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## NOTE

# Adopting Solutions to Orphan Drug Shortages

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*Orphan drugs treat rare diseases affecting less than 200,000 people in the United States. The manufacturing process for orphan drugs is generally complex and time-consuming, making them susceptible to manufacturing quality issues and shortages. Drug shortages of any kind are detrimental to patient health and safety. But orphan drug shortages are especially concerning because orphan drugs treat rare diseases with no other alternative treatments, and one drug maker typically produces the entire supply. The market exclusivity that an orphan drug maker experiences also compounds orphan drug shortages by preventing competitive products in the market. Therefore, when orphan drug shortages occur due to manufacturing interruptions or discontinuances, patients may be left without an available treatment. Recently, courts have held that drug manufacturers do not have a duty to keep manufacturing drugs and supply them to the market. Therefore, patients do not have tort remedies available when there is a disruption in drug supply.*

*Unfortunately, there is not a silver bullet to solve orphan drug shortages, but there are various solutions to mitigate them. This Note focuses specifically on Congress and the FDA, and how both institutions should not only aim to prevent orphan drug shortages, but find alternative, compensatory solutions for patients harmed by these shortages. This Note*

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will explain orphan drug shortages, government efforts to resolve them, discuss Genzyme's recent orphan drug shortage as an example of why there needs to be action, and the negative consequences of failing to act. This Note will then propose various solutions that provide a two-pronged approach of both preventive and compensatory solutions that best serve patients harmed by orphan drug shortages. One such preventative measure is that the FDA should require orphan drug makers to include back-up manufacturing requirements as a part of their New Drug Application or Biological License Application filings. Another solution is for the FDA to consider the establishment of a stockpile repository for orphan drugs. Congress should also pass legislation to allow the FDA to establish a compensation fund that would provide monetary relief to patients harmed by orphan drug shortages. Ultimately, there needs to be more action by Congress and the FDA so that patients in need of orphan drugs or harmed by orphan drug shortages will no longer feel betrayed and "orphaned" by drug companies and the government.

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## INTRODUCTION

Drug shortages are increasing in the United States.<sup>1</sup> Not only do shortages increase healthcare costs, they pose serious threats to public health.<sup>2</sup> Orphan drug shortages are especially concerning since orphan drugs treat rare diseases affecting less than 200,000 people in the United States.<sup>3</sup> Orphan drugs treat rare diseases with no, or very few, alternative treatments, and one drug maker typically produces the drug's entire supply.<sup>4</sup> The market exclusivity that an orphan drug maker experiences also compounds orphan drug shortages by preventing competitive products in the market.<sup>5</sup> Unfortunately, when orphan drug shortages occur due to manufacturing interruptions or discontinuances, patients may be left without an available treatment.<sup>6</sup>

Genzyme is an example of a biotech company that manufactures life-saving medications for rare genetic diseases.<sup>7</sup> When Genzyme shut

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<sup>1</sup> See C. Lee Ventola, *The Drug Shortage Crisis in the United States: Causes, Impact, and Management Strategies*, 36 PHARMACY & THERAPEUTICS 740, 740 (2011); see also Exec. Order No. 13,588, 3 C.F.R. 281 (2012); U.S. FOOD & DRUG ADMIN., A REVIEW OF FDA'S APPROACH TO MEDICAL PRODUCT SHORTAGES 3 (2011) [hereinafter FDA'S APPROACH], available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf>; Letter from Margaret A. Hamburg, Comm'r, U.S. Food & Drug Admin., to Drug Mfg. Indus. (Oct. 31, 2011) [hereinafter Letter to Industry], available at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm277675.htm>.

<sup>2</sup> See Eric Friske, Note, *Addressing Looming Prescription Drug Shortages Through Legislative and Regulatory Approaches*, 14 MINN. J.L. SCI. & TECH. 521, 527 (2013); Andrew Pollack, *Genzyme Drug Shortage Leaves Users Feeling Betrayed*, N.Y. TIMES (Apr. 15, 2010), <http://www.nytimes.com/2010/04/16/business/16genzyme.html> [hereinafter *Genzyme Drug Users Betrayed*].

<sup>3</sup> *The Market for Orphan Drugs*, NAT'L CTR. FOR POLICY ANALYSIS (Aug. 24, 2012), [http://www.ncpa.org/sub/dpd/index.php?Article\\_ID=22290](http://www.ncpa.org/sub/dpd/index.php?Article_ID=22290).

<sup>4</sup> See FDA'S APPROACH, *supra* note 1, at 13, 21-22, 31; Dina Fine Maron, *FDA Moves to Avert Drug Shortages*, SCI. AM. (Oct. 31, 2012), <http://www.scientificamerican.com/article.cfm?id=fda-moves-to-avert-drug-s/>; Richard Dolinar, Chairman, Alliance for Safe Biologic Meds., Presentation at the Annual Drug Information Association (DIA) Conference: Characterizing Drug Shortages and Their Causes: Anticipating Future Trends (June 24, 2013), available at [http://safebiologics.org/resources/wp-content/uploads/2013/07/2013DIA\\_Dolinar\\_FINAL\\_Jun19.pdf](http://safebiologics.org/resources/wp-content/uploads/2013/07/2013DIA_Dolinar_FINAL_Jun19.pdf); *The Market for Orphan Drugs*, *supra* note 3.

<sup>5</sup> See THE PEW CHARITABLE TRUSTS, 2014 DRUG SHORTAGES SUMMIT 12-13 (2014), available at <http://www.pewtrusts.org/~media/Assets/2015/02/2014-Drug-Shortages-Summit.pdf> (discussing how using exclusivity to incentivize market entry can produce the countervailing effect of reduced competition).

<sup>6</sup> See FDA'S APPROACH, *supra* note 1, at 15, 31; Erin R. Fox, *Update to 2012 Emerging Issues Conference Presentation: Where Have All the Drugs Gone? Dealing with Drug Shortages*, HEALTH LAW., Dec. 2012, at 28, 29.

<sup>7</sup> See *About Genzyme*, GENZYME CORP., <http://www.genzyme.com/Company/About-Genzyme.aspx> (last updated Feb. 6, 2015).

down its factories due to manufacturing quality issues, patients relying on the company's orphan drugs suffered serious health consequences and even death.<sup>8</sup> For example, when Jeannine Lipez could not obtain Fabrazyme, Genzyme's drug for Fabry disease, she suffered leg spasms when walking.<sup>9</sup> Her health deteriorated to a point where she will likely need surgery to replace an artery.<sup>10</sup> In a separate, more tragic incident, Dr. William Schubert and his wife did everything they could to replace Fabrazyme.<sup>11</sup> But, by the time they did, it was too late and Dr. Schubert died.<sup>12</sup>

The federal government must act to minimize patient endangerment caused by orphan drug shortages.<sup>13</sup> Action by both Congress and the Food and Drug Administration ("FDA") is particularly important because the judiciary may be the wrong avenue to handle orphan drug shortages.<sup>14</sup> Recently, courts have held that drug manufacturers do not have a duty to keep manufacturing orphan drugs and supply them to the market.<sup>15</sup> Therefore, patients do not have tort remedies available when there is a disruption in orphan drugs' supply.<sup>16</sup> Since Congress statutorily prevents orphan drug competition through a seven-year exclusivity period,<sup>17</sup> both Congress and the FDA should employ additional efforts to prevent orphan drug shortages.

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<sup>8</sup> See *Schubert v. Genzyme Corp.*, No. 2:12CV587DAK, 2013 U.S. Dist. LEXIS 126291, at \*2-4 (D. Utah Sept. 4, 2013); Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>9</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>10</sup> See *id.*

<sup>11</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*4; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>12</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*4; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>13</sup> See Sharona Hoffman, *The Drugs Stop Here: A Public Health Framework to Address the Drug Shortage Crisis*, 67 *FOOD & DRUG L.J.* 1, 14-16 (2012); Kevin Born, Comment, *Time and Money: An Analysis of the Legislative Efforts to Address the Prescription Drug Shortage Crisis in America*, 33 *J. LEGAL MED.* 235, 237 (2012).

<sup>14</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*19 (denying relief for plaintiff by finding no liability on behalf of the manufacturer for the drug shortage); *Lacognata v. Hospira, Inc.*, No. 8:12-cv-822-T-30TGW, 2012 U.S. Dist. LEXIS 102708, at \*9 (M.D. Fla. July 2, 2012) (same).

<sup>15</sup> See, e.g., *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*19 (declining to impose/recognize a duty to supply orphan drugs to market); cf. *Lacognata*, 2012 U.S. Dist. LEXIS 102708, at \*9 (declining to impose/recognize a duty to supply drugs to market).

<sup>16</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*19; *Lacognata*, 2012 U.S. Dist. LEXIS 102708, at \*9.

<sup>17</sup> See FDA'S APPROACH, *supra* note 1, at 31; *The Market for Orphan Drugs*, *supra* note 3; Deborah Weinstein, *Orphan Drugs: Small Is the New Big*, *MED. MARKETING &*

Unfortunately, there is not a silver bullet to solve orphan drug shortages, but there are various solutions to mitigate them. These solutions include congressional, judicial, or administrative (e.g., FDA) action. This Note focuses specifically on Congress and the FDA to argue that they should provide the necessary solutions to reduce orphan drug shortages and compensate patients. Part I will explain orphan drug shortages, government efforts to resolve them, as well as use Genzyme's recent orphan drug shortage as an example of why there needs to be action.<sup>18</sup> Part II will describe additional negative consequences of failing to act.<sup>19</sup> Part III will propose solutions that may prevent or alleviate drug shortages when they occur and assist patients who are affected by orphan drug shortages.<sup>20</sup>

## I. ORPHAN DRUG SHORTAGES AND GOVERNMENT EFFORTS

### A. *Orphan Drug Vulnerability to Shortages and Drug Shortage Effects*

Prescription drug use is prevalent within the United States.<sup>21</sup> Seven out of ten Americans take at least one prescription drug at any one time.<sup>22</sup> More than half take at least two prescriptions.<sup>23</sup> In 2012, the U.S. and worldwide prescription drug market were valued at \$325.7 billion and \$950 billion, respectively.<sup>24</sup> In comparison, the orphan

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MEDIA (Apr. 1, 2012), <http://www.mmm-online.com/orphan-drugs-small-is-the-new-big/article/233445/>.

<sup>18</sup> See *infra* Part I.

<sup>19</sup> See *infra* Part II.

<sup>20</sup> See *infra* Part III.

<sup>21</sup> See Katie Thomas, *U.S. Drug Costs Dropped in 2012, but Rises Loom*, N.Y. TIMES (Mar. 18, 2013), <http://www.nytimes.com/2013/03/19/business/use-of-generics-produces-an-unusual-drop-in-drug-spending.html> [hereinafter *U.S. Drug Costs*]; *Nearly 7 in 10 Americans Take Prescription Drugs*, Mayo Clinic, Olmsted Medical Center Find, MAYO CLINIC (June 19, 2013), <http://www.mayoclinic.org/news2013-rst/7543.html> [hereinafter *Nearly 7 in 10*]; *Study Shows 70 Percent of Americans Take Prescription Drugs*, CBS NEWS (June 20, 2013), [http://www.cbsnews.com/8301-204\\_162-57590305/study-shows-70-percent-of-americans-take-prescription-drugs](http://www.cbsnews.com/8301-204_162-57590305/study-shows-70-percent-of-americans-take-prescription-drugs) [hereinafter *70 Percent of Americans*].

<sup>22</sup> *Nearly 7 in 10*, *supra* note 21; *70 Percent of Americans*, *supra* note 21.

<sup>23</sup> See sources cited *supra* note 22.

<sup>24</sup> See Matthew Herper, *Why Big Pharma Won't Get Its Piece of the \$1.2 Trillion Global Drug Market*, FORBES (July 12, 2012, 7:18 AM), <http://www.forbes.com/sites/matthewherper/2012/07/12/the-global-drug-market-will-swell-to-1-2-trillion-while-big-pharma-treads-water/> [hereinafter *Why Big Pharma*]; Thomas, *U.S. Drug Costs*, *supra* note 21.

drug market was \$83 billion worldwide in 2012,<sup>25</sup> nearly 9% of the worldwide prescription drug market.<sup>26</sup>

With such a prevalence of prescription drug use, drug shortages can have serious consequences. Although drug shortages within the larger prescription drug market do occur, they are rare.<sup>27</sup> While the number of drug shortages in the United States any given year is small,<sup>28</sup> drug shortages have been increasing.<sup>29</sup> From 2005 to 2010, the number of drug shortages tripled from 61 to 178.<sup>30</sup>

With increasing prescription drug usage and drug shortages,<sup>31</sup> healthcare costs are also rising.<sup>32</sup> Drug shortages may cost hospitals over \$416 million a year.<sup>33</sup> When drug shortages affect patients, they tend to visit the hospital more often as their health deteriorates.<sup>34</sup> Hospitals may find the shorted drug to be substantially marked-up.<sup>35</sup> Hospitals may also need to purchase more expensive, alternative therapies.<sup>36</sup> These all result in increased costs to the hospital.<sup>37</sup>

Drug shortages also pose a serious threat to public health and patient safety.<sup>38</sup> When there is a shortage of drugs, health care providers resort to rationing drugs, delaying treatments, and cancelling procedures.<sup>39</sup> Even with drug substitutes, patients can still experience poor treatment

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<sup>25</sup> See *Worldwide Orphan Drug Market to Grow to \$127 Billion by 2018*, BUS. WIRE (Apr. 23, 2013, 9:00 AM EDT), <http://www.businesswire.com/news/home/20130423005249/en/Worldwide-Orphan-Drug-Market-Grow-127-Billion> [hereinafter *Worldwide Orphan Drug Market*].

<sup>26</sup> See Herper, *Why Big Pharma*, *supra* note 24; *Worldwide Orphan Drug Market*, *supra* note 25.

<sup>27</sup> See KEVIN HANINGER ET AL., U.S. DEP'T OF HEALTH & HUMAN SERVS., ECONOMIC ANALYSIS OF THE CAUSES OF DRUG SHORTAGES 1, 3 (2011), available at <http://aspe.hhs.gov/sp/reports/2011/drugshortages/ib.pdf>.

<sup>28</sup> See Exec. Order No. 13,588, 3 C.F.R. 281 (2012).

<sup>29</sup> See *id.*; Hamburg, Letter to Industry, *supra* note 1.

<sup>30</sup> See sources cited *supra* note 29.

<sup>31</sup> See sources cited *supra* note 29 (noting drug shortages); see also *Nearly 7 in 10*, *supra* note 21 (noting increasing prescription drug usage).

<sup>32</sup> See Friske, *supra* note 2, at 527.

<sup>33</sup> See *id.*

<sup>34</sup> Cf. Hoffman, *supra* note 13, at 8-9 (implying how affected patients may experience potential side effects to alternative products or the unavailability of medications, and thereby increasing hospital costs due to increased visits); Friske, *supra* note 2, at 525-26 (same).

<sup>35</sup> See Friske, *supra* note 2, at 527.

<sup>36</sup> See *id.*

<sup>37</sup> See *id.*

<sup>38</sup> See Exec. Order No. 13,588, 3 C.F.R. 281 (2012); Hoffman, *supra* note 13, at 8; Born, *supra* note 13, at 237.

<sup>39</sup> See Hoffman, *supra* note 13, at 8.

outcomes, medical errors, or both.<sup>40</sup> When there are no substitutes, patients suffer detrimental results, including death.<sup>41</sup>

Although the orphan drug market is small when compared with the overall prescription drug market, orphan drugs play a huge role in treating rare diseases.<sup>42</sup> In the United States, the definition of a rare disease is a disease affecting less than 200,000 people.<sup>43</sup> An estimated 25 million people in the United States live with one of the 7,000 rare diseases affecting the world population.<sup>44</sup> Only 250 of these rare diseases have approved treatments.<sup>45</sup>

The recent Ebola outbreak is an example of how important it is to develop drugs for rare diseases.<sup>46</sup> Ebola is a rare disease that occurs more commonly in developing countries, but has recently affected the United States.<sup>47</sup> With very few companies developing Ebola-related drugs, Ebola patients did not have access to life-saving Ebola drugs.<sup>48</sup> Mapp Biopharmaceuticals, one of the few companies developing an Ebola treatment, had limited supplies of its drug, ZMapp.<sup>49</sup> Mapp exhausted its supplies after providing experimental doses to a handful of medical workers who contracted Ebola, including the first two Ebola patients flown from West Africa back to the United States for treatment.<sup>50</sup> There

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<sup>40</sup> See *id.*

<sup>41</sup> See *id.*

<sup>42</sup> See Herper, *Why Big Pharma*, *supra* note 24; *The Market for Orphan Drugs*, *supra* note 3; *Worldwide Orphan Drug Market*, *supra* note 25.

<sup>43</sup> *The Market for Orphan Drugs*, *supra* note 3.

<sup>44</sup> See Ed Silverman, *Orphan Drugs: 'Rare' Opportunities to Make Money*, FORBES (Aug. 23, 2012, 12:33 PM), <http://www.forbes.com/sites/edsilverman/2012/08/23/orphan-drugs-rare-opportunities-to-make-money/>; *The Market for Orphan Drugs*, *supra* note 3.

<sup>45</sup> See *The Market for Orphan Drugs*, *supra* note 3.

<sup>46</sup> E.g., Jason Millman, *Why the Drug Industry Hasn't Come Up with an Ebola Cure*, WASH. POST (Aug. 13, 2014), <http://www.washingtonpost.com/blogs/wonkblog/wp/2014/08/13/why-the-drug-industry-hasnt-come-up-with-an-ebola-cure/>; see Susan E. Swanberg, *The Orphaning of Ebola*, SCILOGS (Aug. 11, 2014), <http://www.scilog.com/tenacious-telomere/the-orphaning-of-ebola/>; Dennis Thompson, *Texas Hospital Worker Tests Positive for Ebola After "Breach in Protocol,"* HEALTH.COM (Oct. 13, 2014), <http://news.health.com/2014/10/13/texas-hospital-worker-tests-positive-for-ebola/>.

<sup>47</sup> See Thompson, *supra* note 46. As noted before, a rare disease in the United States is one that affects less than 200,000 people. See *The Market for Orphan Drugs*, *supra* note 3.

<sup>48</sup> See Millman, *supra* note 46; Swanberg, *supra* note 46.

<sup>49</sup> See Damian Garde, *Feds Rally Behind Mapp as Ebola Spreads, but Production Remains a Challenge*, FIERCEBIOTECH (Oct. 2, 2014), <http://www.fiercebiotech.com/story/feds-rally-behind-mapp-ebola-spreads-production-remains-challenge/2014-10-02>; see also Millman, *supra* note 46.

<sup>50</sup> See Sharon Begley, *U.S. Requests Production Plans for Ebola Drug ZMapp*, REUTERS, Oct. 17, 2014, available at <http://www.reuters.com/article/2014/10/17/us->

were just not enough drug makers in the Ebola rare disease space to develop these orphan drugs, so when the sudden need arose for these treatments, the medical community was caught off guard.

But even if orphan drugs are available to treat rare diseases, they are still prone to shortages due to manufacturing difficulties and the drug class in which most fall.<sup>51</sup> A majority of orphan drugs are biologics — drugs that are produced from living cells.<sup>52</sup> And like sterile injectables, almost all biologics are administered through the same route of administration.<sup>53</sup> Due to this shared delivery mechanism, biologics are susceptible to the same manufacturing quality issues facing sterile injectables.<sup>54</sup> As a result, many orphan drugs fall within a drug class historically most prone to shortages.<sup>55</sup>

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health-ebola-usa-zmapp-exclusive-idUSKCN0I624P20141017; Caroline Chen & Robert Langreth, *Ebola Drug Supply Is Exhausted After Doses Sent to Africa*, BLOOMBERGBUSINESS (Aug. 12, 2014, 2:30 AM), <http://www.bloomberg.com/news/articles/2014-08-11/ebola-drug-supply-is-exhausted-after-doses-sent-to-africa>.

<sup>51</sup> See FDA'S APPROACH, *supra* note 1, at 13, 21, 31; Maron, *supra* note 4; Dolinar, *supra* note 4; Press Release, Alliance for Safe Biologic Meds. (ASBM), Quality, Manufacturing Transparency Key to Avoiding Biologic Drug Shortages: Dolinar Addresses 49th Annual DIA Conference (June 25, 2013), <http://safebiologics.org/resources/2013/06/quality-manufacturing-transparency-key-to-avoiding-biologic-drug-shortages-dolinar-addresses-49th-annual-dia-conference-4/> [hereinafter ASBM Press Release].

<sup>52</sup> See Aarti Sharma et al., *Orphan Drug: Development Trends and Strategies*, 2 J. PHARMACY & BIOALLIED SCI. 290, 290-99 (2010) (noting that biologics account for 64.3% of the orphan drugs market); Andrew Mica et al., *Steps to Ensure Adequate Supply of Biological Medicines: Considerations for the Healthcare Provider*, 2 GENERICS & BIOSIMILARS INITIATIVE J. 136 (2013), <http://gabi-journal.net/steps-to-ensure-adequate-supply-of-biological-medicines-considerations-for-the-healthcare-provider.html>.

<sup>53</sup> See Mica et al., *supra* note 52 (noting how “almost all biologicals are administered parenterally from a sterile dosage form” as are sterile injectables); Dolinar, *supra* note 4 (noting that from 2010–2011, sterile injectables accounted for 80% of drug shortages); ASBM Press Release, *supra* note 51 (explaining how sterile injectables share a delivery mechanism with biologics).

<sup>54</sup> See FDA'S APPROACH, *supra* note 1, at 13, 21 (explaining that biological drug shortages are commonly caused by manufacturing problems); HANINGER ET AL., *supra* note 27, at 13 (noting that 54% of sterile injectable drug shortages are linked to manufacturing quality problems); Maron, *supra* note 4; (explaining how biological drug shortages most frequently arise from poor manufacturing quality control); see, e.g., Katie Thomas, *Lapses at Big Drug Factories Add to Shortages and Danger*, N.Y. TIMES (Oct. 17, 2012), <http://www.nytimes.com/2012/10/18/business/drug-makers-stalled-in-a-cycle-of-quality-lapses-and-shortages.html> [hereinafter *Lapses*] (providing an example of how six of the major sterile injectable drug manufacturers have been warned about serious manufacturing violations within the past three years).

<sup>55</sup> See Dolinar, *supra* note 4. Other sterile injectable drugs affected by shortages include vaccines, cancer medications, antibiotics, surgical anesthetics, emergency medicines, and electrolytes for intravenous feeding. See HANINGER ET AL., *supra* note

Especially for orphan drug shortages, there is a two-fold concern of manufacturing issues and sole-sourced manufacturers.<sup>56</sup> In terms of the manufacturing process for biologics, “the product is the process.”<sup>57</sup> Since living microorganisms are used to produce many orphan drugs, the manufacturing process is complex and time-consuming.<sup>58</sup> Consequently, there is a higher risk of encountering problems since manufacturers need to ensure that the manufacturing process remains the same every single time a drug is made.<sup>59</sup> Even the smallest change in the manufacturing process can affect the finished product.<sup>60</sup> Since orphan drug production is commonly concentrated among a small number of manufacturers or is sole-sourced,<sup>61</sup> this market concentration exaggerates manufacturing problems.<sup>62</sup> With manufacturing concentrated among one or a few players, there are no alternative manufacturers to assist with drug supply disruptions.<sup>63</sup> Thus, orphan drugs are uniquely vulnerable to shortages.<sup>64</sup>

Congressional efforts to incentivize drug makers also compound orphan drug shortage problems.<sup>65</sup> Before Congress passed favorable laws encouraging orphan drug development for rare diseases, drug companies had been reluctant to invest in research and development

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27, at 2; Born, *supra* note 13, at 236.

<sup>56</sup> See FDA’S APPROACH, *supra* note 1, at 13, 21; Mica et al., *supra* note 52; *How Do Drugs and Biologics Differ?*, BIOTECH. INDUS. ORG. (Nov. 10, 2010), <http://www.bio.org/articles/how-do-drugs-and-biologics-differ>.

<sup>57</sup> *How Do Drugs and Biologics Differ?*, *supra* note 56.

<sup>58</sup> See, e.g., FDA’S APPROACH, *supra* note 1, at 13, 21 (explaining how sterile injectables require specialized processes and equipment to manufacture); Maron, *supra* note 4 (explaining how sterile injectables, including biologics, are made in small quantities and have few backup options).

<sup>59</sup> See FDA’S APPROACH, *supra* note 1, at 13, 21; Maron, *supra* note 4; *How Do Drugs and Biologics Differ?*, *supra* note 56.

<sup>60</sup> See *How Do Drugs and Biologics Differ?*, *supra* note 56.

<sup>61</sup> See FDA’S APPROACH, *supra* note 1, at 31 (explaining how a great majority of sterile injectable molecules have only one or two manufacturers and how 60% of sterile injectables in 2010 were virtually sole-sourced); see also 21 C.F.R. § 314.81(b)(3)(iii)(2)(d) (2014) (explaining that a sole-source manufacturer is one who is the only entity manufacturing a drug product of a specific strength, dosage form, or route of administration for sale in the United States).

<sup>62</sup> See FDA’S APPROACH, *supra* note 1, at 31.

<sup>63</sup> See *id.*

<sup>64</sup> See *id.*; Fox, *supra* note 6, at 29.

<sup>65</sup> See Clark Herman, *The Orphan Drug Act at 30 Years: What’s Next?*, PHARMEXEC.COM (Jan. 8, 2013), <http://www.pharmexec.com/orphan-drug-act-30-years-whats-next>; Weinstein, *supra* note 17; cf. THE PEW CHARITABLE TRUSTS, *supra* note 5 (discussing the adverse effects of an exclusivity incentive for drug makers).

for orphan drugs because these drugs were not profitable.<sup>66</sup> Drug companies take about ten to fifteen years, and on average \$1 billion, to shuttle a drug through research and development, human clinical trials, and eventually to market upon FDA approval.<sup>67</sup> To help drug companies recoup their costs, Congress passed the Orphan Drug Act in 1983.<sup>68</sup> The law gives drug companies federal funding for grants and contracts to perform clinical trials of orphan drug products.<sup>69</sup> Orphan drug companies also receive a 50% tax credit for clinical testing costs.<sup>70</sup> The biggest incentive that orphan drug companies receive is a seven-year market exclusivity period for any orphan drug produced.<sup>71</sup>

However, with Congressional incentives come side effects.<sup>72</sup> Market exclusivity effectively stops competitors from selling drugs in that specific rare disease space.<sup>73</sup> For seven years, orphan drug makers do

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<sup>66</sup> Swanberg, *supra* note 46; see Millman, *supra* note 46; *The Market for Orphan Drugs*, *supra* note 3.

<sup>67</sup> See PHARM. RESEARCH & MFRS. OF AM., DRUG DISCOVERY AND DEVELOPMENT: UNDERSTANDING THE R&D PROCESS 1, 10 (2007), available at [http://www.phrma.org/sites/default/files/pdf/rd\\_brochure\\_022307.pdf](http://www.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf); Matthew Herper, *The Truly Staggering Cost of Inventing New Drugs*, FORBES (Feb. 10, 2012, 7:41 AM), <http://www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs/> (estimating that \$1 billion may be a more conservative figure today, and adjusting the figure to include current failure rates, the resulting estimate is \$4 billion of research dollars spent for every drug that is approved); Scott Gavura, *What Does a New Drug Cost? Part II: The Productivity Problem*, SCI-BASED MED. (Dec. 5, 2012), <http://www.sciencebasedmedicine.org/what-does-a-new-drug-cost-part-ii-the-productivity-problem/>.

<sup>68</sup> Orphan Drug Act of 1983, Pub. L. No. 97-414, 96 Stat. 2049 (codified as amended at 21 U.S.C. §§ 360aa–360ee (2012)); see Tamar Nordenberg, *Inside FDA: When a Drug Is in Short Supply*, DRUGS.COM (Oct. 2004), <http://www.drugs.com/news/inside-fda-short-supply-3530.html>; *The Economics of Orphan Drugs*, RARE DISEASE REPORT (Aug. 23, 2012), <http://www.raredr.com/articles/economics-orphan-drugs>; *The Market for Orphan Drugs*, *supra* note 3.

<sup>69</sup> See 21 U.S.C. § 360ee; Nordenberg, *supra* note 68; *The Economics of Orphan Drugs*, *supra* note 68; *The Market for Orphan Drugs*, *supra* note 3.

<sup>70</sup> See 26 U.S.C. § 45C (2012); Nordenberg, *supra* note 68; *The Economics of Orphan Drugs*, *supra* note 68; *The Market for Orphan Drugs*, *supra* note 3. The tax credit is equal to 50% of the development costs attributable to qualified clinical testing in a tax year. Alexander Korniaikov et al., *The Orphan Drug and Research Tax Credits: The “Substantially All” Rule*, AM. INST. OF CPAs (Oct. 1, 2014), [http://www.aicpa.org/publications/taxadviser/2014/october/pages/korniaikov\\_oct14.aspx](http://www.aicpa.org/publications/taxadviser/2014/october/pages/korniaikov_oct14.aspx). Costs include employee wages paid for qualified clinical testing services and activities. See *id.*

<sup>71</sup> See 21 U.S.C. § 360cc; *The Economics of Orphan Drugs*, *supra* note 68.

<sup>72</sup> Cf. THE PEW CHARITABLE TRUSTS, *supra* note 5 (explaining the adverse effects of an exclusivity incentive that leads to reduced competition and indirect consequences of having no backup options to sole produced drugs).

<sup>73</sup> See Matthew Perrone, *Drug Firms Find Profits in Niche ‘Orphan Drugs,’*

not have to worry about competitors vying for their market share.<sup>74</sup> Exclusivity provides orphan drug companies an easier time recouping the development costs of high-valued drugs for such small patient markets.<sup>75</sup> However, without competitive products, patients of a specific rare disease have only one treatment option for their rare conditions.<sup>76</sup> The concentration of orphan drug production among a small number of manufacturers compounds the problem.<sup>77</sup> The drug development incentives that Congress offered to orphan drug companies may eventually backfire when the combination of market exclusivity and drug shortages occur. Therefore, if an orphan drug maker enjoys market exclusivity but experiences a drug shortage, patients are left without an available treatment.<sup>78</sup>

### B. *Government Efforts to Address Drug Shortages*

Congress has made various efforts to address drug shortages by mandating that drug makers provide advance notice of drug discontinuances or interruptions.<sup>79</sup> In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act (“FD&C Act”).<sup>80</sup> The FD&C Act formed the FDA and gave it the authority to regulate food, drugs, medical devices, and cosmetic safety.<sup>81</sup> But, the FD&C Act mandates

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MANUFACTURING.NET (Jan. 25, 2012, 9:25 AM), <http://www.manufacturing.net/news/2012/01/drug-firms-find-profits-in-niche-orphan-drugs>.

<sup>74</sup> See *id.*

<sup>75</sup> See *id.*

<sup>76</sup> See FDA’S APPROACH, *supra* note 1, at 31; Fox, *supra* note 6, at 29; Weinstein, *supra* note 17.

<sup>77</sup> See FDA’S APPROACH, *supra* note 1, at 31.

<sup>78</sup> See Fox, *supra* note 6, at 29; *cf.* THE PEW CHARITABLE TRUSTS, *supra* note 5 (explaining the adverse effects of an exclusivity incentive that leads to reduced competition and indirect consequences of having no backup options to sole produced drugs). I want to be clear that I am not proposing that Congress ends orphan drug incentives and cause drug makers to develop no treatments at all. I am merely pointing out some weaknesses in the current incentivized system that contribute to or compound orphan drug shortages. Proposed changes to the Orphan Drug Act is beyond the scope of my Note.

<sup>79</sup> See Food and Drug Administration Safety and Innovation Act of 2012, Pub. L. No. 112-144, 126 Stat. 993 (codified as amended in scattered sections of 21 U.S.C.); Preserving Access to Life-Saving Medications Act of 2011, H.R. 2245, 112th Cong. § 2(a) (2011); 21 C.F.R. § 314.81(b)(3)(iii)(2)(d) (2014).

<sup>80</sup> Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301–399f (2012)).

<sup>81</sup> See *Overview of Federal Food, Drug, and Cosmetic Act*, DAVIES, BARRELL, WILL, LEWELLYN & EDWARDS, PLC., <http://www.dbwle.com/newsletters-2/products-liability/overview-of-federal-food-drug-and-cosmetic-act/> (last visited Mar. 24, 2015).

that only sole-source and medically necessary drug manufacturers are required to provide six months advance notice of drug discontinuances or interruptions to the FDA.<sup>82</sup> In 2011, Congress introduced the Preserving Access to Life-Saving Medications Act (“PALSM Act”).<sup>83</sup> The PALSM Act allows the FDA to distribute information about shortages, prioritize inspections, identify vulnerable drugs, and collaborate with manufacturers to address shortages.<sup>84</sup> The PALSM Act also requires all drug manufacturers (regardless of the sole-source or medically necessary designation) to provide six months’ notice to the FDA before discontinuing or interrupting drug production.<sup>85</sup> But, Congress has not yet enacted the PALSM Act.<sup>86</sup> Instead, Congress passed the Food and Drug Administration Safety and Innovation Act (“FDASIA”) in 2012.<sup>87</sup> Unlike the proposed PALSM Act, the FDASIA requires only that the medically necessary drug manufacturers, sole-source or not, provide six months advance notice if they anticipate discontinuances or interruptions.<sup>88</sup> But if the PALSM Act had passed, the FDA would then receive adequate, advance manufacturer notice to intervene more strategically, find alternative suppliers, and better inform clinicians of potential future drug shortages.<sup>89</sup> Instead, congressional efforts have not significantly mitigated or reduced drug shortages.<sup>90</sup>

Currently, the FDA has some options to mitigate the effects of a confirmed drug shortage,<sup>91</sup> but they are not enough.<sup>92</sup> The FDA can notify and encourage manufacturers of same or similar products to increase production.<sup>93</sup> The FDA can expedite review of new

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<sup>82</sup> See 21 C.F.R. § 314.81(b)(3)(iii)(2)(d); FDA’S APPROACH, *supra* note 1, at 18 (defining “medically necessary” as any drug product used to treat or prevent a serious disease or medical condition for which there is no other adequately available drug product that is judged by medical staff to be an appropriate substitute).

<sup>83</sup> H.R. 2245; Hoffman, *supra* note 13, at 14.

<sup>84</sup> See H.R. 2245 § 2(a).

<sup>85</sup> See *id.*; Born, *supra* note 13, at 244.

<sup>86</sup> See Hoffman, *supra* note 13, at 15.

<sup>87</sup> Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, 126 Stat. 993 (2012) (codified as amended in scattered sections of 21 U.S.C.).

<sup>88</sup> See *id.* § 1001, 21 U.S.C. § 356c (Supp. I 2013).

<sup>89</sup> See Hoffman, *supra* note 13, at 15.

<sup>90</sup> See Hoffman, *supra* note 13, at 14-16; Born, *supra* note 13, at 236, 244-46.

<sup>91</sup> See FDA’S APPROACH, *supra* note 1, at 16; Born, *supra* note 13, at 242-43; Hamburg, Letter to Industry, *supra* note 1.

<sup>92</sup> See Hoffman, *supra* note 13, at 11; Born, *supra* note 13, at 247.

<sup>93</sup> See 21 C.F.R. § 1303.13 (2014); FDA’S APPROACH, *supra* note 1, at 4, 16; Born, *supra* note 13, at 242-43.

manufacturing lines or raw material sources to assist companies with production increases.<sup>94</sup> The FDA can find another manufacturer to begin producing the product.<sup>95</sup> The FDA can also exercise its regulatory discretion to grant a “compassionate use exception” for experimental drugs or the controlled importation of equivalent products approved outside of the United States.<sup>96</sup>

The FDA may also take action against a drug maker — in the form of a consent decree — that is facing a drug shortage caused by manufacturing quality issues.<sup>97</sup> A consent decree is a judicial order recognizing the legal agreement between the FDA and a drug maker.<sup>98</sup> Under a consent decree, a drug maker allows a third-party to inspect and review its factory operations for a certain time.<sup>99</sup> The third-party will certify the drug maker’s compliance with FDA regulations.<sup>100</sup> As a result of the regulatory action, the FDA may fine drug companies for their manufacturing quality problems.<sup>101</sup> The FDA may also require companies to pay specified amounts of past and future profits from products made at their troubled factories.<sup>102</sup> Federal fines can be costly.<sup>103</sup> For example, Wyeth Pharmaceuticals violated manufacturing protocols while producing a flu vaccine in 2000.<sup>104</sup> Wyeth paid \$297 million in fines, plus 18.5% of its flu vaccine sales.<sup>105</sup> In 2002, Schering-Plough, now owned by Merck, paid \$500 million to the FDA for drug manufacturing violations produced at four factories.<sup>106</sup> In

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<sup>94</sup> See 21 C.F.R. § 314.70 (2014); FDA’S APPROACH, *supra* note 1, at 4, 16; Born, *supra* note 13, at 242-43.

<sup>95</sup> See *supra* note 94.

<sup>96</sup> See 21 C.F.R. §§ 312.305–310 (2014); FDA’S APPROACH, *supra* note 1, at 4, 16; Born, *supra* note 13, at 242-43.

<sup>97</sup> See Andrew Pollack, *Genzyme Says FDA Will Oversee Its Factory*, N.Y. TIMES (Mar. 24, 2010), <http://www.nytimes.com/2010/03/25/business/25genzyme.html> [hereinafter *Genzyme Says FDA*]; Thomas, *Lapses*, *supra* note 54; Nordenberg, *supra* note 68.

<sup>98</sup> *FDA Consent Decree*, COMPLIANCE INSIGHT, INC., <http://compliance-insight.com/fda-483-warning-letters/fda-consent-decree/> (last visited Jan. 25, 2015).

<sup>99</sup> See *id.*; Tracy Staton, *Genzyme Submits to \$175M Fine, FDA Consent Decree*, FIERCEPHARMA (May 25, 2010), <http://www.fiercepharma.com/story/genzyme-submits-175m-fine-fda-consent-decree/2010-05-25> [hereinafter *Genzyme Submits*].

<sup>100</sup> See Pollack, *Genzyme Says FDA*, *supra* note 97.

<sup>101</sup> See *id.*

<sup>102</sup> See *id.*

<sup>103</sup> See *id.*; Staton, *Genzyme Submits*, *supra* note 99.

<sup>104</sup> See *Wyeth - Pharma Manufacturing Consent Decrees*, FIERCEPHARMA MANUFACTURING (Oct. 19, 2010), <http://www.fiercepharmamanufacturing.com/special-reports/pharma-manufacturing-consent-decrees/wyeth-pharma-manufacturing-consent-decrees>.

<sup>105</sup> *Id.*

<sup>106</sup> Pollack, *Genzyme Says FDA*, *supra* note 97.

2010, Genzyme paid the FDA a \$175 million fine for a virus contamination in its key Boston plant.<sup>107</sup>

Specifically for orphan drug shortages, the FDA has specialized options under federal laws.<sup>108</sup> If the FDA believes an orphan drug maker cannot produce enough drugs to meet patient need, the Director offers the company one of two options.<sup>109</sup> First, the drug maker may provide information on how the company can produce sufficient orphan drug quantities within a reasonable time.<sup>110</sup> Second, the drug maker may agree to allow the FDA to approve competitor drugs before the company's market exclusivity expires.<sup>111</sup> If the orphan drug company fails to fulfill either option, then the Director will withdraw the drug's exclusive approval.<sup>112</sup> The FDA cannot reinstate a drug's market exclusivity after a company loses it.<sup>113</sup>

Recently, FDA efforts to mitigate drug shortages have produced some positive results.<sup>114</sup> In October 2011, FDA Commissioner Margaret Hamburg issued a letter to all drug manufacturers to bring attention to the rising incidence of drug shortages. Commissioner Hamburg expressed concern over the shortages, especially those involving drugs without alternative therapies.<sup>115</sup> She asked drug manufacturers to work with the FDA and notify the agency of potential disruptions.<sup>116</sup> After six months, Commissioner Hamburg reported that her letter made the industry aware of the increases in drug shortages.<sup>117</sup> The letter resulted in a six-fold increase of early manufacturer notifications.<sup>118</sup> The FDA prevented 128 drug shortages during the six-month timeframe.<sup>119</sup> A fewer number of shortages have

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<sup>107</sup> Staton, *Genzyme Submits*, *supra* note 99.

<sup>108</sup> See 21 C.F.R. § 316.36 (2014).

<sup>109</sup> See *id.* § 316.36(a).

<sup>110</sup> See *id.* § 316.36(a)(1).

<sup>111</sup> See *id.* § 316.36(a)(2).

<sup>112</sup> See *id.* § 316.36(b).

<sup>113</sup> See *id.*

<sup>114</sup> See Hamburg, Letter to Industry, *supra* note 1; Margaret Hamburg, *Six Month Check-up: FDA's Work on Drug Shortages*, FDA VOICE (May 3, 2012), <http://blogs.fda.gov/fdavoices/index.php/2012/05/six-month-check-up-fdas-work-on-drug-shortages> [hereinafter *Six Month Check-up*].

<sup>115</sup> See Hamburg, Letter to Industry, *supra* note 1.

<sup>116</sup> See *id.*

<sup>117</sup> See Hamburg, *Six Month Check-up*, *supra* note 114.

<sup>118</sup> *Id.*

<sup>119</sup> *Id.*

occurred since then, with 117 drug shortages in 2012 and 44 shortages in 2013.<sup>120</sup>

The White House has also recognized the seriousness of drug shortages.<sup>121</sup> In October 2011, President Obama signed an Executive Order to address the recent increases in drug shortages.<sup>122</sup> The order increased the FDA's jurisdiction in preventing and reducing drug shortages of life-saving drugs.<sup>123</sup> President Obama granted the FDA broader reporting of discontinuances, expedited regulatory review, and the ability to report drug profiteering activities to the Department of Justice.<sup>124</sup>

### C. Case Study: Genzyme's Orphan Drug Shortage

Genzyme's recent manufacturing woes provide an excellent case study of an orphan drug shortage and its effect on patient lives.<sup>125</sup> In June 2009, Genzyme shut down its main Boston manufacturing plant when a virus contaminated two of its drug products.<sup>126</sup> The affected drugs were Cerezyme, for Gaucher disease, and Fabrazyme, for Fabry disease.<sup>127</sup>

Genzyme's drugs treat very rare genetic diseases.<sup>128</sup> Gaucher and Fabry disease are both rare inherited enzyme deficiencies that allow fatty substances to build up in the body.<sup>129</sup> Untreated, the build-up causes organ damage.<sup>130</sup> Both Cerezyme and Fabrazyme provide the missing enzyme for their respective diseases.<sup>131</sup> In the United States,

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<sup>120</sup> Valerie Jensen, *FDA Actions Reduce Drug Shortages but Critical Issues Remain*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/NewsEvents/ucm401553.htm> (last modified June 20, 2014).

<sup>121</sup> See Exec. Order No. 13,588, 3 C.F.R. 281 (2012).

<sup>122</sup> *Id.*

<sup>123</sup> See *id.*

<sup>124</sup> See *id.*

<sup>125</sup> See generally *Schubert v. Genzyme Corp.*, No. 2:12CV587DAK, 2013 U.S. Dist. LEXIS 126291 (D. Utah Sept. 4, 2013) (illustrating how Genzyme's drug shortage allegedly killed a patient who relied on the company's drug); Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2 (illustrating Genzyme's manufacturing troubles and the effects and consequences it has on patients who depend on Genzyme's orphan drugs to survive); Pollack, *Genzyme Says FDA*, *supra* note 97 (explaining Genzyme's manufacturing quality problems and the regulatory actions the FDA took as a result).

<sup>126</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>127</sup> See *id.*

<sup>128</sup> See *id.*

<sup>129</sup> See *id.*

<sup>130</sup> See *id.*

<sup>131</sup> See *id.*

there are only 1,500 Cerezyme users and fewer than 1,000 Fabrazyme users.<sup>132</sup>

Genzyme's drug shortage lasted much longer than anticipated.<sup>133</sup> Initially, Genzyme predicted that the shortages would last six to eight weeks.<sup>134</sup> But, Genzyme encountered additional manufacturing problems when it found steel, rubber, and fibers in its drug vials.<sup>135</sup> Consequently, what began as a temporary drug shortage lasted about a year.<sup>136</sup>

Genzyme's drug shortage had severe consequences.<sup>137</sup> Genzyme rationed drugs and gave them to patients with the most severe cases.<sup>138</sup> Genzyme also began decreasing drug doses.<sup>139</sup> Worse yet, 80% of patients received no drugs for several months.<sup>140</sup> Patients experienced increased pain and fatigue.<sup>141</sup> Even though serious medical results have been rare, devastating consequences, such as death, have occurred.<sup>142</sup> Dr. William Schubert, a Genzyme patient, allegedly died because of the Fabrazyme shortage.<sup>143</sup> After Genzyme rationed Dr. Schubert's Fabrazyme doses, his health deteriorated quickly.<sup>144</sup>

At the time, there was a Canadian bioequivalent drug available to treat Fabry disease.<sup>145</sup> Under a "compassionate use exception," the FDA allowed patients to receive the Canadian drug for free.<sup>146</sup> The Canadian drug does not have market approval in the United States,

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<sup>132</sup> *Id.*

<sup>133</sup> *See id.*

<sup>134</sup> *See id.*

<sup>135</sup> *See id.*

<sup>136</sup> *See id.*

<sup>137</sup> *See id.*

<sup>138</sup> *See id.*

<sup>139</sup> *See Schubert v. Genzyme Corp.*, No. 2:12CV587DAK, 2013 U.S. Dist. LEXIS 126291, at \*3 (D. Utah Sept. 4, 2013); Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>140</sup> *See* Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>141</sup> *See id.*

<sup>142</sup> *See id.*

<sup>143</sup> *See Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*4 (noting that Mrs. Schubert alleged the delay in obtaining proper Fabrazyme dosages caused Dr. Schubert's death); Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2 (noting that Genzyme executives deny the drug shortage directly caused Dr. Schubert's death).

<sup>144</sup> Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; *see Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*3.

<sup>145</sup> *See Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*4; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>146</sup> *See* Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

but the FDA allowed the importation of the drug into the country.<sup>147</sup> Sadly, Dr. Schubert did not hear about the Canadian drug until December 2009, and he was only able to obtain it two months later.<sup>148</sup> When Dr. Schubert finally received the drug, it was too late.<sup>149</sup> He died soon afterwards.<sup>150</sup>

After Dr. Schubert's death, Mrs. Schubert sued Genzyme for negligence.<sup>151</sup> She argued that Genzyme owed Dr. Schubert a duty of reasonable care to ensure a continued supply of Fabrazyme.<sup>152</sup> The trial court disagreed and found that Genzyme's failure to supply enough drugs was an act of omission.<sup>153</sup> The conduct was nonfeasance, not malfeasance.<sup>154</sup> The court also discussed how public policy forbids the court to impose a duty of care on drug manufacturers.<sup>155</sup> If the court imposed such a duty, drug developers would be discouraged from entering the market.<sup>156</sup> Therefore, the court granted Genzyme's motion to dismiss on the pleadings.<sup>157</sup>

## II. PROBLEMS AND ISSUES RELATING TO ORPHAN DRUG SHORTAGES

### A. *The Shortage of Efforts to Mitigate Drug Shortages*

Congressional efforts to mitigate drug shortages have been encouraging, but there is more work to accomplish.<sup>158</sup> Although Congress introduced the PALSM Act, it has not been able to pass the proposed legislation.<sup>159</sup> The proposed legislation would require all drug makers to inform the FDA of drug discontinuances or interruptions six months in advance.<sup>160</sup> Even with such a disclosure

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<sup>147</sup> Cf. FDA's APPROACH, *supra* note 1, at 4 (“[The] FDA . . . exercised regulatory discretion regarding controlled importation of similar products approved abroad but not approved in the United States . . .”).

<sup>148</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*4; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>149</sup> See sources cited *supra* note 148.

<sup>150</sup> See sources cited *supra* note 148.

<sup>151</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*4.

<sup>152</sup> See *id.*

<sup>153</sup> See *id.* at \*19.

<sup>154</sup> See *id.*

<sup>155</sup> See *id.* at \*18.

<sup>156</sup> See *id.*

<sup>157</sup> See *id.* at \*19-20.

<sup>158</sup> See Hoffman, *supra* note 13, at 14-16; Born, *supra* note 13, at 237; *supra* Part I.B.

<sup>159</sup> See Hoffman, *supra* note 13, at 14-15.

<sup>160</sup> See H.R. 2245, 112th Cong. § 2(a)-(b) (2011); Hoffman, *supra* note 13, at 14;

mandate, drug makers may not always fulfill the requirement since shortages are unpredictable.<sup>161</sup> The FDA is currently able to expedite review of manufacturing lines or seek manufacturers of similar products to increase production during shortages.<sup>162</sup> But, these options are not effective for orphan drug shortages since there are usually no similar drug products or manufacturers in the disease space.<sup>163</sup> Also, the current and proposed legislation does not address compensatory remedies for patients negatively affected by drug shortages.<sup>164</sup> Congress does not have legislative reforms providing compensatory remedies on its agenda in the near future.<sup>165</sup>

Judicial remedies for patients harmed by drug shortages are also not readily available.<sup>166</sup> After *Schubert*, courts may be unwilling to extend tort liability for drug makers who discontinue or temporarily stop production of drug supplies.<sup>167</sup> *Schubert* is the latest of two existing cases that explore the issue of a drug maker's duty to continue drug production.<sup>168</sup> Courts in these cases have sided with the drug company and rejected such a duty.<sup>169</sup> These rulings illustrate how judicial tort remedies are currently unavailable for patients harmed by discontinued or interrupted drug products.<sup>170</sup>

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Born, *supra* note 13, at 244.

<sup>161</sup> See Born, *supra* note 13, at 245-46; Fox, *supra* note 6, at 29 (indicating that communication alone will not fix drug shortage problems).

<sup>162</sup> See FDA'S APPROACH, *supra* note 1, at 4, 16.

<sup>163</sup> See *id.* at 3, 31.

<sup>164</sup> See generally 21 U.S.C. §§ 301-399f (2012) (providing no compensatory remedies for patients negatively affected by drug shortages).

<sup>165</sup> See generally H.R. 2245 (presenting proposed legislation that does not encompass compensatory remedies for patients negatively affected by drug shortages). H.R. 2245 is an example where Congress did not propose any compensatory reforms.

<sup>166</sup> See, e.g., *Schubert v. Genzyme Corp.*, No. 2:12CV587DAK, 2013 U.S. Dist. LEXIS 126291, at \*19 (D. Utah Sept. 4, 2013) (ruling that Genzyme had no duty to meet all market demand for its drug and therefore had no liability); *Lacognata v. Hospira, Inc.*, No. 8:12-cv-822-T-30TGW, 2012 U.S. Dist. LEXIS 102708, at \*9 (M.D. Fla. July 2, 2012) (ruling that Hospira was not liable to plaintiff for personal injury damages).

<sup>167</sup> Cf. *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*19 (holding that Genzyme did not have a duty to continue supplying patients of the drug in short supply); *Lacognata*, 2012 U.S. Dist. LEXIS 102708, at \*9 (holding that Hospira did not have a duty to supply the drug to the Plaintiff and the market in general).

<sup>168</sup> See generally *Schubert*, 2013 U.S. Dist. LEXIS 126291 (analyzing and ruling on the issue of drug maker duty to continue drug production); *Lacognata*, 2012 U.S. Dist. LEXIS 102708 (same).

<sup>169</sup> See cases cited *supra* note 167.

<sup>170</sup> See *Schubert*, 2013 U.S. Dist. LEXIS 126291, at \*19; *Lacognata*, 2012 U.S. Dist. LEXIS 102708, at \*9.

B. *The Consequences of Inadequate Efforts to Mitigate Drug Shortages*

Healthcare systems, patients and their families, and orphan drug companies all face serious concerns and consequences when confronted with drug shortages.<sup>171</sup> Most of these issues are financial in nature or relate to safety concerns.<sup>172</sup> The negative consequences can also affect drug companies' reputations.<sup>173</sup> But, patients are ultimately the ones who suffer the most from orphan drug shortages.<sup>174</sup>

Healthcare providers experience increased costs and have trouble treating patients with limited orphan drug supplies.<sup>175</sup> Drug vendors and distributors engage in price gouging by charging health providers 10–1,000 times the ordinary price for drugs in shortage, thereby increasing hospital costs.<sup>176</sup> This exploitative environment creates grey markets.<sup>177</sup> A grey market is the trade of legally made products through unauthorized, unofficial, or unintended distribution channels.<sup>178</sup> The same drugs sold in other countries can cost a fraction of their drug prices in the United States.<sup>179</sup> Unauthorized distributors can import the drugs into the United States and sell them at heavily marked up prices.<sup>180</sup> A pharmacy survey estimated that U.S. hospitals spent at least \$200 million on grey market and alternative drugs.<sup>181</sup>

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<sup>171</sup> See Hoffman, *supra* note 13, at 9-11; Born, *supra* note 13, at 237-39; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Andrew Pollack, *Precious Drugs that Come at a Cost Few Can Afford to Meet*, N.Y. TIMES (Apr. 15, 2010), <http://www.nytimes.com/2010/04/16/business/16genzymeside.html> [hereinafter *Precious Drugs*].

<sup>172</sup> See Hoffman, *supra* note 13, at 9-11; Born, *supra* note 13, at 237-39.

<sup>173</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171.

<sup>174</sup> E.g., Schubert, 2013 U.S. Dist. LEXIS 126291, at \*4 (providing an example of a patient who died); see Born, *supra* note 13, at 237; Friske, *supra* note 2, at 525-26; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171.

<sup>175</sup> See FDA'S APPROACH, *supra* note 1, at 29; Hoffman, *supra* note 13, at 9-11; Born, *supra* note 13, at 239.

<sup>176</sup> See Hoffman, *supra* note 13, at 9; Kara Stencel, *Health Policy Brief: Drug Shortages*, HEALTH AFF. (Sept. 11, 2014), [http://www.healthaffairs.org/healthpolicybriefs/brief.php?brief\\_id=124](http://www.healthaffairs.org/healthpolicybriefs/brief.php?brief_id=124).

<sup>177</sup> See Hoffman, *supra* note 13, at 9; Born, *supra* note 13, at 239; Stencel, *supra* note 176.

<sup>178</sup> Jonny Balfus, *Keep It to Yourself: 50 States of Grey*, POPDOSE (June 26, 2014, 8:48 PM), <http://popdose.com/keep-it-to-yourself-50-states-of-grey/>.

<sup>179</sup> See *id.*

<sup>180</sup> See Hoffman, *supra* note 13, at 9; Balfus, *supra* note 178.

<sup>181</sup> Hoffman, *supra* note 13, at 10.

Even worse than grey markets, black markets can develop.<sup>182</sup> Black markets differ from grey markets by providing consumers with illegal products or products that cannot be acquired through authorized channels.<sup>183</sup> Like grey markets, black market vendors sell short supply drugs at exorbitant prices.<sup>184</sup> Fraudulent, counterfeit, and expired drugs are also concerns in the black market.<sup>185</sup> A side effect of grey and black markets is that patients may resort to stockpiling and hoarding.<sup>186</sup> This can also exacerbate the severity of the drug shortage.<sup>187</sup>

For patients and their families, they encounter financial and safety concerns when facing drug shortages.<sup>188</sup> Drug shortages may force patients to forgo treatments, take reduced drug doses, or receive alternative drug treatments that increase adverse reaction risks and dosing errors.<sup>189</sup> Patients taking reduced doses or less-effective alternative treatments may have deteriorating health.<sup>190</sup> These patients may require frequent visits to the hospital, increasing healthcare costs and consuming resources.<sup>191</sup> For patients who may need to take substitute, alternative treatments, insurance providers may be unwilling to pay.<sup>192</sup> As a result, patients need to cover these treatments out-of-pocket.<sup>193</sup> And if patients die as a consequence of ineffective treatments or drug shortages, family members are the ones left to shoulder the grief and expense of funeral costs.<sup>194</sup>

But, even if orphan drugs are available and not in shortage, orphan disease patients still pay an exorbitant amount for their orphan drugs.

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<sup>182</sup> See DEVON HERRICK, NAT'L CTR. FOR POLICY ANALYSIS, ISSUE BRIEF NO. 104, WHAT TO DO ABOUT DRUG SHORTAGES 4 (2011), available at <http://www.ncpa.org/pdfs/ib104.pdf>; Richard N. Fogoros, *What's Really Causing the Drug Shortages*, COVERT RATIONING BLOG (Nov. 8, 2011, 6:33 AM), <http://coverrationingblog.com/healthcare-policy/whats-really-causing-the-drug-shortages>.

<sup>183</sup> See Balfus, *supra* note 178; Fogoros, *supra* note 182.

<sup>184</sup> See HERRICK, *supra* note 182, at 4; Born, *supra* note 13, at 239.

<sup>185</sup> See HERRICK, *supra* note 182, at 4.

<sup>186</sup> See *id.*

<sup>187</sup> See *id.*

<sup>188</sup> See Hoffman, *supra* note 13, at 8-11; Born, *supra* note 13, at 237-39; Pollack, *Precious Drugs*, *supra* note 171.

<sup>189</sup> See Born, *supra* note 13, at 237-39; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171.

<sup>190</sup> See Friske, *supra* note 2, at 525-26.

<sup>191</sup> See *id.*

<sup>192</sup> See Hoffman, *supra* note 13, at 11.

<sup>193</sup> See *id.*

<sup>194</sup> See Lisa Gibbs & Ismat Sarah Mangla, *The High Cost of Saying Goodbye: Part 1 of 3*, MONEY MAG., Nov. 2012, at 108, 110-12.

Orphan drug patients typically pay \$100,000 to \$300,000 each year for their drugs.<sup>195</sup> Even patients with insurance pay \$2,000 to \$4,000 out of pocket each month.<sup>196</sup> Patients may take extreme measures to afford their drugs.<sup>197</sup> Examples of such measures are patients selling their houses, not paying bills, leaving careers for jobs with better insurance, and ruining their credit ratings.<sup>198</sup> The high drug prices that patients pay, and the extreme measures they take to afford them, should be unacceptable to the ethical and moral conscience of society.

The government is aware of the high, and sometimes increasing drug prices that companies are charging patients with rare diseases.<sup>199</sup> The concern is that drug companies are exploiting patients with rare diseases.<sup>200</sup> The government already provides incentives to orphan drug companies to develop orphan drugs and recoup their costs, but orphan drugs are still highly priced in comparison to other drugs.<sup>201</sup> Even after orphan drug makers enjoy the first seven years without competitors, orphan drug companies are still unlikely to encounter competitors after seven years pass (which keep orphan drug prices high),<sup>202</sup> and also unlikely to experience generic competition (that would then lower orphan drug costs).<sup>203</sup> However, the tide may shift

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<sup>195</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171; Max Nisen, \$300,000 a Year 'Orphan Drugs' Are Becoming a Hugely Profitable Business, *BUS. INSIDER* (Jan. 31, 2013, 6:43 AM), <http://www.businessinsider.com/the-business-of-orphan-drugs-2013-1>; Aaron Smith, *From Orphan to Blockbuster?*, *CNNMONEY* (July 8, 2005, 2:06 PM), <http://money.cnn.com/2005/07/08/news/midcaps/orphan>.

<sup>196</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171.

<sup>197</sup> See sources cited *supra* note 196.

<sup>198</sup> See sources cited *supra* note 196.

<sup>199</sup> See generally *Small Market Drugs, Big Price Tags: Are Drug Companies Exploiting People with Rare Disease?: Hearing Before the J. Econ. Comm.*, 110th Cong. (2008) [hereinafter *Hearings*] (noting how Congress's Joint Economic Committee conducted a hearing on this exact issue of how drug companies are exploiting people with rare diseases).

<sup>200</sup> See *Hearings*, *supra* note 199, at 2-5 (statement of Sen. Amy Klobuchar, Member, J. Econ. Comm.).

<sup>201</sup> See *id.* at 4-5; Perrone, *supra* note 73. Examples of government incentives include tax credits, R&D grants, waived FDA fees, favorable reimbursement, lower marketing costs, longer market exclusivity, and premium pricing. See *The Economics of Orphan Drugs*, *supra* note 68.

<sup>202</sup> See *Hearings*, *supra* note 199, at 5 (statement of Sen. Amy Klobuchar, Member, J. Econ. Comm.); Perrone, *supra* note 73.

<sup>203</sup> See *Hearings*, *supra* note 199, at 5 (statement of Sen. Amy Klobuchar, Member, Joint Econ. Comm.). Generic biological drugs are called "biosimilars." See *Biosimilars*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/drugs/developmentapprovalprocess/>

as the FDA recently approved Novartis's Zarxio, the first biosimilar drug in the United States.<sup>204</sup> But it is still to be seen if there will be enough incentive for biosimilar drug companies to enter an orphan drug market with a small patient population and established orphan drug brand.

Since many detrimental consequences result from orphan drug shortages, orphan drug companies face intense scrutiny and bad publicity.<sup>205</sup> Patients are aware that drug makers profit immensely from orphan drugs.<sup>206</sup> In exchange for paying these high prices, patients expect companies to ensure that large-scale manufacturing violations would not occur and that enough drugs are available.<sup>207</sup> Therefore, patients are outraged when orphan drug companies reduce drug dosages or stop providing the drugs altogether.<sup>208</sup> Patients wonder about a drug maker's sense of corporate and social responsibility.<sup>209</sup> As a result, patients perceive that drug makers have been unfair and unethical.<sup>210</sup>

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howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/default.htm (last updated Jan. 2, 2015).

<sup>204</sup> See Deena Beasley & Ben Hirschler, *Novartis Wins Approval for First U.S. Biosimilar Drug*, REUTERS (Mar. 6, 2015), <http://www.reuters.com/article/2015/03/06/us-health-biosimilars-novartis-idUSKBN0M21HI20150306> (noting that Zarxio is the copied version of Amgen's Neupogen, which generated \$1.2 billion in sales worldwide during 2014). Congress passed the Biologics Price Competition and Innovation Act in 2009, allowing the FDA to review and approve biosimilars. See Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, §§ 7001–7003, 124 Stat. 119, 804-21 (2010) (codified as amended at 21 U.S.C. §§ 355(b)(5)(B), 35 U.S.C. 271(e), 42 U.S.C. 262, 262(i) (2012)); *Biosimilars*, *supra* note 203.

<sup>205</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171.

<sup>206</sup> See Pollack, *Precious Drugs*, *supra* note 171 (quoting an orphan drug user as saying “[drug makers] are essentially financially raping people” (internal quotation marks omitted)).

<sup>207</sup> See generally *id.* (reporting orphan drug users' sentiments about drug manufacturers).

<sup>208</sup> See *supra* note 205.

<sup>209</sup> See Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2.

<sup>210</sup> See Andrew Pollack, *Cutting Dosage of Costly Drug Spurs a Debate*, N.Y. TIMES (Mar. 16, 2008), <http://www.nytimes.com/2008/03/16/business/16gaucher.html>; Pollack, *Genzyme Drug Users Betrayed*, *supra* note 2; Pollack, *Precious Drugs*, *supra* note 171.

## III. SOLUTIONS TO MITIGATE ORPHAN DRUG SHORTAGES

A. *Redundant and Back-up Manufacturing*

The FDA should require orphan drug companies to create redundant or back-up manufacturing processes and systems.<sup>211</sup> Since the FDA approves every new drug in the United States,<sup>212</sup> the FDA could condition orphan drug approval upon the specification of back-up manufacturing plans.<sup>213</sup> At the beginning of the approval process, drug makers file either a New Drug Application (“NDA”) or a Biologic License Application (“BLA”).<sup>214</sup> In these applications, drug makers need to include information about the manufacturer, the manufacturing process, and regulatory compliance.<sup>215</sup> The FDA has the ability to inspect the manufacturer to review the facilities, equipment, and skills to manufacture the new drug.<sup>216</sup>

Currently, drug makers favor efficiency over preparedness.<sup>217</sup> Drug makers select only one or two manufacturers to produce each drug a company develops.<sup>218</sup> They do so because the manufacturing process for biological orphan drugs is complex and expensive.<sup>219</sup> If an orphan drug maker employs only one manufacturer, the FDA should require

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<sup>211</sup> See Hoffman, *supra* note 13, at 21; Friske, *supra* note 2, at 534; Daphne Allen, Editorial, *Should Industry Step Up Redundancy to Prevent Drug Shortages?*, PHARM. & MED. PACKAGING NEWS (Nov. 3, 2011), <http://www.pmpnews.com/news/editorial-should-industry-step-redundancy-prevent-drug-shortages>.

<sup>212</sup> See *How Drugs Are Developed and Approved*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm> (last updated Nov. 10, 2014).

<sup>213</sup> See Hoffman, *supra* note 13, at 21 (alluding that drug makers currently do not indicate to the FDA whether they will create redundancy in their manufacturing plans to avoid shortages); Friske, *supra* note 2, at 534 (suggesting that drug makers need to improve communications with the FDA regarding “manufacturing redundancies or backup supplies”); Allen, *supra* note 211 (recommending that manufacturers should consider “redundant or parallel manufacturing processes” to mitigate drug supply disruptions).

<sup>214</sup> See *Types of Applications*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/default.htm> (last updated Oct. 23, 2014).

<sup>215</sup> See *Drug Applications and Current Good Manufacturing Practice (CGMP) Regulations*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/drugs/developmentapprovalprocess/manufacturing/ucm090016.htm> (last updated Dec. 17, 2014).

<sup>216</sup> See *id.*

<sup>217</sup> See FDA’S APPROACH, *supra* note 1, at 30-31; Friske, *supra* note 2, at 534; Allen, *supra* note 211.

<sup>218</sup> See FDA’S APPROACH, *supra* note 1, at 30-31.

<sup>219</sup> See Allen, *supra* note 211.

the company to submit manufacturing information for a second, back-up manufacturer.<sup>220</sup> With a back-up contract manufacturer organization (“CMO”), the drug company would have an alternative system in place if the first manufacturer encounters problems.<sup>221</sup>

Critics will argue that such a requirement is burdensome, time-consuming, and costly for drug makers.<sup>222</sup> But, drug makers receive many incentives to enter the orphan drug business,<sup>223</sup> and an additional FDA requirement should not be a deterrent.<sup>224</sup> The advantages of entering the orphan drug space may outweigh the negatives.<sup>225</sup> Orphan drugs are an \$83 billion business and it is booming.<sup>226</sup> Orphan drug makers receive seven-year market exclusivity on new orphan drugs.<sup>227</sup> Drug makers also obtain direct grants and tax credits equivalent to half their drug development costs.<sup>228</sup> These incentives make orphan drugs cheaper to develop, but companies are still able to charge high prices for them.<sup>229</sup> Therefore, companies have been profiting from their orphan drugs.<sup>230</sup>

Critics also overstate the amount of time and money needed to employ a second CMO.<sup>231</sup> The advantages of having a back-up

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<sup>220</sup> See *id.*

<sup>221</sup> See Friske, *supra* note 2, at 534.

<sup>222</sup> See Fox, *supra* note 6, at 29; Allen, *supra* note 211.

<sup>223</sup> See Nisen, *supra* note 195 (discussing the enormous profitability of some companies after entering the orphan drug business); Perrone, *supra* note 73; Smith, *supra* note 195.

<sup>224</sup> See Nisen, *supra* note 195; Smith, *supra* note 195; *The Economics of Orphan Drugs*, *supra* note 68.

<sup>225</sup> See *supra* note 224.

<sup>226</sup> See Anthony Raeside, *Worldwide Orphan Drug Market to Grow to \$127 Billion by 2018*, BIOTECHNOW (Apr. 23, 2013), <http://www.biotech-now.org/health/2013/04/worldwide-orphan-drug-market-to-grow-to-127-billion-by-2018> (noting the figure accounted for 2012, but said to grow to \$127 billion by 2018).

<sup>227</sup> See 21 U.S.C. § 360cc (2012).

<sup>228</sup> See 26 U.S.C. § 45C (2012); 21 U.S.C. § 360ee (2012).

<sup>229</sup> See *The Economics of Orphan Drugs*, *supra* note 68; see, e.g., Pollack, *Precious Drugs*, *supra* note 171 (illustrating that Genzyme’s orphan drugs can cost more than \$200,000 a year); Andrew Pollack, *Questcor Finds Profits, at \$28,000 a Vial*, N.Y. TIMES (Dec. 29, 2012), <http://www.nytimes.com/2012/12/30/business/questcor-finds-profit-for-acthar-drug-at-28000-a-vial.html> (illustrating a typical course of Questcor’s orphan drug treatment can cost over \$100,000).

<sup>230</sup> See Smith, *supra* note 195.

<sup>231</sup> See Thomas, *Lapses*, *supra* note 54; Allen, *supra* note 211; Ed Miseta, *5 Characteristics to Look for in a Backup Supplier*, OUTSOURCED PHARMA (Sept. 20, 2013), <http://www.outsourcedpharma.com/doc/characteristics-to-look-for-in-a-backup-supplier-0001>.

manufacturer outweigh not having one.<sup>232</sup> Maintaining manufacturing redundancies and back-ups is expensive, but the drug maker can incur even greater costs if it encounters manufacturing disruptions without a back-up plan.<sup>233</sup> Manufacturing problems can take a long time to solve, and companies can lose profits and customers during drug shortages.<sup>234</sup> The manufacturing issues can be so severe that manufacturers need to spend hundreds of millions of dollars to improve their facilities.<sup>235</sup> Also, once a CMO has developed a manufacturing process, a drug maker can transfer the process to a second CMO.<sup>236</sup> Thus, a back-up manufacturer can protect the drug maker from drug shortages,<sup>237</sup> and can ultimately benefit patients.<sup>238</sup>

### B. A Stockpile Repository

The FDA should also develop an orphan drug stockpile repository program.<sup>239</sup> After the FDA approves an orphan drug for market, the FDA should require the orphan drug maker to manufacture excess drugs every year.<sup>240</sup> Drug makers should maintain excess orphan drugs as part of a repository.<sup>241</sup>

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<sup>232</sup> See Born, *supra* note 13, at 246-49; Jensen, *supra* note 120; Miseta, *supra* note 231.

<sup>233</sup> See Fox, *supra* note 6, at 29; Miseta, *supra* note 231.

<sup>234</sup> See sources cited *supra* note 233.

<sup>235</sup> See, e.g., Thomas, *Lapses*, *supra* note 54 (noting how Ben Venue spent more than \$300 million to upgrade its factories and build a new plant, while Hospira anticipates spending up to \$375 million to address FDA concerns over its facilities).

<sup>236</sup> See Angelo DePalma, *Ins & Outs of Tech Transfer*, PHARM. MFG. (Mar. 13, 2013), <http://www.pharmamanufacturing.com/articles/2013/1303-ins-outs-tech-transfer/>.

<sup>237</sup> See Miseta, *supra* note 231.

<sup>238</sup> See Hoffman, *supra* note 13, at 21; Friske, *supra* note 2, at 534; Allen, *supra* note 211.

<sup>239</sup> See Hoffman, *supra* note 13, at 17. See generally Sam Lister, 'Shocking Example of Incompetence' over Stockpiled Flu Drug Tamiflu, INDEPENDENT (May 21, 2013), <http://www.independent.co.uk/news/uk/politics/shocking-example-of-incompetence-over-stockpiled-flu-drug-tamiflu-8625528.html> (illustrating an example of a stockpile that an orphan drug repository may be modeled after); Andrew C. Revkin, *Buried Seed Vault Opens in Arctic*, N.Y. TIMES DOT EARTH BLOG (Feb. 26, 2008, 7:18 AM), <http://dotearth.blogs.nytimes.com/2008/02/26/buried-seed-vault-opens-in-arctic/> (same).

<sup>240</sup> Cf. Nick Taylor, *UK Issues Supply Chain Guide to Prevent Drug Shortages*, IN-PHARMA TECHNOLOGIST.COM (Feb. 7, 2011, 11:56 AM), <http://www.in-pharmatechnologist.com/Regulatory-Safety/UK-issues-supply-chain-guide-to-prevent-drug-shortages> (suggesting a similar regime in the United Kingdom).

<sup>241</sup> Cf. Hoffman, *supra* note 13, at 17 (noting that national stockpiles are beneficial in times of emergency). See generally Lister, *supra* note 239 (illustrating an example of a stockpile that an orphan drug repository may be modeled after); Revkin, *supra* note 239 (demonstrating the success of repositories in the agricultural context).

Stockpiling programs have succeeded in other contexts.<sup>242</sup> The Strategic National Stockpile includes medical supplies and medicines that may be necessary in case of public health emergencies.<sup>243</sup> When concerns over bird flu began in 2006, the government started a national stockpile of Roche's Tamiflu.<sup>244</sup> The government began pushing corporations to accumulate corporate stockpiles for their employees as a way to supplement the national stockpile.<sup>245</sup> Another type of repository is located in the Arctic.<sup>246</sup> The Arctic repository contains a back-up supply of seeds from different plant varieties.<sup>247</sup> Although current stockpile repositories exist for different purposes, the FDA can turn to them for guidance in creating an orphan drug repository.<sup>248</sup>

Critics will argue that collecting and maintaining stockpiles can be costly and logistically complicated.<sup>249</sup> But this argument fails because the number of orphan drugs needed to collect and manage is relatively small.<sup>250</sup> Since 1983, the FDA has approved only 425 orphan drugs.<sup>251</sup> Orphan drugs comprise about 12% of the global pharmaceutical market by volume,<sup>252</sup> so there are fewer drugs to collect to maintain a stockpile. The FDA should work with drug companies to determine

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<sup>242</sup> See Hoffman, *supra* note 13, at 17; Lister, *supra* note 239; Revkin, *supra* note 239; Tracy Staton, *Roche Touts Corporate Tamiflu Stockpiling*, FIERCEPHARMA (June 27, 2008), <http://www.fiercepharma.com/story/roche-touts-corporate-tamiflu-stockpiling/2008-06-27> [hereinafter *Roche Touts*]; see, e.g., *Svalbard Global Seed Vault*, NOR. MINISTRY OF AGRIC. & FOOD, <http://www.regjeringen.no/en/dep/lmd/campaign/svalbard-global-seed-vault.html?id=462220> (last visited Jan. 18, 2014) (providing an example of a successful government-sponsored stockpiling endeavor in another context).

<sup>243</sup> See Hoffman, *supra* note 13, at 17.

<sup>244</sup> See Lister, *supra* note 239; Staton, *Roche Touts*, *supra* note 242.

<sup>245</sup> See Staton, *Roche Touts*, *supra* note 242.

<sup>246</sup> See Revkin, *supra* note 239; *Svalbard Global Seed Vault*, *supra* note 242.

<sup>247</sup> See sources cited *supra* note 246.

<sup>248</sup> See Hoffman, *supra* note 13, at 17; see, e.g., Lister, *supra* note 239 (illustrating on example of a stockpile that an orphan drug repository may be modeled after); Revkin, *supra* note 239 (same).

<sup>249</sup> See Hoffman, *supra* note 13, at 17; Lister, *supra* note 239; *Flu Drug Stockpiles Save Lives, Too Costly for Many*, REUTERS (Feb. 2, 2011, 5:17 AM EST), <http://www.reuters.com/article/2011/02/02/flu-stockpiling-idUSLDE7101YN20110202>.

<sup>250</sup> See *supra* Part I.A; cf. Hoffman, *supra* note 13, at 17 (noting that this stockpile is limited to only medicines and supplies necessary for a public health emergency); Revkin, *supra* note 239 (noting that this stockpile is limited to only plant seed varieties); Staton, *Roche Touts*, *supra* note 242 (noting that this stockpile is limited to only Tamiflu).

<sup>251</sup> Raeside, *supra* note 226.

<sup>252</sup> See *id.*; *Statistics*, DRUG BANK, <http://www.drugbank.ca/stats> (last visited Mar. 26, 2015) (noting that there are 3,360 approved drugs worldwide).

the excess drug amounts necessary for the stockpile so that companies can manufacture excess drugs during production of its normally scheduled drugs.<sup>253</sup>

Critics will also argue that drugs have limited shelf lives and companies need to replace them periodically.<sup>254</sup> If drug shortages do not occur, then the drugs may go to waste.<sup>255</sup> However, commercial drug companies have supply chain managers and processes in place to manage drug supplies.<sup>256</sup> When the manufacturer produces a new drug batch, supply chain personnel can designate a certain amount into the repository, with the rest for consumer use.<sup>257</sup> Supply chain managers can then monitor the repository and rotate out the drugs nearing their shelf lives.<sup>258</sup> They can filter repository drugs into the regular supply chain, and deliver the drugs to consumers.<sup>259</sup> Supply chain managers should be able to prevent drug waste because they can monitor, rotate out, and replace repository drugs with newly manufactured drugs.<sup>260</sup>

### C. Compensation Fund

Congress should propose and pass legislation that would allow the FDA to establish an orphan drug compensation fund that would

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<sup>253</sup> Cf. Nordenberg, *supra* note 68 (illustrating FDA efforts to mitigate drug shortages and the potential to extend its efforts to creating and maintaining an orphan drug shortage).

<sup>254</sup> See Hoffman, *supra* note 13, at 17.

<sup>255</sup> See *id.*

<sup>256</sup> See Ryan McBride, *Prizer Tapes Cloud Computing to Gain Control of Supply Chain*, FIERCEBIOTECHIT (Sept. 12, 2012), <http://www.fiercebiotechit.com/story/pfizer-taps-cloud-computing-gain-control-supply-chain/2012-09-12>. See generally Robert Handfield, *What Is Supply Chain Management?*, SUPPLY CHAIN RES. COOP., N.C. STATE UNIV. (Jan. 11, 2011), <http://scm.ncsu.edu/scm-articles/article/what-is-supply-chain-management> (explaining supply chain management); Victoria Taylor, *Supply Chain Management: The Next Big Thing?*, BLOOMBERG BUS. (Sept. 12, 2011), <http://www.businessweek.com/business-schools/supply-chain-management-the-next-big-thing-09122011.html> (describing increasing demand for supply chain management professionals).

<sup>257</sup> Cf. Nordenberg, *supra* note 68 (illustrating how a drug allocation program can properly manage demand and supply).

<sup>258</sup> See Hoffman, *supra* note 13, at 17.

<sup>259</sup> Cf. *id.* (noting how drugs are wasted if drug expiration dates are not tracked and are not replaced periodically); Nordenberg, *supra* note 68 (illustrating how a properly managed drug allocation program can distribute drugs to consumers who need them).

<sup>260</sup> Cf. Nordenberg, *supra* note 68 (illustrating how a properly managed drug allocation program can distribute drugs efficiently and effectively).

provide monetary relief for patients harmed by orphan drug shortages.<sup>261</sup> Currently, patients suffering from orphan drug shortages have no remedy.<sup>262</sup> Victims probably cannot successfully sue for negligence.<sup>263</sup> Therefore, a solution that compensates orphan drug shortage victims would provide the monetary relief they would otherwise not receive.<sup>264</sup>

Victims have successfully utilized compensation funds in lieu of tort remedies in other situations.<sup>265</sup> In the past, different entities have established compensation funds to compensate victims.<sup>266</sup> When the British Petroleum (“BP”) oil spill occurred in 2010,<sup>267</sup> the company established a compensation fund to compensate those affected by the oil spill.<sup>268</sup> Albeit nearly ten years after the 9/11 terrorist attacks, President Obama established the September 11th Victim Compensation Fund (“Fund”).<sup>269</sup> The Fund compensated any individual who suffered physical harm, and the families of those who were killed, because of the attacks.<sup>270</sup>

The National Childhood Vaccine Injury Act (“NCVI Act”) is a representative example of a successful compensation fund for medical issues.<sup>271</sup> Congress enacted the NCVI Act in 1986.<sup>272</sup> The NCVI Act

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<sup>261</sup> Cf. *About the Victim Compensation Fund*, SEPTEMBER 11TH VICTIM COMP. FUND, <http://www.vcf.gov/genProgramInfo.html> (last visited Jan. 18, 2014) [hereinafter *Victim Compensation Fund*] (providing an example of another type of compensation fund to provide victims monetary relief); David Goguen, *BP Oil Spill Claims and Compensation*, NOLO, <http://www.nolo.com/legal-encyclopedia/bp-oil-spill-filing-claim-33441.html> (last visited Mar. 26, 2015) (same); *National Childhood Vaccine Injury Act of 1986*, AM. TORT REFORM ASS'N, <http://www.atra.org/legislation/federal/national-childhood-vaccine-injury-act-of-1986> (last visited Jan. 18, 2014) [hereinafter *National Childhood Vaccine Act*] (same).

<sup>262</sup> See *supra* Part I.B.

<sup>263</sup> See *supra* Part II.A.

<sup>264</sup> See *supra* Part II.A.

<sup>265</sup> See sources cited *supra* note 261.

<sup>266</sup> See sources cited *supra* note 261.

<sup>267</sup> See *Deepwater Horizon Accident and Response*, BP, PLC, <http://www.bp.com/en/global/corporate/gulf-of-mexico-restoration/deepwater-horizon-accident-and-response.html> (last visited Jan. 18, 2014).

<sup>268</sup> See Goguen, *supra* note 261.

<sup>269</sup> *Victim Compensation Fund*, *supra* note 261.

<sup>270</sup> See *id.*

<sup>271</sup> See *Frequently Asked Questions*, HEALTH RES. & SERVS. ADMIN., <http://www.hrsa.gov/vaccinecompensation/faq.html> (last visited Jan. 18, 2014); *National Childhood Vaccine Act*, *supra* note 261; *National Vaccine Injury Compensation Program*, HEALTH RES. & SERVS. ADMIN., <http://www.hrsa.gov/vaccinecompensation/index.html> (last visited Jan. 18, 2014); *Vaccine Injury Compensation Programs*, COLL. OF PHYSICIANS OF PHILA., <http://www.historyofvaccines.org/content/articles/vaccine-injury-compensation-programs> (last updated July 31, 2014).

compensated people who experienced vaccination side effects, but had little recourse for compensation from manufacturers, doctors, and the government.<sup>273</sup> The NCVI Act also created a no-fault, claim-based compensation program for vaccine-related injuries or death (“NCVI Fund”).<sup>274</sup> Additionally, the NCVI Act offered liability protections to vaccine manufacturers.<sup>275</sup> Therefore, the NCVI Fund became an alternative to the traditional tort system for resolving vaccine injury claims.<sup>276</sup> For people suffering, or representatives of those who died, from vaccine injuries, they must first exhaust the remedies available under the NCVI Act before taking separate legal action.<sup>277</sup> To date, the NCVI Fund has paid out over \$2 billion to claimants.<sup>278</sup>

The FDA should establish a fund similar to the NCVI Fund.<sup>279</sup> The FDA should use the manufacturing fines that the agency collects to fund the program.<sup>280</sup> Through a claim procedure, the fund would disburse monetary relief to patients who were injured and died because of orphan drug shortages.<sup>281</sup>

Critics will argue that compensation funds are complicated and hard to manage.<sup>282</sup> But new processes and procedures have their challenges. The FDA can use the fund to pay claim administrators to run the claim process system.<sup>283</sup> Patients may use the fund to obtain

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<sup>272</sup> National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, §§ 301–322, 100 Stat. 3743, 3755 (codified as amended at 42 U.S.C. §§ 300aa-1 to 300aa-34 (2012)); see *National Childhood Vaccine Act*, *supra* note 261.

<sup>273</sup> See *Vaccine Injury Compensation Programs*, *supra* note 271.

<sup>274</sup> See 42 U.S.C. § 300aa-11 (2012); *History of Vaccine Safety*, CDC, [http://www.cdc.gov/vaccinesafety/Vaccine\\_Monitoring/history.html](http://www.cdc.gov/vaccinesafety/Vaccine_Monitoring/history.html) (last updated Nov. 4, 2014); *National Childhood Vaccine Act*, *supra* note 261.

<sup>275</sup> See *Frequently Asked Questions*, *supra* note 271.

<sup>276</sup> *National Vaccine Injury Compensation Program*, *supra* note 271.

<sup>277</sup> See *Frequently Asked Questions*, *supra* note 271.

<sup>278</sup> See *Vaccine Injury Compensation Programs*, *supra* note 271.

<sup>279</sup> *Cf. id.* (providing an example of a healthcare-related compensation fund that the FDA can use as a model for an orphan drug compensation fund).

<sup>280</sup> *Cf. id.* (providing an example of how an excise tax is imposed on each vaccine dose to fund the Vaccine Injury Compensation Fund).

<sup>281</sup> *Cf. id.* (providing an example of how a claim procedure can be used for an orphan drug compensation fund).

<sup>282</sup> See, e.g., Barbara Loe Fisher, *Why Vaccine-Injured Kids Are Rarely Compensated*, MERCOLA.COM (Dec. 13, 2008), <http://articles.mercola.com/sites/articles/archive/2008/12/13/why-vaccine-injured-kids-are-rarely-compensated.aspx> (arguing that the vaccine compensation program is not working as intended and should thus be repealed).

<sup>283</sup> *Cf. How to File a Claim*, HEALTH RES. & SERVS. ADMIN., <http://www.hrsa.gov/vaccinecompensation/fileclaim.html> (last visited Jan. 18, 2014) (providing an example of how the Office of Special Masters within the U.S. Court of

compensation they would otherwise not receive from the common law tort system.<sup>284</sup> If this fund is not established, orphan drug patients will have a slim chance of compensation elsewhere.<sup>285</sup> Ultimately, the benefits of having an orphan drug compensation fund may outweigh the disadvantages.<sup>286</sup>

#### CONCLUSION

Orphan drug shortages are detrimental to patient health and safety.<sup>287</sup> Both Congress and the FDA should not only aim to prevent orphan drug shortages, but find alternative, compensatory solutions for patients harmed by these shortages.<sup>288</sup> Therefore, a two-pronged approach of both preventive and compensatory solutions will best serve patients harmed by orphan drug shortages.<sup>289</sup>

One of the FDA's preventative measures should require orphan drug makers to include back-up manufacturing requirements as a part of their NDA or BLA filings.<sup>290</sup> The FDA should also establish stockpile repository requirements for orphan drugs.<sup>291</sup> Since the traditional tort reform system does not provide monetary relief for patients injured by orphan drug shortages, Congress should pass legislation to allow the FDA to establish a compensation fund.<sup>292</sup> FDA manufacturing fines can supply the fund.<sup>293</sup> If these actions are taken, patients in need of orphan drugs or harmed by orphan drug shortages may no longer feel left behind and "orphaned" by drug companies and the government.

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Federal Claims is designated to handle claim processing).

<sup>284</sup> See *supra* Part I.A.

<sup>285</sup> See *supra* Part II.A.

<sup>286</sup> Cf. *supra* note 261 (providing examples of how without the compensation funds, victims would have had a difficult time obtaining monetary relief). There may be difficulties associated with running and managing an orphan drug shortage compensation fund, but it is hard to justify that these costs would exceed the social and monetary benefits of allowing victims to receive compensation from such a fund.

<sup>287</sup> See *supra* Parts I.A, II.B.

<sup>288</sup> See *supra* Part III.A–C.

<sup>289</sup> See *supra* Part III.A–C.

<sup>290</sup> See *supra* Part III.A.

<sup>291</sup> See *supra* Part III.B.

<sup>292</sup> See *supra* Part III.C.

<sup>293</sup> See *supra* Part III.C.