750 patients have been infected and 64 have died.<sup>3</sup> Within weeks of Lovelace's death, the FDA instructed NECC to recall thousands of potentially contaminated doses of at least nine of its products. The production facility was shut down, and NECC was forced to surrender its pharmacy license to the Massachusetts Board of Registration in Pharmacy (MBRP).<sup>4</sup>

The FDA's response did not end there, however. In the face of growing criticism from the medical community, the news media, and Congress for allegedly lax agency oversight, FDA officials went into overdrive to shift responsibility and deny any role in the tragedy. Even though the agency had inspected the NECC facility and threatened enforcement action several times before the meningitis outbreak, senior FDA officials claimed the agency was powerless to have prevented the outbreak and insisted it needed

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additional authority to prevent such problems from occurring again. It did not take long for members of Congress to introduce new legislation to hand the agency such power.

Yet, the real problem behind this tragedy is not one of FDA impotence. Agency officials have indirectly acknowledged in congressional hearings that they already possess sufficient authority to have prevented the meningitis outbreak.<sup>5</sup> Arguably, the problem can be chalked up to *over*-regulation and the agency's abuse of its existing enforcement discretion. The FDA has long neglected its existing authority to regulate large-scale drug compounding, even as agency inspectors knew of specific quality control problems at the NECC facility. In stark contrast, in recent years the agency has become distracted by ever more aggressive enforcement of minor regulatory infractions against manufacturers of approved drugs. All the while, a host of other public policies have contributed to a rapidly rising demand for compounded medicines.

Adding new federal regulations to further restrict compounding would do little but raise the price and reduce the availability of important products for patients who need them.

**What Is Compounding?** Compounding pharmacies create customized drugs that are not available on the normal FDA-regulated market, generally by reformulating, repackaging, or changing the dosage of already approved products, or by combining two or more approved ingredients into single, multi-drug doses. This allows physicians and pharmacists to better tailor drugs to their individual patients' specific medical needs.

For example, some patients may be unable to take off-the-shelf medicines because of an allergy to coloring agents, preservatives, or other inactive ingredients. In many such cases, a pharmacist can reformulate the active components into a product that does not contain the problem-causing inactive ingredients. Other patients, including children, may be unable to swallow pills, so a compounding pharmacy may transform pills into liquids for easier use, or add a flavoring agent to make the medicine more palatable. Compounders also frequently repack large, multi-dose vials of sterile injectable medicines into single-use doses.

Because compounded drugs are intended to be customized for individual patients, compounding pharmacies are exempted from FDA regulations applicable to conventional drug manufacturers.<sup>6</sup> The exemption applies when drugs are compounded to fill a physician's prescription written for a specific patient. In such cases, the compounding pharmacy is regulated by a state agency—typically the board of pharmacy in the state where the compounding is done.

The exemption is not applicable when a pharmacy produces large quantities of compounded drugs for broad distribution, which is legally considered to be “manufacturing” and is regulated by both the state pharmacy board and the FDA. However, where a pharmacy produces small batches of compounded drugs in anticipation of receiving individual prescriptions, the FDA tends to use its enforcement discretion and defers to state oversight.

The FDA also has oversight authority when:

- Any bulk ingredients used by a compounding pharmacy are not already approved by the agency;
- The compounding is done for third parties for resale; or
- The pharmacy replicates drugs that are commercially available from an FDA-regulated manufacturer.<sup>7</sup>

However, the FDA has often turned a blind eye toward even large-scale compounding, preferring for state regulators to perform the bulk of enforcement activity even when FDA inspectors have identified quality control problems.

**Growth in the Market for Compounded Drugs.** Until the 1950s, around 80 percent of the prescriptions filled in the United States were compounded.<sup>8</sup> But after passage of the Drug Act Amendments of 1962, which substantially increased the premarket approval requirements for pharmaceuticals, large FDA-regulated manufacturers soon came to dominate the market with mass-produced drugs. Most pharmacies remained capable of preparing compounded medicines, but the typical pharmacist became more a dispenser of mass-manufactured drugs than a producer of custom-made products.

In recent years, however, demand for compounded drugs has rebounded significantly, giving rise to an industry of specialist compounding pharmacies. By 2006, an estimated 5 percent of the total of 30 million prescriptions written in the U.S. each year was being filled by dedicated compounding pharmacies.<sup>9</sup> And over the past decade, these specialized pharmacies have taken ever greater advantage of their ability to supply physicians and patients with both traditionally compounded drugs and slightly altered or repackaged versions of commercially available mass-produced products. Today, roughly half of the nation's 56,000 pharmacies are capable of offering basic compounding services, and the number of dedicated compounding pharmacies has increased to 7,500.<sup>10</sup>

The reasons for this rapid growth in compounding pharmacies are many, but two major contributing factors appear to be the sharp increase in drug shortages during the last decade and a desire to source lower-priced versions of commercially available, mass-produced drugs.

**Compounding Pharmacies Offer Relief from Shortages.** Since 2006, the number of drug shortages has increased by more than four times, from 70 that year to 300 in April 2013.<sup>11</sup> Roughly 80 percent of the shortages are of sterile injectable drugs that are used every day to treat cardiac patients, surgical patients undergoing anesthesia, psychiatric patients, seizure patients, and cancer patients.<sup>12</sup> They include—in addition to injectable, sterile methylprednisolone—numerous injectable cancer treatments, the heart medicine nitroglycerine, the injectable analgesic fentanyl, injectable ophthalmologic drugs used for eye surgery, the numbing solution lidocaine, the pain killers morphine and hydromorphone, the injectable hypnotic agent propofol, which is used to induce and maintain general anesthesia, and the first-line anti-tuberculosis drug, isoniazid (INH), which has been in use since 1951.<sup>13</sup>

In 2011, more than 80 percent of hospitals were forced to delay treatment for some patients because of a drug shortage, according to an American Hospital Association survey.<sup>14</sup> Thus, an increasing number of hospitals, neighborhood pharmacies, and clinics have turned to compounding pharmacies for their critical medical supply needs.

Although shortages and supply disruptions occur for a number of reasons, such as a lack of raw materials, unanticipated high demand, and manufacturer decisions to reduce production or discontinue a product, aggressive FDA enforcement actions have also been a major contributor to the problem. A June 2012 report by the U.S. House of Representatives Committee on Oversight and Government Reform concluded that widespread shortages of generic injectable drugs are due to two main factors:

1. Reduced profitability and growing market concentration for several classes of drugs over the past decade; and
2. Increased FDA enforcement and regulation, which “has shut down a substantial amount of manufacturing capacity.”<sup>15</sup>

Despite acknowledging the complex interplay of several factors, the report was clear: “FDA actions over the past several years are the primary reason for the severity of the drug shortage crisis.”<sup>16</sup>

**Overzealous FDA Enforcement.** In recent years, the agency has become far more aggressive in its enforcement actions against licensed drug manufacturing facilities. The number of FDA warning letters, which often result in the closing of a manufacturing facility, increased by 42 percent between 2009 and 2010, and by an additional 156 percent between 2010 and 2011.<sup>17</sup> Today, about 30 percent of the capacity to produce sterile, injectable drugs at the largest generic drug makers has been curtailed because of FDA enforcement actions.<sup>18</sup>

Such quality or safety concerns are often merited, but, as health policy expert John Goodman notes, the agency’s rules are “rigid, inflexible, and unforgiving.”<sup>19</sup> It has instituted a strict “zero tolerance” policy for manufacturing facilities. At times, this results in shutting down facilities for paperwork violations, inappropriate handling issues that would not materially impact safety or efficacy, or even small quality control problems. And rather than work with the firms to remediate minor problems quickly, while the facility remains online, FDA rules too often require closing such facilities altogether.

In most cases, the temporary closing of a production facility occurred because quality control problems were suspected of compromising the safety or efficacy of a manufacturer’s drug. However, the House Oversight and Government Reform Committee report also found no evidence that drugs from any of the facilities involved had actually harmed patients. Nevertheless, when drug manufacturing facility closures result in drug shortages, physicians and hospitals are often forced to source drugs from compounding pharmacies.<sup>20</sup>

**Price Controls and Industry Economics.** Two economic factors contribute to the spate of drug shortages:

1. High fixed costs associated with producing FDA-regulated medicines; and
2. Increasing pressure from insurers and government health care programs to lower drug prices.

Many of the drugs in short supply are generic products that command very thin profit margins, so only a small number of manufacturers produce the drugs, and they attempt to limit production to the smallest level that will satisfy current demand. When one of these manufacturers leaves the market, has a supply chain problem, or is temporarily closed by the FDA, a shortage of the drug is more likely to occur.

For example, demand for NECC's sterile injectable methylprednisolone greatly increased after the two FDA-approved manufacturers left the business because of FDA actions at their manufacturing plants.<sup>21</sup> Sterile injectable generic drugs, such as injectable methylprednisolone, have higher manufacturing costs and lower profit margins than those of other, simpler drugs.

Shortages persist at times even when the drug in question is produced by multiple manufacturers, because the FDA not only regulates the safety and effectiveness of drugs, but also the quantities produced and their schedules of production.<sup>22</sup> This means that if a shortage arises because one manufacturer is no longer producing a given product, competing manufacturers cannot respond by increasing their own output without securing FDA approval, which generally cannot be obtained quickly.

Government price controls also play a role in drug shortages by making low-profit margin products uneconomical to produce. Price controls date from at least 1992, when Congress created the federal 340B drug rebate program to help uninsured and indigent patients receive important medicines. The law requires drug manufacturers to give significant discounts to Public Health Service hospitals and clinics and to others that have a large number of indigent and Medicaid patients. In 2002, around 8,000 hospitals and clinics were eligible for discounted drugs. By 2011 this number had nearly doubled,<sup>23</sup> leading some to speculate that physicians and clinics may be skewing their prescription decisions to take undue advantage of the program. Whether this is true or not, the program's dramatic growth has put unanticipated downward pressure on drug prices.

In 2003, Congress added additional price controls in an attempt to further reduce drug prices. The Medicare Prescription Drug Improvement and Modernization Act of 2003 fixes the price Medicare will pay for drugs to a government-estimated "average sales price" plus 6 percent. It also restricts the calculated average price from increasing by more than 6 percent every six months.<sup>24</sup> In addition to reducing the incentives for manufacturers to produce drugs with very small profit margins, this pricing rigidity means that when drug shortages arise, prices—which are already too low—cannot increase appropriately to incentivize doctors to conserve on their use of the scarce products or to attract manufacturers to increase their production to meet the market demand.

**FDA Regulatory Failure.** The FDA’s hyper-aggressiveness in shutting down licensed pharmaceutical manufacturing facilities stands in stark contrast with its enforcement approach to compounding pharmacies that are effectively engaged in manufacturing. Indeed, the FDA had inspected the New England Compounding Center on several occasions prior to the 2012 meningitis outbreak and had repeatedly identified contamination problems, but failed to take any meaningful action.

The Massachusetts Board of Registration in Pharmacy had also repeatedly documented contamination problems and cited NECC for possible safety violations as far back as 1999, the year after the compounding center began operations.<sup>25</sup> MBRP had investigated 12 separate complaints since that time, several of which were associated with serious adverse events.

The FDA inspected NECC in April and in October 2002, after a spate of adverse event reports indicated contamination issues. The Center was cited both times for lack of sterility and threatened with enforcement action if it did not address the problems. The FDA and MBRP conducted a joint inspection of the NECC facility in September 2004, following complaints by pharmacists who alleged that the Center was acting as a manufacturing pharmacy—compounding copies of FDA-approved drugs available from commercial manufacturers.<sup>26</sup> But it was not until December 4, 2006 that FDA issued a warning letter regarding its findings from the inspection that occurred over two years earlier.

The warning letter claimed NECC was guilty of compounding and distributing copies of FDA-approved drugs, compounding drugs without valid prescriptions for individual patients, misbranding local anesthetic drug products, and repackaging an approved injectable drug without individual prescription orders.<sup>27</sup> NECC denied all of FDA’s allegations in a letter the following month, January 2007. For some reason, however, the FDA delayed its response to the NECC’s denials for another two years, until October 31, 2008, when the agency threatened enforcement action due to the findings of its September 2004 inspection. Startlingly, though, FDA took no further action against NECC, despite continuing to receive numerous complaints about the Center’s products and practices, including many that questioned the safety of its products.<sup>28</sup>

When investigators inspected the Center after the meningitis outbreak, they found “greenish-black foreign matter” in vials of methylprednisolone. They also discovered that NECC’s own environmental monitoring program had documented the presence of bacteria and mold in two of its clean rooms on at least 79 occasions between January and September of 2012. That is, NECC’s own records indicated that the Center’s employees were fully aware of the potential for contamination, but these results had not been investigated.<sup>29</sup>

Hearings in November 2012 and April 2013 by the House Committee on Energy and Commerce’s Subcommittee on Oversight and Investigation documented that the FDA had known for years that NECC was a manufacturing pharmacy and that the agency had

clear authority to regulate it. The committee compiled, from submitted FDA documents, a list of more than 30 complaints and adverse event reports, many concerning NECC, which the agency had received over the 10-year period from March 2002 to July 2012.<sup>30</sup>

The message was clear: The FDA was fully aware of NECC's quality control problems and was aware that NECC's mass production of compounded drugs made it subject to federal authority. Seeking to deflect criticism, however, FDA Commissioner Margaret Hamburg testified that the agency faced "complex issues" that prevented effective oversight, and she repeatedly requested that Congress pass new legislation in order to give the agency more authority. But she could not explain why the agency had not taken enforcement action to prevent the outbreak, stating only: "We should have been more aggressive," and "I regret that we didn't do more."<sup>31</sup>

The hearings also revealed that FDA had suspended all inspections and enforcement actions against compounding pharmacies, including NECC, for a year, from 2011 until the 2012 outbreak occurred, for which Hamburg provided no explanation. She also did not explain why, in an about-face early in 2013, the agency was able to complete nearly 50 inspections of compounding pharmacies that resulted in product recalls by five firms.

Similarly, Dr. Lauren Smith, interim commissioner of the Massachusetts Department of Public Health, in testimony at the November 14, 2012 hearings, admitted her agency had the authority to shut down compounding pharmacies and that it had acted too slowly.<sup>32</sup> But other witnesses, including Dr. Madeline Brondolillo, Director of the Massachusetts Department of Public Health's Bureau of Health Care Safety and Quality, demanded a stepped-up federal response anyway.

At no time did FDA or Massachusetts officials acknowledge their own complicity in the NECC outbreak. Nor did they seem to recognize that excessive regulatory burdens might contribute to greater problems for patients by restricting the source and raising the price of essential treatment options for thousands, if not millions, of Americans.

**Congress' Response.** In the wake of the fungal meningitis outbreak, the news media, public health advocates, and other experts demanded explanations. Both state and federal regulators, wishing to deflect blame from their own lapses, called for new restrictions on compounding and new enforcement authority for themselves. Members of Congress rushed to provide the new laws, even though at best the proposals would mask the symptoms, not treat the underlying causes. Few stopped long enough to ask whether regulatory agencies had sufficient oversight authority already and whether regulators simply failed in their duties. The so-called crisis became an excuse to expand the FDA's power.

Mere weeks after the FDA traced the meningitis outbreak to the NECC's products, Massachusetts representative Edward Markey introduced the Verifying Authority and Legality in Drug (VALID) Compounding Act—reintroduced with minor changes in the 113<sup>th</sup> Congress as H.R. 2186.<sup>33</sup> It would require a valid prescription order written for an individually named patient—except in the case of a drug shortage—before a pharmacy

could legally compound a drug unless the pharmacy registers with the FDA and meets certain, as yet undetermined, safety standards. That would prevent compounders from preparing even small batches of specialty products ahead of individualized orders.

The bill would also reinforce the existing prohibition on compounding drugs that are commercially available from FDA-licensed manufacturers, but add an exception for cases in which there is a commercial shortage in those products. It would authorize the FDA to maintain a list of drugs and dosages that may never be compounded and authorize the agency to forbid the use of certain ingredients in compounding. It would further institute for all compounding pharmacies:

1. New FDA registration;
2. New inspection procedures;
3. Annual registration fees;
4. Fees for each inspection.

By August 2013, the bill had been the subject of several hearings by the House Energy and Commerce Committee, which was simultaneously considering a bill reported by the Senate Health, Education, Labor, and Pensions (HELP) Committee.

The Pharmaceutical Quality and Accountability Act (S. 959) was reported out of the Senate HELP Committee in May 2013.<sup>34</sup> In addition to its compounding rules, the bill includes a broad number of new, generally applicable regulatory requirements for licensed drug manufacturers, distributors, and pharmacies. For drug compounders, it would establish a new regulatory category for “compounding manufacturers” that would encompass, among others, any pharmacy that compounds sterile products prior to receiving individual prescription orders or that repackages or pools preservative-free sterile drugs—with an exception for hospital pharmacies that compound such products for use by the hospitals’ own patients. All other pharmacies, however, would be prohibited from compound drugs before receiving a prescription order for individually named patients.

In addition, the Senate bill would subject compounded drugs to all of the regulatory requirements applicable to drugs produced by conventional licensed manufacturers. It also would establish several categories of products that could never be compounded lawfully and give the FDA authority to add additional products to that list. Like the House bill, the Senate bill would also permit compounding of commercially available, FDA-approved drugs in the case of a shortage. In addition, it would require registration and inspection of compounding pharmacies and establish new fees for each.

In September 2013, House and Senate committee staffers struck a compromise that would require registration and direct FDA oversight of pharmacies wishing to operate as “outsourcing facilities,” beyond the scope of traditional pharmacy compounding. Traditional pharmacies that prepare compounded drugs from a restricted class of ingredients, and only for filling prescription orders for individual patients, would continue to be regulated primarily by state governments.

Pharmacy outsourcing facilities that prepare large volumes of compounded drugs without individual prescriptions, or those that use certain specified bulk ingredients, such as substances on the FDA's drug shortage list, would be directly regulated by the FDA in much the same way as manufacturers are. They would have to register with the agency, pay annual revenue-based fees, comply with FDA-determined quality assurance and reporting standards, and be subject to regular inspections by the FDA. In addition, outsourcing facilities would be prohibited from compounding drugs the FDA determines are "demonstrably difficult" to compound safely. And special labeling rules would require drugs compounded by an outsourcing facility to, among other things, indicate lot or batch numbers and identify the products as compounded drugs.

The House and Senate compromise language was hastily combined with another House bill addressing supply chain security for drug manufacturers and passed by the full House as the Drug Quality and Security Act (H.R. 3204) on September 28.<sup>35</sup> It was introduced in the Senate in November 2013 and is expected to be enacted with little opposition.

None of these proposed measures would address the quality control or contamination problems associated with the NECC outbreak. FDA and Massachusetts state officials have both acknowledged that they already possess sufficient authority to regulate pharmacies like NECC, which mass produce compounded drugs before receiving prescription orders for individual patients. Indeed, both FDA and MBRP inspectors repeatedly documented ongoing safety and contamination problems with the NECC facility and various NECC products over the course of the decade leading up to the 2012 fungal meningitis outbreak, but neither took any meaningful action to sanction NECC or close its production facility until after the tragic loss of more than 50 lives.

The obvious solution to this problem requires no additional regulatory authority or further restrictions on the ability of pharmacies to engage in compounding. It merely requires that Congress hold the FDA accountable for the choices it made in the exercise of its enforcement discretion.

**Cure Worse than the Disease.** The proposed new restrictions would increase the costs of producing compounded drugs and reduce convenience for many thousands of patients. Requiring pharmacies to have an individual order identifying a single, named patient for every prescription they fill would limit the batch size of the drugs they compound and render it impossible to plan ahead for anticipated future demand.

Mandating smaller batch sizes would necessarily increase labor costs per prescription filled. In many cases, it would lead to waste of raw ingredients, because once sterile containers containing raw ingredients are opened or their seals breached, quantities remaining after the initial use generally must be discarded. And forcing pharmacies to wait until they receive a physician's order would increase the time necessary for prescriptions to be filled. A ban on advance preparation would drastically increase the length of time patients must wait to have their prescriptions filled and may result in overly rushed and inadequate preparation, particularly in cases where the pharmacist must perform potency, purity, and sterility testing of compounded doses.

The restrictions pose another problem. The availability of medical supplies, including various drugs, for in-office use is essential to the practice of medicine. The individual prescription requirement would make it difficult, if not impossible, for hospitals, clinics, and other physician offices to order batches of compounded drugs ahead of time to stock shelves for their in-office use of those products. Some physician professional associations, including the American Academy of Ophthalmology (AAO), have warned that the prescription order requirement could have severe unintended consequences for millions of American doctors and their patients by removing valuable treatment supplies from physician offices. Furthermore, as the AAO points out, “there is no evidence to suggest that labeling a drug with a patient’s name increases the safety” of that product.<sup>36</sup>

Finally, the costs associated with the new registration and inspection fees will fall most heavily on smaller pharmacies. As with other taxes and regulatory costs, smaller firms are least able to absorb such expenses and spread their impact across a larger range of products and sales. For the most part, they will have to be passed on to consumers in the form of higher prices, giving larger competitors an even greater pricing advantage. The net result is likely to increase, rather than decrease, the dominance of large-scale compounding pharmacies in the health care market—precisely the opposite outcome that FDA officials and members of Congress appear to want.

**Conclusion.** The 2012 deadly fungal meningitis outbreak could have been prevented under existing laws had responsible agencies regulated properly. The NECC repeatedly violated state law, but the Massachusetts Board of Registration in Pharmacy failed to enforce existing rules. The FDA knew the NECC to be in violation of federal law, but failed to act within its statutory authority in a timely manner. Giving FDA more power as a reward for its demonstrated failings would not solve the problem, but only magnify it.

Grandstanding politicians and officials, along with a compliant press, mislead the public by proposing feel good measures that are designed to convince Americans they are “doing something” about a given problem. The new laws they propose are largely designed to treat the symptoms of the problem, not to correct its fundamental underlying causes.

Arguably, the only need for congressional action at this time is more aggressive oversight of the FDA’s priority setting. Rather than expand FDA’s regulatory powers, Congress should examine ways in which reducing the agency’s authority could help to improve public health. Expanding FDA authority over drug compounding is not only unnecessary, but will make it more difficult for patients to access the medicines they need by placing additional burdens on the countless compounding pharmacies that practice their craft in a safe and effective manner.

The use of regulation rather, than market forces, makes the entire U.S. health care system more expensive and less safe. Reforming the FDA and eliminating government price controls would largely address the problem of drug shortages and greatly reduce the demand for compounding, to which shortages greatly contribute. More production then would shift back to the more sophisticated, commercial manufacturing facilities that have

more effective quality control measures. This would tend to increase quality and purity while lowering the costs of drugs on the market. It would also lighten the burden on states and the FDA to oversee the compounding that remains, while preserving the flexibility of compounders to meet the needs of patients and physicians.

## Notes

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<sup>5</sup> U.S. House of Representatives Energy and Commerce Committee hearing video, “A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented,” April 16, 2013, <http://www.energycommerce.house.gov/hearing/continuing-investigation-fungal-meningitis-outbreak-and-whether-it-could-have-been-prevented>.

<sup>6</sup> Judith M. Glassgold, “Compounded Drugs,” Congressional Research Service Report R43082, June 3, 2013, <http://www.fas.org/sgp/crs/misc/R43082.pdf>.

<sup>7</sup> Scott Gottlieb, “Compounding a Crisis,” *The American*, October 16, 2012, <http://www.american.com/archive/2012/october/compounding-a-crisis>.

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<sup>9</sup> Ibid.

<sup>10</sup> The International Academy of Compounding Pharmacists, “The International Academy of Compounding Pharmacists Responds to Meningitis Outbreak Tied to Compounding Pharmacy,” October 4, 2012, <http://www.prnewswire.com/news-releases/the-international-academy-of-compounding-pharmacists-responds-to-meningitis-outbreak-tied-to-compounding-pharmacy-172725431.html>.

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<sup>13</sup> Thomas Sullivan, “Drug Shortages Remain in 2013,” *Policy and Medicine*, June 19, 2013, <http://www.policymed.com/2013/06/drug-shortages-remain-in-2013.html>.

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<sup>17</sup> Ibid., p. 5.

<sup>18</sup> Ibid., p. 3.

<sup>19</sup> John Goodman, “Death by Regulation,” Health Policy Blog, June 20, 2011, <http://healthblog.ncpa.org/death-by-regulation>.

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<sup>21</sup> Gottlieb, “Compounding a Crisis.”

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<sup>22</sup> Goodman.

<sup>23</sup> Government Accountability Office, *Drug Pricing: Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement*, Report GAO-11-836, September 23, 2011, pp. 27–28.

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<sup>28</sup> Committee on Energy and Commerce, *FDA’s Oversight of NECC and Ameridose: A History of Missed Opportunities?*

<sup>29</sup> Elizabeth Weise, “‘Greenish-black’ material tied to meningitis deaths,” *USA Today*, October 26, 2012, <http://www.usatoday.com/story/news/nation/2012/10/26/meningitis-outbreak-deaths-fda/1661155>.

<sup>30</sup> U.S. House of Representatives Committee on Energy and Commerce, “Complaints FDA Received Associated with NECC and Ameridose,” <http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/Hearings/OI/20130416/Complaints-FDA-Received-Associated-with-NECC-and-Ameridose.pdf>, accessed September 6, 2013.

<sup>31</sup> U.S. House of Representatives Energy and Commerce Committee hearing video, “A Continuing Investigation into the Fungal Meningitis Outbreak and Whether It Could Have Been Prevented.”

<sup>32</sup> *Ibid.*

<sup>33</sup> “VALID Compounding Act,” H.R. 2186, 113th Congress, Text as of May 23, 2013, <http://www.govtrack.us/congress/bills/113/hr2186/text>.

<sup>34</sup> “Pharmaceutical Quality, Security, and Accountability Act,” S. 959, 113th Congress, Text as of May 15, 2013, <http://www.govtrack.us/congress/bills/113/s959/text>.

<sup>35</sup> “Drug Quality and Security Act,” H.R. 3204, 113th Congress, Text as of November 4, 2012, <https://www.govtrack.us/congress/bills/113/hr3204>.

<sup>36</sup> American Academy of Ophthalmology, “Statement on Provisions to Pharmaceutical Compounding Quality and Accountability Act,” May 29, 2013, <http://www.aao.org/newsroom/release/20130529.cfm>.