

## The Drug Shortage Crisis: When Generic Manufacturers “Just Say No”

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#### INTRODUCTION

Jenny Morrill, a mother and former arts administrator, has been battling ovarian cancer since 2007.<sup>1</sup> When she recently went to her scheduled chemotherapy treatment, the hospital presented her with both good and bad news.<sup>2</sup> The good news was that she was responding well to the prescribed chemotherapy drug, Doxil.<sup>3</sup> The bad news was that due to nationwide shortages, the hospital had no more Doxil to give her.<sup>4</sup> Ms. Morrill said her “jaw dropped.”<sup>5</sup> In describing her health predicament, Ms. Morrill said,

A lot of things can go wrong when you’re in cancer treatment—your white count can go down, you can become too frail to get treatment, the chemo can stop working. One of the things you never consider is that treatment might just not be available. It’s like you’re out in the ocean and the guy on the lifeboat says, “Sorry, they ran out of life rings.”<sup>6</sup>

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<sup>1</sup> Roni Caryn Rabin, *Drug Scarcity’s Dire Cost, and Some Ways to Cope*, N.Y. TIMES, (Dec. 12, 2001), <http://www.nytimes.com/2011/12/13/health/policy/the-personal-price-paid-for-shortages-of-doxil-and-other-drugs.html?pagewanted=all>.

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

<sup>3</sup> *Id.*

<sup>4</sup> *Id.*

<sup>5</sup> *Id.*

<sup>6</sup> *Id.*

This scenario is playing out with increasing frequency, as Ms. Morrill and thousands of other cancer patients cannot get access to lifesaving medications. Doxil shortages began in 2011, when the manufacturer temporarily halted production to address Food and Drug Administration (FDA) manufacturing and sanitation issues.<sup>7</sup> The facility’s remediation efforts continued over the next two years.<sup>8</sup> During that time, the facility produced only seventeen of sixty-five expected batches of Doxil.<sup>9</sup> Claiming required upgrades to restore full operation were too costly, the owner of the facility shut down production in 2013.<sup>10</sup> The facility was the sole supplier of Doxil.<sup>11</sup> Adding to Ms. Morrill’s health predicament—the Doxil shortage will continue at least through 2014.<sup>12</sup>

In the past five years, the number of drug shortages in the United States has nearly quintupled.<sup>13</sup> The majority of shortages involve sterile injectables used to fight infectious diseases and treat cancer.<sup>14</sup> These complex drugs are produced in a concentrated market consisting of only a few manufacturers.<sup>15</sup> Any disruption in supply can result in shortages that leave patients without access to lifesaving drugs.<sup>16</sup> In some cases, the drugs are the only treatment for their condition.<sup>17</sup> These shortages have been the result of many factors,

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<sup>7</sup> Eric Palmer, *Updated: J&J’s Doxil Shortage to Last Until at Least End of 2014*, FIERCE PHARMA (Oct. 7, 2013), <http://www.fiercepharma.com/story/jjs-doxil-shortage-last-until-least-end-2014/2013-10-07>.

<sup>8</sup> *See id.*

<sup>9</sup> *Id.*

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

<sup>11</sup> Jef Feeley & Michelle Fay Cortez, *J&J Says Boehringer Fight May Cause Cancer-Drug Shortage*, BLOOMBERG (Oct. 1, 2013), <http://www.bloomberg.com/news/2013-10-01/j-j-says-boehringer-doxil-dispute-may-cause-shortage.html>.

<sup>12</sup> Palmer, *supra* note 7.

<sup>13</sup> Rachel Wallach, *Plenty of Demand, Hurting for Supply*, CHANGING BUS. (Sept. 24, 2014), <http://changeinbusiness.johnshopkins.edu/blog/2014/09/24/plenty-of-demand-hurting-for-supply/>.

<sup>14</sup> FDA, A REVIEW OF FDA’S APPROACH TO MEDICAL PRODUCT SHORTAGES 13 (2011) [hereinafter FDA 2011 REVIEW], available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf>; see also FDA, STRATEGIC PLAN FOR PREVENTING AND MITIGATING DRUG SHORTAGES 8 (2013) [hereinafter FDA 2013 PLAN], available at <http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf>.

<sup>15</sup> See FDA 2011 REVIEW, *supra* note 14, at 4.

<sup>16</sup> *Id.* at 11.

<sup>17</sup> See Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products, 78 Fed. Reg. 65,904 (to be codified at 21 C.F.R. pts 20, 310, 314, and 600) (proposed Nov. 4, 2013) [hereinafter Discontinuance or Interruption].

including product quality concerns, discontinuation of product lines, changes in supply and demand, and manufacturing problems.<sup>18</sup>

In response to the serious effects these shortages have on public health, recent federal legislation attempts to address the drug shortage problem by focusing on manufacturers' notification responsibilities.<sup>19</sup> This legislation authorizes the FDA to require manufacturers of lifesaving and life-supporting drugs to alert the Agency of impending shortages.<sup>20</sup> While this requirement may alleviate some of the factors associated with drug shortages, the FDA receiving advance notice of shortages fails to address the underlying causes.

Despite reoccurring drug shortages, manufacturers have not increased production of these lifesaving medicines. Using generic manufacturers as the lens, this Article explores the confluence of regulatory constraints and market forces behind the shortages. As noted in the Doxil example, shortages have occurred among branded pharmaceuticals; however, more than eighty percent of drugs in short supply are generic injectable medications.<sup>21</sup> Understanding the unique aspects of the generic drug industry is critical to ending shortages.

Part I of this Article provides an overview of current drug shortages and their impact on patient care and healthcare providers. Part II offers an economic analysis of the root causes of the drug shortages. Specifically, Section A provides background on the manufacturers who produce many of the drugs in shortage. This Section also examines how these drugs' complex production processes affect manufacturers' ability to meet increases in demand. Section B looks at unique features of the healthcare drug market and examines their influence on traditional notions of supply and demand. Section C explores the role market consolidations and healthcare reimbursement rates play in current shortages. This Section also expands the analysis to examine how Group Purchasing Organizations' (GPOs) contract practices influence generic manufacturers' production decisions. Section D focuses on the FDA's role in current shortages. According to the FDA, a leading cause of

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<sup>18</sup> FDA 2011 REVIEW, *supra* note 14, at 15–16 fig.4.

<sup>19</sup> Food, Drugs, and Cosmetics Act § 506C(a), 21 U.S.C. § 356c(a) (2012), *amended by* Food and Drug Administration Safety and Innovation Act (FDASIA), Pub. L. No. 112-144, § 1001(a), 126 Stat. 993, 1099 (2012).

<sup>20</sup> *Id.*

<sup>21</sup> Alina Selyukh, *Study Finds U.S. Drug Shortage Problem Concentrated*, REUTERS (Nov. 14, 2011, 10:32 AM), <http://www.reuters.com/article/2011/11/14/us-drugs-shortages-imshealth-idUSTRE7AD1CJ20111114>.

drug shortages is quality problems at manufacturing sites that precipitate production disruptions.<sup>22</sup> This Section challenges that notion. After examining FDA policy decisions, this Section posits that poor agency execution has helped to transform manageable facility improvements into the current drug shortage. Part III analyzes current legislative, regulatory, and industry efforts to address drug shortages. While these approaches may mitigate shortages, this Part concludes they do not go far enough. Part IV acknowledges that shortages will continue until it is profitable for generic manufacturers to maintain production levels sufficient to meet patient demand. Accordingly, this Part offers a multipronged approach that balances patient needs, regulatory safeguards, and manufacturer incentives in a manner sufficient to end drug shortages.

## I

### OVERVIEW OF THE DRUG SHORTAGE CRISIS

#### *A. The Current State of Drug Shortages*

According to the FDA Drug Shortage Index, there is a “shortage” of more than eighty medically necessary drugs.<sup>23</sup> The FDA defines a “drug shortage” as a situation in which the total supply of all clinically interchangeable versions of an FDA-regulated drug is inadequate to meet the current or projected demand at the patient level.<sup>24</sup> Some may be surprised to learn that, notwithstanding the United States’ free market economy and robust patient demand for lifesaving medicines, drug shortages are neither new nor decreasing. In 2005, there were sixty-one reported new drug shortages.<sup>25</sup> By 2011, that number had quadrupled to more than 250 new shortages.<sup>26</sup>

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<sup>22</sup> U.S. GOV’T ACCOUNTABILITY OFFICE, DRUG SHORTAGES: PUBLIC HEALTH THREAT CONTINUES, DESPITE EFFORTS TO HELP ENSURE PRODUCT AVAILABILITY 21 (2014) [hereinafter GAO DRUG SHORTAGES], available at <http://www.gao.gov/assets/670/660785.pdf>.

<sup>23</sup> See *Current and Resolved Drug Shortages and Discontinuations Reported to FDA*, FDA, <http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm> (last visited Oct. 11, 2014) [hereinafter *Current and Resolved Drug Shortages*].

<sup>24</sup> See CTR. FOR DRUG EVALUATION & RESEARCH, DRUG SHORTAGE MANAGEMENT 12 (2014), available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffPoliciesandProcedures/ucm079936.pdf>.

<sup>25</sup> FDA 2011 REVIEW, *supra* note 14, at 10 fig.1.

<sup>26</sup> GAO DRUG SHORTAGES, *supra* note 22, at 11–12 fig.2. It should be noted that drug shortage statistics vary depending on which entity is conducting the study. For example, the American Society of Health-System Pharmacists (ASHP) has a broader definition of drug shortage than the FDA definition. The ASHP takes into account all instances in

Drug shortages, however, typically continue for extended periods so the actual number of shortages at any point in time is often higher.<sup>27</sup> While the number of new shortages decreased in 2012, more than 300 shortages remained active by the end of the year.<sup>28</sup>

The majority of drug shortages have been concentrated among older generic sterile injectables.<sup>29</sup> In 2011, the FDA published a study of 127 long-duration drug shortages that had significant public health implications.<sup>30</sup> The study revealed that the three most common classes of drugs in shortage were oncology (28%), antibiotics (13%), and electrolyte nutrition drugs (11%).<sup>31</sup> Recent shortages have been documented in “crash cart” medicines, which can be lifesaving drugs needed in emergency ambulatory centers while waiting for emergency medical staff to arrive.<sup>32</sup> There are also ongoing shortages in outpatient chemotherapy drugs that must be administered within rigid timeframes of a few days or weeks to provide maximum patient benefit.<sup>33</sup>

In 2011, an American Hospital Association (AHA) survey found that 99.5% of the 820 hospitals surveyed had experienced at least one drug shortage during the last six months.<sup>34</sup> Forty-four percent reported having experienced 21 or more shortages during this same time, and 64% indicated that the shortages created significant patient risks.<sup>35</sup> In a 2012 survey conducted by the American Society of

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which “a supply issue . . . affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent.” Erin R. Fox et al., *ASHP Guidelines on Managing Drug Product Shortages in Hospitals and Health Systems*, 66 AM. J. HEALTH-SYS. PHARMACY 1399, 1400 (2009). ASHP reported 211 drug shortages in 2010 compared to the FDA’s finding of 178. Sharona Hoffman, *The Drugs Stop Here: A Public Health Framework to Address the Drug Shortage Crisis*, 67 FOOD & DRUG L.J. 1, 3 (2012).

<sup>27</sup> FDA 2013 PLAN, *supra* note 14, at 8. Seventy-four percent of the drugs reported to the Drug Shortage Program in 2010 were sterile injectables. FDA 2011 REVIEW, *supra* note 14, at 13.

<sup>28</sup> FDA 2013 PLAN, *supra* note 14, at 8.

<sup>29</sup> FDA 2011 REVIEW, *supra* note 14, at 13.

<sup>30</sup> *Id.* at 13–15.

<sup>31</sup> *Id.* at 14–15 fig.3.

<sup>32</sup> FDA 2011 REVIEW, *supra* note 14, at 11; MINIMUM CRASH CART SUPPLIES AND DRUGS (BASED ON 2010 ACLS PROTOCOLS), <https://www.ttuhsu.edu/provost/clinic/forms/ACForm2.03.A.pdf> (last visited Oct. 12, 2014).

<sup>33</sup> FDA 2011 REVIEW, *supra* note 14, at 11.

<sup>34</sup> AHA SURVEY ON DRUG SHORTAGES, AM. HOSP. ASS’N 2, 4, *available at* [www.aha.org/content/11/drugshortagesurvey.pdf](http://www.aha.org/content/11/drugshortagesurvey.pdf).

<sup>35</sup> *Id.* at 5–8; *see Drug Shortages: National Survey Reveals High Level of Frustration, Low Level of Safety*, INST. FOR SAFE MED. PRACTICES (Sept. 23, 2010), <https://www.ismp.org/newsletters/acutecare/articles/20100923.asp> [hereinafter ISMP].

Anesthesiologists, almost 98% of the 3063 members surveyed reported current shortages of at least one anesthetic.<sup>36</sup> Of those, 96% indicated having to use an alternative drug, 50% had to change an anesthetic procedure because of the shortage, 7% had to postpone treatment, and 4% had to cancel procedures.<sup>37</sup> Finally, the group purchasing organization (GPO) Premier Healthcare Alliance conducted a survey of 311 pharmacy experts representing 228 hospitals.<sup>38</sup> Of those surveyed, 89% reported drug shortages that may have caused a safety issue or medical error, and 80% reported that a drug shortage resulted in delay or cancellation of a patient care intervention.<sup>39</sup> Behind these statistics are patients who are in need of drugs to provide required parenteral nutrition, address serious infections, and treat life-threatening diseases such as cancer.

### *B. Effect of Drug Shortages on Patient Care and Healthcare Providers*

Drug shortages have had serious and immediate effects on patients and healthcare providers. The unavailability of lifesaving treatments has resulted in providers prescribing second-line alternatives.<sup>40</sup> Providers prescribe a specific drug for a number of reasons. In their medical opinion, the ordered drug is the most effective, has the fewest side effects, and is compatible with other medication the patient is taking.<sup>41</sup> When healthcare providers are forced to use second-line alternatives, which may not be as effective as the first-line option, the risk of adverse reactions and errors increases.<sup>42</sup> Shortages require

<sup>36</sup> 2012 ASA Drug Shortage Survey Results, AM. SOC’Y ANESTHESIOLOGISTS (Apr. 17, 2012), <http://www.asahq.org/For-Members/Advocacy/Washington-Alerts/2012-ASA-Drug-Shortage-Survey-Results.aspx>.

<sup>37</sup> *Id.*

<sup>38</sup> Coleen Cherici et al., *Navigating Drug Shortages in American Healthcare: A Premier Healthcare Alliance Analysis*, PREMIER 1, 3 (Mar. 2011), <https://legacy.premierinc.com/about/news/11-mar/drug-shortage-white-paper-3-28-11.pdf>.

<sup>39</sup> *Id.* at 3.

<sup>40</sup> *Examining the Increase in Drug Shortages: Hearing on H.R. 2245 Before the Subcomm. on Health of the Comm. on Energy & Commerce*, 112th Cong. 117 (2011) (statement of W. Charles Penley, Chair, Gov’t Relations Comm., Am. Soc’y of Clinical Oncology).

<sup>41</sup> *See id.*; C. Lee Ventola, *The Drug Shortage Crisis in the United States: Causes, Impact, and Management Strategies*, 36 PHARMACY & THERAPEUTICS 740, 750–51 (2011).

<sup>42</sup> Maryn McKenna, *Hospital Pharmacists Scrambling Amid Vast Drug Shortages: Emergency Physicians Between Roc and a Hard Place*, 57 ANNALS OF EMERGENCY MED. 13A, 13A–14A (2011); *see* AHA SURVEY ON DRUG SHORTAGES, *supra* note 34, at 8.

healthcare providers to redirect their therapeutic efforts from applying the optimum course of treatment to searching through alternative drugs to determine proper dosages and interactions with other medications.<sup>43</sup> Sixty-nine percent of the AHA survey respondents indicated that shortages resulted in patients receiving a less effective drug, and thirty-five percent reported that patients have experienced adverse outcomes as a result of this treatment.<sup>44</sup>

When healthcare providers are unable to use an alternative treatment option because the specified drug is the only available treatment for a particular illness, patients forgo treatment, and hospitals must ration the supplies they have.<sup>45</sup> According to the AHA survey, seventy-eight percent of respondents reported rationing or restricting drugs.<sup>46</sup> As one physician noted, when there is no alternative to a lifesaving drug, “I guess patients just have to die.”<sup>47</sup>

In addition to the toll shortages have taken on patient care, an American Society of Health-System Pharmacists (ASHP) survey has estimated the financial toll of these shortages to the healthcare system. Pharmacists and pharmacy technicians reported devoting on average nine and eight hours a week, respectively, to drug shortages.<sup>48</sup> This translates into estimated labor costs of \$216 million per year.<sup>49</sup> Added to these expenses are the higher prices hospitals and healthcare providers pay for alternative drugs, as well as shipping costs to ensure the drugs arrive in time.<sup>50</sup>

As a result of drug shortages, some hospitals have resorted to purchasing lifesaving drugs on the “gray market.”<sup>51</sup> This market consists of distributors who offer their short supply drugs to healthcare providers at exorbitant prices.<sup>52</sup> The average markup is

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<sup>43</sup> See AHA SURVEY ON DRUG SHORTAGES, *supra* note 34, at 14.

<sup>44</sup> *Id.* at 8.

<sup>45</sup> See Ventola, *supra* note 41, at 751.

<sup>46</sup> AHA SURVEY ON DRUG SHORTAGES, *supra* note 34, at 9.

<sup>47</sup> ISMP, *supra* note 35.

<sup>48</sup> Rola Kaakeh et al., *Impact of Drug Shortages on U.S. Health Systems*, 68 AM. J. HEALTH-SYS. PHARMACY 1811, 1814 (2011).

<sup>49</sup> *Id.* at 1811.

<sup>50</sup> Joseph M. Hill & Cynthia Reilly, *Can the United States Ensure an Adequate Supply of Critical Medications?*, 1 FOOD & DRUG POL’Y F. 1, 5 (2011).

<sup>51</sup> *Drug Shortages Blamed in at Least 15 Deaths*, ASSOC. PRESS (Sept. 23, 2011, 6:55 AM), available at <http://www.cbsnews.com/news/drug-shortages-blamed-in-at-least-15-deaths/>; see Coleen Cheric, Patrick McGinnis & Wayne Russell, *Buyer Beware: Drug Shortages and the Gray Market*, PREMIER 1, 1–2 (Aug. 2011), <http://www.chcablog.com/wp-content/uploads/2011/08/Gray-Market-Analysis-David-Edit.pdf>.

<sup>52</sup> Fox et al., *supra* note 26, at 1401.



650% above normal prices.<sup>53</sup> The cost for drugs used to treat critically ill patients and those needing anesthesia for surgery can be even higher.<sup>54</sup> In 2011, a vendor offered to sell the generic antihypertensive drug Labetalol for \$1200.<sup>55</sup> According to a *Buyer Beware* report, this is a 4533% markup from the drug’s customary cost of \$25.90 per dose.<sup>56</sup> To combat shortages, U.S. hospitals will spend almost half a billion dollars in enhanced labor and inflated pharmaceutical costs.<sup>57</sup>

In addition to paying exorbitant prices, hospitals acquiring drugs through the gray market have no guarantee of the drug’s quality.<sup>58</sup> Diverted drugs sold through the gray market may be diluted, expired, contaminated, or relabeled with the wrong information.<sup>59</sup> In a study by the Institute for Safe Medication Practices, a patient safety advocacy group, more than half of the 549 U.S. hospitals acknowledged that they had purchased one or more prescription drugs from gray market vendors.<sup>60</sup> Twelve percent reported side effects or other problems attributable to drugs supplied by the gray market.<sup>61</sup>

There are several conflicting theories as to the cause of drug shortages. However, in the end, there is agreement on one key fact—drug shortages persist, in part, because generic manufacturers are either unable or unwilling to supply drugs sufficient to meet current

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<sup>53</sup> Cherici, McGinnis & Russell, *supra* note 51, at 2.

<sup>54</sup> See *Drug Shortages Blamed in at Least 15 Deaths*, *supra* note 51.

<sup>55</sup> *Id.*; Cherici, McGinnis & Russell, *supra* note 51, at 2; Omudhome Ogbru, *Iabetalol, Normodyne, Trandate*, MEDICINENET.COM, <http://www.medicinenet.com/labetalol/article.htm> (last visited Nov. 7, 2014).

<sup>56</sup> Cherici, McGinnis & Russell, *supra* note 51, at 2; *Drug Shortages Blamed in at Least 15 Deaths*, *supra* note 51.

<sup>57</sup> *Examining the Increase in Drug Shortages: Hearing on H.R. 2245 Before the Subcomm. on Health of the Comm. on Energy & Commerce*, 112th Cong. 101 (2011) (statement of Mike Alkire, Chief Operating Officer, Premier Healthcare Alliance).

<sup>58</sup> Cherici, McGinnis & Russell, *supra* note 51, at 4. Rep. Elijah Cummings, member of the House Committee on Oversight and Government Reform, introduced H.R. 5853, a bill which “includes several provisions to address weaknesses in the drug supply chain, deter price gouging, and improve drug safety and efficacy.” *Investigation of the “Gray Market,”* Comm. on Oversight & Gov’t Reform, <http://democrats.oversight.house.gov/investigations/investigation-of-the-gray-market> (last visited Oct. 15, 2014); Gray Market Drug Reform and Transparency Act of 2013, H.R. 1958, 113th Cong. (1st Sess. 2013).

<sup>59</sup> Cherici, McGinnis & Russell, *supra* note 51, at 4–5.

<sup>60</sup> *Gray Market, Black Heart: Pharmaceutical Gray Market Finds a Disturbing Niche During the Drug Shortage Crisis*, INST. FOR SAFE MEDICATION PRACS. 1, 1–2 (Aug. 25, 2011), <http://www.ismp.org/Newsletters/acutecare/showarticle.aspx?id=3>.

<sup>61</sup> *Id.* at 3.

patient and provider demand. The next Part explores some of the reasons for the shortages.

## II

### THE ECONOMICS OF THE DRUG SHORTAGES

#### *A. Role of Generic Manufacturers*

More than eighty percent of all drug shortages involve sterile injectables and generic brands.<sup>62</sup> To understand why shortages are so frequent in these areas necessitates a closer examination of sterile injectable generic manufacturers and their production processes. The generic sterile injectable market is highly concentrated with seven manufacturers producing the vast majority of all the drugs.<sup>63</sup> In fact, the majority of the production of a given sterile injectable is done by three or fewer manufacturers.<sup>64</sup> A 2010 study of thirty-three injectable oncology drugs shows that for twenty-eight of the drugs, at least ninety percent of the total production unit sales were done by three or fewer manufacturers.<sup>65</sup> If one refines the analysis down to specific drug classes, the concentration order increases. In 2008, Teva Pharmaceutical Industries held a sixty-eight percent market share of Bleomycin, a cancer drug.<sup>66</sup> In the same year, Bedford Laboratories®, held a sixty-two percent market share of Cytarabine, a chemotherapy agent.<sup>67</sup>

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<sup>62</sup> *Most Products Are Injectables and Multi-Sourced Generics*, IMS HEALTH, <http://www.imshealth.com/portal/site/ims/menuitem.748f6639e159b2ab41d84b903208c22a/?vgnextoid=8dbc6a9876493310VgnVCM100000ed152ca2RCRD> (last visited Nov. 7, 2014).

<sup>63</sup> KEVIN HANINGER, AMBER JESSUP & KATHLEEN KOEHLER, U.S. DEP'T OF HEALTH & HUMAN SERVS., *ECONOMIC ANALYSIS OF THE CAUSES OF DRUG SHORTAGES 6* (2011) [hereinafter U.S. DEP'T OF HEALTH & HUMAN SERVS.], available at <http://aspe.hhs.gov/sp/reports/2011/drugshortages/ib.pdf>; GAO DRUG SHORTAGES, *supra* note 22, at 28; FDA, DRUG SHORTAGE WORKSHOP 43–44 (2011) [hereinafter DRUG SHORTAGE WORKSHOP], available at <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM275801.pdf>.

<sup>64</sup> U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 6; *see, e.g.*, GAO DRUG SHORTAGES, *supra* note 22, at 28 (noting that in 2008, three manufacturers made seventy-one percent of all generic sterile injectable oncology drugs, and three manufacturers produced ninety-one percent of generic sterile injectable supplements).

<sup>65</sup> U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 2, 6.

<sup>66</sup> Thomas, Sullivan, *Drug Shortages*, POL'Y & MED. (Oct. 23, 2014), <http://www.policymed.com/drug-shortages/>.

<sup>67</sup> *Id.*

To produce sterile injectables, each of these manufacturers operates a small number of highly specialized facilities.<sup>68</sup> Production must take place in a “clean room” environment to assure that the drugs are sterile. In this context, sterile drugs are free of contamination from all microorganisms and visible matter.<sup>69</sup> Many of these sterilized products require dedicated lines and specialized manufacturing equipment.<sup>70</sup> As a result, there is limited production fungibility within the facilities.<sup>71</sup> The production time for these drugs ranges from hours to weeks.<sup>72</sup>

Given the highly specialized facilities required to produce sterile injectables, companies have chosen to meet growing demand by increasing production levels rather than expanding their manufacturing infrastructure.<sup>73</sup> Manufacturers justify this production approach by balancing the cost of building redundancy into their facilities against the purported slim profit margins available in the injectable generic market.<sup>74</sup> This has created an industry in which facilities are on tighter schedules—any need for facility repairs or equipment maintenance could cripple a manufacturer’s ability to maintain sufficient output levels to prevent a shortage.<sup>75</sup> Inspection reports from key manufacturing sites indicate that several facilities experiencing current production shortages have been in continuous operation since the 1960s.<sup>76</sup> These reports note that some facilities’ “manufacturing lines have undergone only limited upgrades during that time while running 24 hours a day, 7 days per week . . . .”<sup>77</sup> In summary, much of the market for generic injections is highly concentrated and composed of manufacturers who have opted, in several cases, to meet demand by running aging production equipment at high capacity. Against this backdrop, we examine the

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<sup>68</sup> See FDA, GUIDANCE FOR INDUSTRY: STERILE DRUG PRODUCTS PRODUCED BY ASEPTIC PROCESSING—CURRENT GOOD MANUFACTURING PRACTICES 5–12 (2004) [hereinafter CURRENT GOOD MANUFACTURING PRACTICES], available at <http://www.fda.gov/downloads/Drugs/.../Guidances/ucm070342.pdf>.

<sup>69</sup> *Id.* at 5.

<sup>70</sup> *See id.* at 8–12.

<sup>71</sup> J. Woodcock & M. Wosinska, *Economic and Technological Drivers of Generic Sterile Injectable Drug Shortages*, 93 CLINICAL PHARMACOLOGY & THERAPEUTICS 170, 170–73 (2012).

<sup>72</sup> *Id.*

<sup>73</sup> U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 63, at 8–12.

<sup>74</sup> *See id.* at 13.

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

<sup>76</sup> Woodcock & Wosinska, *supra* note 71, at 173.

<sup>77</sup> *Id.*

economic underpinnings and generic manufacturers' role in the current drug shortage.

*B. Underlying Conditions of the Shortage*

*1. Market Forces—Inelasticity of Demand and Supply*

The unique nature of the healthcare market makes it particularly susceptible to drug shortages. In the majority of markets, shortages are rare because prices change to maintain equilibrium between the quantity of products supplied and the quantity demanded.<sup>78</sup> For example, when a supply disruption reduces the availability of a product, prices increase, and consumer demand recalibrates.<sup>79</sup>

By contrast, the prescription drug market is relatively inflexible and constrained in its ability to react effectively to demand and supply changes. Patient demand for these drugs is often unaffected by changes in price for two reasons.<sup>80</sup> First, a majority of these drugs are medically necessary, which suggests that there are few substitutes.<sup>81</sup> Insufficient supplies generally do not precipitate a reduced demand for drugs because patients cannot control what illnesses they will suffer and the specific medications they require.<sup>82</sup> Second, manufacturers are prevented from raising prices to influence demand because patient health insurance contracts typically pay providers using pre-negotiated payment rates.<sup>83</sup> These pre-set rates do not allow manufacturers to alter prices during the contract term.<sup>84</sup>

Price inelasticity is present on the supply side as well. Here, low price responsiveness influences manufacturer inventory decisions.<sup>85</sup> If a manufacturer has a surplus of a particular oncology drug, there may be no market for it even at a highly discounted price.<sup>86</sup> “Drugs have a limited shelf life and holding excess inventory is costly.”<sup>87</sup> As noted in a recent industry report, this produces a scenario in which “manufacturers face an asymmetry of incentives: there is little cost

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<sup>78</sup> U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 3.

<sup>79</sup> *Id.*

<sup>80</sup> *Id.* at 4; Hoffman, *supra* note 26, at 6.

<sup>81</sup> U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 4; Hoffman, *supra* note 26, at 6; DRUG SHORTAGE WORKSHOP, *supra* note 63, at 25.

<sup>82</sup> Hoffman, *supra* note 26, at 6.

<sup>83</sup> *Id.*; U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 4.

<sup>84</sup> Hoffman, *supra* note 26, at 6.

<sup>85</sup> See U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 4.

<sup>86</sup> See *id.*

<sup>87</sup> *Id.* at 4.

. . . of producing too little of one drug . . . , but a potentially high cost of producing too much of that drug.”<sup>88</sup> Rather than carry excess product, manufacturers commonly use “just in time” inventory practices.<sup>89</sup> Using this approach, facilities manufacture drugs in amounts calculated to satisfy current demand.<sup>90</sup> While efficient from a manufacturing perspective, any sudden change in supply or demand could render a drug vulnerable to shortage.<sup>91</sup>

Another feature of the sterile injectable market is that high front-end costs, dedicated production lines, and strict regulatory requirements prevent new manufacturers from quickly entering the market to increase supply.<sup>92</sup> It generally takes two to three years for a manufacturer to get FDA approval for a new production facility.<sup>93</sup> In addition, raw materials for production are often difficult to source, must be validated by manufacturers, and require regulatory approvals.<sup>94</sup> As a result of these factors, it generally takes years for the industry to expand capacity in response to an increase in demand.<sup>95</sup> Moreover, if the increase in demand is expected to be temporary (i.e., a shortage due to a production line disruption), investments in increased capacity are unlikely to occur.<sup>96</sup>

In the sterile injectable market, maintaining excess production capacity to meet unanticipated demand is an uneconomical business approach; it would result in a generic manufacturer having high costs compared to its competitors.<sup>97</sup> In the highly competitive generic drug market, no generic manufacturer would choose this strategy unless it could receive a higher price in the market.<sup>98</sup> As discussed in the

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<sup>88</sup> *Id.* at 6; *see also* Woodcock & Wosinska, *supra* note 71, at 170–76 (While contracts generally place a penalty for failure to supply product, that penalty structure is the difference between the contracted rate and the rate that a provider must pay for an alternative source. Drug shortages generally do not trigger these clauses because there is often no alternative source.).

<sup>89</sup> FDA 2011 REVIEW, *supra* note 14, at 5–6, 21–22.

<sup>90</sup> *Id.* at 23, 32.

<sup>91</sup> *Id.* at 32.

<sup>92</sup> U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 63, at 13.

<sup>93</sup> *See Prescription Drug Shortages: Examining a Public Health Concern and Potential Solutions: Hearing of the Comm. on Health, Educ., Labor, & Pensions*, 112th Cong. 18 (2011) (statement of Sherry Glied, Assistant Sec’y for Planning and Educ., U.S. Dep’t of Health & Human Servs.).

<sup>94</sup> U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 63, at 19.

<sup>95</sup> *See id.* at 4.

<sup>96</sup> *Id.*

<sup>97</sup> *Id.*

<sup>98</sup> *Id.*

following Section, Medicare Modernization Act (MMA) price controls forestall that possibility.

## 2. Legislative Constraints

The MMA has a significant effect on the profit margins for generic sterile injectable drugs. In pertinent part, the law changed the reimbursement system for physician-administered drugs under Medicare Part B.<sup>99</sup> The MMA capped provider reimbursement at the actual average sales price (ASP) recorded in the market place plus a six percent markup, which is intended to cover the drug cost.<sup>100</sup> Prior to the MMA, providers received ninety-five percent of the average wholesale price (AWP) for each covered drug.<sup>101</sup> Despite the name, the AWP was not actually the average wholesale price, but rather the manufacturer's suggested list price.<sup>102</sup> In 2001, the Government Accounting Office (GAO) and Centers for Medicare and Medicaid Services (CMS) found that, under the AWP system, "Medicare overpaid for Part B drugs by over \$1 billion" per year.<sup>103</sup> Congress addressed the overpayment issue by including provisions in the MMA to change the Medicare reimbursement system.<sup>104</sup>

In 2005, Medicare converted to the ASP-based reimbursement system.<sup>105</sup> In practice, this limited manufacturer price increases for generic drugs to no more than six percent every six months "because raising the price more than that would cause reimbursement for the

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<sup>99</sup> ACAD. OF MANAGED CARE PHARMACY, AMCP GUIDE TO PHARMACEUTICAL PAYMENT METHODS 10 (2007) [hereinafter AMCP GUIDE], available at <http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9856>.

<sup>100</sup> Michael P. Link, Karen Hagerty & Hagop M. Kantarjian, *Chemotherapy Drug Shortages in the United States: Genesis and Potential Solutions*, 30 J. CLINICAL ONCOLOGY 692, 693 (2012).

<sup>101</sup> COMM. ON WAYS AND MEANS, REIMBURSEMENT FOR PART B DRUGS: AVERAGE WHOLESALE PRICE REFORM 1 (2004) [hereinafter REIMBURSEMENT FOR PART B DRUGS], available at <http://waysandmeans.house.gov/media/pdf/healthdocs/awpreform.pdf>.

<sup>102</sup> AMCP GUIDE, *supra* note 99, at 3.

<sup>103</sup> REIMBURSEMENT FOR PART B DRUGS, *supra* note 101, at 1.

<sup>104</sup> *Id.* at 2–3 (discussing changes in reimbursement for oncologists).

<sup>105</sup> Mireille Jacobson et al., *How Medicare's Payment Cuts for Cancer Chemotherapy Drugs Changed Patterns of Treatment*, 29 HEALTH AFF. 1391, 1391 (2010); *2014 ASP Drug Pricing Files: ASP Drug Pricing Files October 2014 Update*, CTRS. FOR MEDICARE & MEDICAID SERVS., <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2014ASPFiles.html> (last modified Sept. 9, 2014, 3:51 PM) (stating that repayment amounts are "106 percent of the Average Sales Price (ASP) calculated from data submitted by drug manufacturers" with "quarter to quarter price changes").

drug to be less than the actual selling price.”<sup>106</sup> The ASP cap leaves little flexibility for prices to adapt to supply and demand.<sup>107</sup> This hurts manufacturers because, in the generic market, drug prices can decrease quickly. As noted by former healthcare adviser to the Obama administration, physician Ezekiel Emanuel:

In the first two or three years after a cancer drug goes generic, its price can drop by as much as 90 percent as manufacturers compete for market share. But if a shortage develops, the drug’s price should be able to increase again to attract more manufacturers. Because the 2003 act effectively limits drug price increases, it prevents this from happening.<sup>108</sup>

Because traditional notions of supply and demand do not apply to cancer drugs, the market cannot self-correct to address shortages.<sup>109</sup> Typically, the market would respond to increased demand with increased prices.<sup>110</sup> “[T]he Medicare payment system has made it difficult to raise prices, creating a situation in which—for low-cost drugs with dwindling profit margins—there is little incentive for continued production.”<sup>111</sup> This theory, along with a Department of Health and Human Services (DHHS) study that reviewed Medicare Part B volume of service data, suggests that drug shortages are likely to occur when a drug’s price falls.<sup>112</sup> The study found that within “the group of drugs that eventually experience[d] a shortage, average prices decreased in every year leading up to that shortage. In contrast, the average prices of drugs that never experienced a shortage over this period did not change . . . .”<sup>113</sup>

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<sup>106</sup> Link, Hagerty & Kantarjian, *supra* note 100, at 693. The MMA applied to all drugs administered in a provider setting. *Id.*

<sup>107</sup> See Ezekiel J. Emanuel, *Shortchanging Cancer Patients*, N.Y. TIMES (Aug. 6, 2011), <http://www.nytimes.com/2011/08/07/opinion/sunday/ezekiel-emanuel-cancer-patients.html>.

<sup>108</sup> *Id.*

<sup>109</sup> *See id.*

<sup>110</sup> *See id.*

<sup>111</sup> Link, Hagerty & Kantarjian, *supra* note 100, at 693.

<sup>112</sup> U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 63, at 7.

<sup>113</sup> *Id.* at 8. The study

found that 44 drugs with declining sales in 2006–2008 were in shortage in subsequent years, and 28 drugs with increased sales in 2006–2008 were never involved in a shortage. The study also found that the prices of 44 drugs in shortage had steadily decreased, while the prices of the 28 drugs whose supply was adequate did not change significantly.

Hoffman, *supra* note 26, at 7–8.

The ASP reimbursement system also exerts price pressure on generic manufacturers because it incentivizes physicians to prescribe costly brand-name drugs over generics.<sup>114</sup> Physicians who prescribe drugs that are more expensive receive a higher dollar amount than those who prescribe generics.<sup>115</sup> For example, six percent of the cancer drug Abraxane, which sells for \$5824, generates a significantly higher payment for a provider than six percent of the generic paclitaxel, priced at \$312.<sup>116</sup>

For nearly a decade, the MMA's reimbursement system has applied a steady downward pressure on sterile injectables drug prices.<sup>117</sup> In the short-run, these falling prices are favorable to patients and payers. However, when the cost of a drug falls below a certain price, patients can run the risk of manufacturers abandoning production in favor of more lucrative product lines.<sup>118</sup> Consider the long-term viability of producing a one dollar sterile injectable cancer drug from a manufacturer's perspective: faced with diminishing returns from low prices, manufacturers have a reduced incentive to remain in the market of generic sterile injectables. As recent market activity suggests, fewer manufacturers choose to produce these drugs.<sup>119</sup> With a limited number of manufacturers, any production line disruption magnifies the impact on the supply of product.<sup>120</sup> Currently, providers treat patients with lifesaving cancer drugs that cost less than a can of soda. In the end, this pricing scheme may not be economically viable for generic manufacturers.

### *C. Exacerbating Economic Factors*

#### *1. Business Decisions and Market Consolidations*

The MMA reimbursement policies and market forces described above influence generic manufacturers' decisions regarding not only how much to produce, but where to sell their products. Some generic manufacturers have made the business decision to sell their products

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<sup>114</sup> Mandy L. Gatesman & Thomas J. Smith, *The Shortage of Essential Chemotherapy Drugs in the United States*, 365 NEW ENG. J. MED. 1653, 1653–54 (2011).

<sup>115</sup> *Id.* at 1654.

<sup>116</sup> Hoffman, *supra* note 26, at 7.

<sup>117</sup> BRIAN RYE, BLOOMBERG GOV'T, MEDICARE PRICE CONTROLS WORSEN DRUG SHORTAGES, BOOST GRAY MARKET 1, 6 (Oct. 1, 2012).

<sup>118</sup> Link, Hagerty & Kantarjian, *supra* note 100, at 693.

<sup>119</sup> See GAO DRUG SHORTAGES, *supra* note 22, at 28.

<sup>120</sup> U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 13.



abroad rather than in the U.S. market.<sup>121</sup> Medicare-type reimbursement caps do not exist in Europe, and generic drug prices are higher.<sup>122</sup> As a result, generic drugs manufactured in the United States can be sold abroad at a higher profit.<sup>123</sup> When manufacturers focus on more profitable markets, needed drugs are diverted to foreign countries.<sup>124</sup> These business practices, in turn, contribute to drug shortages in the United States.<sup>125</sup>

High production costs and comparatively low profit margins associated with sterile injectables have prompted generic manufacturers to reduce or discontinue production.<sup>126</sup> In 2000, vaccines used against diphtheria and tetanus were in shortage because one manufacturer, citing low revenues, stopped.<sup>127</sup> In the case of the cancer drug leucovorin, a generic manufacturer decided to stop production eight months after a brand-name version with a higher profit margin became available.<sup>128</sup> For more than seventy years, several manufacturers have produced the cancer drug.<sup>129</sup> In 2008, the FDA approved a patented active l-isomer of the generic drug.<sup>130</sup> Though the brand-name drug was no more effective than the generic, it was fifty-eight times more expensive than the thirty-two dollar generic.<sup>131</sup> Prescriptions for the brand-name version of the drug became increasingly popular.<sup>132</sup> Eight months after the FDA approved the branded version, there was a shortage of the generic.<sup>133</sup> The high manufacturing costs and insufficient financial return made it no longer in generic manufacturers' business interests to continue production.<sup>134</sup>

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<sup>121</sup> See Bruce A. Chabner, *Drug Shortages—A Critical Challenge for the Generic-Drug Market*, 365 NEW ENG. J. MED. 2147, 2149 (2011).

<sup>122</sup> Link, Hagerty & Kantarjian, *supra* note 100, at 693.

<sup>123</sup> Chabner, *supra* note 121, at 2149.

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

<sup>125</sup> See Hoffman, *supra* note 26, at 6.

<sup>126</sup> See Hill & Reilly, *supra* note 50, at 4.

<sup>127</sup> Fox et al., *supra* note 26, at 1401.

<sup>128</sup> Hoffman, *supra* note 26, at 6.

<sup>129</sup> Gatesman & Smith, *supra* note 114, at 1653–54.

<sup>130</sup> *Id.* at 1653.

<sup>131</sup> *Id.* at 1654.

<sup>132</sup> Hoffman, *supra* note 26, at 6.

<sup>133</sup> *Id.*

<sup>134</sup> See Gatesman & Smith, *supra* note 114, at 1653.

Industry consolidations have also affected the availability of drugs.<sup>135</sup> When generic manufacturers combine, the merged entity often streamlines or transfers product lines to new facilities.<sup>136</sup> These actions can result in a complete cessation of, or delays in, a drug's manufacturing.<sup>137</sup> In addition, if the two consolidated companies have a similar product line, often single-source productions result from the merger.<sup>138</sup> "As the number of manufacturers of a product decreases, resiliency in the supply chain also decreases . . . ."<sup>139</sup> The net result is that those drugs become more vulnerable to shortages.<sup>140</sup>

Consolidations from 2007 and 2008 within the generic drug industry include Teva's acquisition of Barr Pharmaceuticals<sup>141</sup> and Mylan Pharmaceuticals' acquisition of Merck's KGaA generics.<sup>142</sup> Mergers of this type often result in competing financial interests within an organization that can affect availability of lower priced pharmaceuticals.<sup>143</sup> A DHHS report indicates that mergers could considerably contribute "to drug shortages . . . if the consolidations have resulted in closures of manufacturing facilities that reduced production capacity."<sup>144</sup> As noted by Assistant Secretary of Health Howard Koh:

Industry consolidation has also contributed to the drug shortage problem. . . . [W]hen a firm has a manufacturing or quality problem they will often voluntarily suspend production so they can identify and address the root cause of the product quality problem. . . . Consolidation has led to fewer firms making these drugs and the firms have a limited number of manufacturing lines. When one firm experiences a quality problem which results in production holds or

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<sup>135</sup> *Examining the Increase in Drug Shortages: Hearing on H.R. 2245 Before the Subcomm. on Health of the Comm. on Energy & Commerce*, 112th Cong. 8 (2011) [hereinafter Statement of Howard K. Koh] (statement of Howard K. Koh, Assistant Sec'y for Health, U.S. Dep't of Health & Human Servs.).

<sup>136</sup> Fox et al., *supra* note 26, at 1401.

<sup>137</sup> *Id.*

<sup>138</sup> *Id.*

<sup>139</sup> *Id.*

<sup>140</sup> *Id.*

<sup>141</sup> Shirley S. Wang, *Teva to Buy U.S. Generic Rival Barr for \$7.46 Billion*, WALL ST. J. (July 19, 2008), <http://online.wsj.com/articles/SB121637960357665065>.

<sup>142</sup> Press Release, Mylan Inc., Mylan Completes Acquisition of Generics Business of Merck KGaA (Oct. 2, 2007), *available at* [investor.mylan.com/releasedetail.cfm?releaseid=406511](http://investor.mylan.com/releasedetail.cfm?releaseid=406511).

<sup>143</sup> See Ventola, *supra* note 41, at 742.

<sup>144</sup> U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 6.

slowdowns, the remaining firms are usually not able to make up the shortfall due to capacity constraints.<sup>145</sup>

## 2. *The Role of GPOs*

Currently, the GAO is investigating the extent to which GPOs contribute to ongoing shortages.<sup>146</sup> GPOs are purchasing intermediaries that leverage the buying power of their members and negotiate contracts with manufacturers and vendors.<sup>147</sup> In the healthcare setting, GPOs negotiate contracts with drug manufacturers on behalf of hospital groups and healthcare organizations.<sup>148</sup> As the intermediary between manufacturers and hospitals, GPOs create value by reducing transaction costs and negotiating lower prices than a single hospital could achieve alone.<sup>149</sup> GPOs derive a majority of this value (and their operating revenue) by charging drug manufacturers for contracting services.<sup>150</sup> Referred to as “contract administrative fees,” these payments are on a percentage of each drug manufacturers’ GPO-negotiated contract sales.<sup>151</sup> By law, this fee should not exceed three percent, but in special cases, GPOs have charged higher fees.<sup>152</sup> GPOs can charge these fees through a “safe harbor” amendment to the Social Security Act’s “anti-kickback” statute.<sup>153</sup>

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<sup>145</sup> Statement of Howard K. Koh, *supra* note 135, at 14.

<sup>146</sup> Jaimy Lee, *Group Blames GPOs for Generic Drug Shortages*, MODERN HEALTHCARE (Sept. 4, 2013), <http://www.modernhealthcare.com/article/20130904/blog/309049998>.

<sup>147</sup> GAO, GROUP PURCHASING ORGANIZATIONS: FEDERAL OVERSIGHT AND SELF-REGULATION 1–2 (2012) [hereinafter GPO OVERSIGHT AND SELF-REGULATION], available at <http://www.gao.gov/assets/590/589778.pdf>.

<sup>148</sup> *Id.*

<sup>149</sup> Kathleen E. McKone-Sweet, Paul Hamilton & Susan B. Willis, *The Ailing Healthcare Supply Chain: A Prescription for Change*, 41 J. SUPPLY CHAIN MGMT. 4, 8 (2005).

<sup>150</sup> GAO, GROUP PURCHASING ORGANIZATIONS: USE OF CONTRACTING PROCESSES AND STRATEGIES TO AWARD CONTRACTS FOR MEDICAL-SURGICAL PRODUCTS 6 (2003) [hereinafter GROUP PURCHASING ORGANIZATIONS].

<sup>151</sup> *Id.* at 2.

<sup>152</sup> *Id.* at 6; McKone-Sweet, Hamilton & Willis, *supra* note 149, at 8–9.

<sup>153</sup> GROUP PURCHASING ORGANIZATIONS, *supra* note 150, at 6. “The Anti-Kickback statute prohibits the knowing or willful solicitation, receipt, offer, or payment of fees, or other remuneration, to induce the purchase of an item or service for which payment may be made under a federal health care program.” GPO OVERSIGHT AND SELF-REGULATION, *supra* note 147, at 2 n.3 (citing 42 U.S.C. § 1320a-7b(b) (2006)).

By 2011, more than ninety percent of all hospital purchases were made through GPO contracts.<sup>154</sup> In the same year, the two largest GPOs, Novation and Premier, negotiated contracts worth approximately seventy billion dollars.<sup>155</sup> The consolidation of GPO purchasing power has raised several policy concerns. In particular, contract provisions frequently used when negotiating with generic manufacturers have raised anti-competitive concerns.<sup>156</sup> Most recently, these practices have been linked to drug shortages.

GPO contracts are structured to take advantage of large economies of scale in drug production.<sup>157</sup> In the sterile injectable market, this results in only a few large manufacturers producing each medication.<sup>158</sup> “GPOs tend to favor large manufacturers since they have a wider variety of products and are financially capable of paying the contract fees.”<sup>159</sup> In exchange for the administration fees, GPOs offer drug manufacturers a variety of contractual incentives that limit competition among sources of supply to their member hospitals.<sup>160</sup> The GAO indicates that GPOs frequently use sole-source contracts.<sup>161</sup> In such contracts, a GPO grants a generic manufacturer the exclusive right to offer its drugs to the GPO member hospitals.<sup>162</sup> Other GPO contracts offer minimum volume purchase requirements to specific drug manufacturers.<sup>163</sup> GPOs set the volume requirements at levels that essentially block smaller generic manufacturers from competing for these contracts.<sup>164</sup> GPOs also offer select manufacturers bundling arrangements.<sup>165</sup> In these contracts, GPO member hospitals can purchase combinations of products from specific manufacturers. The manufacturer benefits from these arrangements through increased sales from items that may not generate adequate revenue as stand-

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<sup>154</sup> Roger D. Blair & Christine Piette Durrance, *Group Purchasing Organizations, Monopsony, and Antitrust Policy*, MANAGERIAL & DECISION ECON. (2013).

<sup>155</sup> *Id.*

<sup>156</sup> *Id.*

<sup>157</sup> *See id.*

<sup>158</sup> COMM. ON OVERSIGHT AND GOV'T REFORM, 112TH CONG., FDA'S CONTRIBUTION TO THE DRUG SHORTAGE CRISIS 10 (2012) [hereinafter COGR 2012 REPORT].

<sup>159</sup> McKone-Sweet, Hamilton & Willis, *supra* note 149, at 9.

<sup>160</sup> *See id.* at 8–9.

<sup>161</sup> GROUP PURCHASING ORGANIZATIONS, *supra* note 150, at 3, 11–12.

<sup>162</sup> *Id.* at 5; Blair & Durrance, *supra* note 154.

<sup>163</sup> COGR 2012 REPORT, *supra* note 158, at 10; GROUP PURCHASING ORGANIZATIONS, *supra* note 150, at 5.

<sup>164</sup> COGR 2012 REPORT, *supra* note 158, at 10.

<sup>165</sup> GROUP PURCHASING ORGANIZATIONS, *supra* note 150, at 3.

alone items.<sup>166</sup> As noted in the GAO report, in each of these instances, there is a tendency for one manufacturer to thrive while rivals are either marginalized or excluded entirely from the market.<sup>167</sup>

In 2012, a House Committee on Oversight and Government Reform (House Committee) report indicated that these GPO practices contribute to the current shortage of generic injectable medications.<sup>168</sup> Because GPO networks are a guaranteed source of demand, drug manufacturers compete aggressively for GPO contracts.<sup>169</sup> As previously noted, GPOs favor drug manufacturers who can produce drugs in high volumes because economies of scale in drug manufacturing result in declining average costs as the amount of production increases.<sup>170</sup> The heightened competition among manufacturers to obtain GPO contracts drives prices down.<sup>171</sup> As a result, however, the House Committee report notes, “companies that cannot produce a drug at large enough output levels to take advantage of the economies of scale . . . will stop producing the drug or will neglect to enter the market.”<sup>172</sup> These practices contract the market. In contracted markets dominated by single-source suppliers, drugs are more vulnerable to shortage.<sup>173</sup>

Critics contend that these exclusive contracting provisions have given GPOs monopolistic control over the industry, and they jeopardize market competition.<sup>174</sup> In response to these concerns, six senior members from the House of Representatives turned to the GAO to determine whether GPO contract practices and safe harbor administration fees are a “driving cause” of drug shortages.<sup>175</sup> The GAO report is due out in 2014.<sup>176</sup>

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<sup>166</sup> *Id.* at 6.

<sup>167</sup> *Id.*

<sup>168</sup> COGR 2012 REPORT, *supra* note 158, at 4.

<sup>169</sup> Blair & Durrance, *supra* note 154, § 4.

<sup>170</sup> See RYE, *supra* note 117, at 6; COGR 2012 REPORT, *supra* note 158, at 10.

<sup>171</sup> COGR 2012 REPORT, *supra* note 158, at 10.

<sup>172</sup> *Id.* at 4.

<sup>173</sup> Ventola, *supra* note 41, at 749–50.

<sup>174</sup> *Some MDs Blame GPOs for Chronic Drug Shortages*, PHARMACY PRAC. NEWS (June 2013), [http://www.pharmacypracticenews.com/ViewArticle.aspx?d=Policy&d\\_id=51&I=June+2013&i\\_id=964&a\\_id=23481](http://www.pharmacypracticenews.com/ViewArticle.aspx?d=Policy&d_id=51&I=June+2013&i_id=964&a_id=23481).

<sup>175</sup> *Id.*

<sup>176</sup> Lee, *supra* note 146.

#### *D. The FDA's Role in Drug Shortages*

According to a report published by the FDA, quality problems at generic manufacturing facilities, which resulted in supply disruptions of lifesaving medicines, caused current drug shortages.<sup>177</sup> The report further notes that, while product disruptions and other primary causes of drug shortages “lie outside the purview of FDA . . . , the Agency has taken on the task of working with manufacturers to prevent and mitigate such shortages.”<sup>178</sup> The FDA report, however, mischaracterizes both the leading cause, and the Agency’s role, in the current drug shortages.

The root cause of current shortages can be traced back to 2009, when President Barack Obama appointed Dr. Margaret Hamburg FDA Commissioner.<sup>179</sup> Her appointment followed news that contaminated batches of a sterile injectable, heparin, were linked to more than eighty deaths in the United States from 2007 to 2008.<sup>180</sup> As the new commissioner, Hamburg made preventing contaminated drugs a top priority.<sup>181</sup> Specifically, she announced that “[t]he FDA is fortunate to have received significant funding increases for the current and next fiscal year that will be devoted to additional inspection and compliance activities that will support the elements of an effective enforcement strategy that I have outlined.”<sup>182</sup>

Due to the FDA’s new policy of increased inspection and compliance oversight, four of the United States’ five largest generic injectable manufacturers simultaneously commenced remediation efforts.<sup>183</sup> As part of addressing issues raised in FDA warning letters, all of the recipients temporarily halted production.<sup>184</sup> When

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<sup>177</sup> FDA 2011 REVIEW, *supra* note 14, at 15.

<sup>178</sup> *Id.* at 8.

<sup>179</sup> Press Release, White House, President Barack Obama Announces Key FDA Appointments and Tougher Food Safety Measures (Mar. 14, 2009), *available at* [http://www.whitehouse.gov/the\\_press\\_office/Weekly-Address-President-Barack-Obama-Announces-Key-FDA-Appointments-and-Tougher-F/](http://www.whitehouse.gov/the_press_office/Weekly-Address-President-Barack-Obama-Announces-Key-FDA-Appointments-and-Tougher-F/).

<sup>180</sup> RYE, *supra* note 117, at 6.

<sup>181</sup> Margaret A. Hamburg, Comm’r, Food & Drug Admin., Remarks on Effective Enforcement and Benefits to Public Health at the Food and Drug Law Institute (Aug. 6, 2009), *available at* <http://www.fda.gov/NewsEvents/Speeches/ucm175983.htm>.

<sup>182</sup> *Id.*

<sup>183</sup> COGR 2012 REPORT, *supra* note 158, at 16.

<sup>184</sup> *See id.* An FDA warning letter is:

[A] correspondence that notifies regulated industry about violations that FDA has documented during its inspections or investigations. Typically, a Warning Letter notifies a responsible individual or firm that the Agency considers one or more products, practices, processes, or other activities to be in violation of the Federal

explaining these concurrent production stoppages to Congress, the FDA stated that they were voluntary manufacturer decisions.<sup>185</sup> However, given the explicit threat contained in FDA warning letters (“[f]ailure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction”),<sup>186</sup> the “voluntariness” of such action is questionable.

By February 2012, fifty-eight percent of the drugs in short supply were manufactured by one or more of the facilities that had received a warning letter from the FDA and were undergoing remediation efforts.<sup>187</sup> Under Hamburg’s direction, FDA agents increased their efforts in conducting facility inspections and issuing citations.<sup>188</sup> According to the House Report, these field agents did not believe it was their responsibility to consider the implications of their increased enforcement action, even if it resulted in production disruptions, facility closures, and eventual shortages.<sup>189</sup>

A troubling aspect of the FDA’s heightened enforcement strategy was that, in some instances, the validity of the allegations in the warning letter was questionable. The FDA conducted three separate investigations of a Sandoz manufacturing plant in Québec during 2011.<sup>190</sup> In November 2011, the Agency issued a warning letter citing possible contamination of some of Sandoz’s sterile injectable

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Food, Drug, and Cosmetic Act (the Act), its implementing regulations and other federal statutes. Warning Letters should only be issued for violations of regulatory significance, i.e., those that may actually lead to an enforcement action if the documented violations are not promptly and adequately corrected. A Warning Letter is one of the Agency’s principal means of achieving prompt voluntary compliance with the Act.

FDA, *Procedures for Clearing FDA Warning Letters and Untitled Letters*, in REGULATORY PROCEDURES MANUAL—JULY 2012 § 4.1 (2012), available at <http://www.fda.gov/downloads/ICECI/ComplianceManuals/RegulatoryProceduresManual/UCM176965.pdf>.

<sup>185</sup> COGR 2012 REPORT, *supra* note 158, at 18.

<sup>186</sup> Letter from Alonza E. Cruse, Dist. Dir., FDA, to Teva Parenterals Medicines, Inc. (Dec. 11, 2009), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm209222.htm>.

<sup>187</sup> COGR 2012 REPORT, *supra* note 158, at 5, 18.

<sup>188</sup> *See id.* at 16, 18.

<sup>189</sup> *Id.* at 18–19.

<sup>190</sup> *Sandoz Suspends Some Drug Production After U.S. Warning*, GENERICLICENSING.COM, <http://genericlicensing.com/news/view/146> (last visited Oct. 15, 2014) [hereinafter *Sandoz Suspends Some Drug Production*]; Letter from Steven Lynn, Acting Dir. of Pub. Health Serv., FDA, to Joseph Jimenez, Chief Exec. Officer, Novartis International AG, available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm281843.htm>.

drugs.<sup>191</sup> The Canadian drug authority conducted a separate inspection soon thereafter and identified no problems.<sup>192</sup> Faced with possible FDA sanctions, however, Sandoz decided to scale back production of several drugs while addressing Agency concerns.<sup>193</sup> Sandoz's experience of having no identifiable problems is not uncommon. During the House Committee's investigation of the FDA's role in drug shortages, it found no "evidence that any products produced . . . at the facilities undergoing remediation had harmed anyone beyond typical side effects associated with any type of medication."<sup>194</sup>

The House Committee's finding does not dispute that many of the facilities were older and that upgrades were preferable.<sup>195</sup> However, as pointed out by former FDA Deputy Commissioner and senior official at CMS, Dr. Scott Gottlieb,<sup>196</sup> the FDA has largely contributed to the drug shortage crisis with inflexible and outdated policies:

With its vigilance heightened, the FDA has required manufacturers to undergo major plant renovations, suspend facilities or stop shipping goods from suspect production lines. The FDA and the manufacturers often don't understand the drug-production processes well enough to detect the root cause of problems. Instead of calling for targeted fixes of troubled plants, the agency has often required manufacturers to undertake costly, general upgrades to facilities.<sup>197</sup>

Between fiscal years 2009 and 2011, the number of FDA-issued warning letters increased by 250%.<sup>198</sup> Compliance with the warning letters essentially required all U.S. manufacturers of sterile injectables to remediate their facilities at the same time, causing their available capacity to reduce by thirty percent in comparison to capacity in 2009.<sup>199</sup> This created a vacuum in the generic drug market which, due to the highly complex manufacturing processes, could not be filled

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<sup>191</sup> *Sandoz Suspends Some Drug Production*, *supra* note 190.

<sup>192</sup> *Id.*

<sup>193</sup> *Id.*

<sup>194</sup> COGR 2012 REPORT, *supra* note 158, at 18.

<sup>195</sup> *Id.* at 20.

<sup>196</sup> *Drug Shortage Crisis: Lives Are in the Balance: Hearing Before the Subcomm. on Health Care*, 112th Cong. 25, 28–29 (2011) (statement of Scott Gottlieb, resident fellow, American Enterprise Institute).

<sup>197</sup> *Id.*

<sup>198</sup> COGR 2012 REPORT, *supra* note 158, at 19.

<sup>199</sup> *Id.* at 18.



immediately.<sup>200</sup> For facilities with genuine manufacturing problems, the FDA could have directed facilities to make targeted improvements carried out over a timeframe that would have significantly diminished the public health crisis the country is now facing from drug shortages.

Perhaps in recognition that its enforcement strategy was contributing to drug shortages, the FDA revised its warning letters. The letters now include the following directive:

If as a result of receiving this Warning Letter or in general, you are considering making a decision that will result in a decreased number of finished drug products or active pharmaceutical ingredients produced by your manufacturing facility, FDA requests that you contact CDER’s Drug Shortages Program immediately, as you begin your internal discussions, . . . in order to ensure that your action(s) does not adversely affect the public health.<sup>201</sup>

### III

#### THE NEED FOR A NEW APPROACH

##### *A. Current Administrative and Legislative Solutions to the Drug Shortage Crisis*

This Section examines current legislative, regulatory, and private sector approaches to mitigate and prevent drug shortages. These efforts will ameliorate some of the effects of drug shortages. As the analysis shows, however, in several critical areas, these approaches are insufficient.

##### *1. Executive Order 13588—Reducing Prescription Drug Shortages*

On October 31, 2011, President Obama issued an Executive Order in response to the rising number of drug shortages and its impact on healthcare in the United States.<sup>202</sup> The order directs the FDA to take steps to prevent future disruptions in the supply of lifesaving medicines.<sup>203</sup> An important element in that process is “ensuring that the FDA and the public receive adequate advance notice of shortages whenever possible.”<sup>204</sup> To that end, the order tasks the FDA with a two-part directive. The first part instructs the Agency to require drug manufacturers to provide advance notice of production interruptions

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<sup>200</sup> See *id.* at 20 (citing U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 63, at 13).

<sup>201</sup> COGR 2012 REPORT, *supra* note 158, at 19.

<sup>202</sup> See Exec. Order No. 13,588, 3 C.F.R. 13588 (2011).

<sup>203</sup> *Id.*

<sup>204</sup> *Id.*

that could lead to shortages of certain drugs.<sup>205</sup> The second part requires the FDA to expand and expedite its regulatory reviews of new drug suppliers and manufacturing facilities.<sup>206</sup>

## 2. *Food and Drug Administration Safety and Innovation Act (FDASIA)*

### a. *Expanded Notification Requirements*

In July 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act (FDASIA) into law.<sup>207</sup> The Act amends existing Food, Drug, & Cosmetic Act (FD&C) drug shortage notification requirements and adds new notice provisions.<sup>208</sup> Title X of the Act: (1) expands drug supply disruption and reporting requirements, (2) directs the FDA to take specific actions to prevent or mitigate shortages, (3) creates a mechanism for tracking drug shortage data and sharing that information with key stakeholders, and (4) establishes a task force to analyze the causes of drug shortages and devise strategic plans that address the shortages.<sup>209</sup>

The FDASIA substantially revises the scope of drug shortage reporting requirements. The Act's notice requirements now apply to all manufacturers of medically important, approved and unapproved drugs.<sup>210</sup> Previously, only sole manufacturers of approved drugs were required to alert the FDA of a drug shortage.<sup>211</sup> Title X also expands the scope of drugs subject to shortage notification to include drugs used during emergency medical care or surgery.<sup>212</sup> Prior FD&C notice provisions applied only to drugs that were life-supporting, life-sustaining, or intended for use in the prevention of a debilitating disease or condition.<sup>213</sup>

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<sup>205</sup> *Id.*

<sup>206</sup> *Id.* In response to the Executive Order's instruction to address the growing number of drug shortages, the FDA published an interim final rule (IFR) that required sole manufacturers of certain drugs to provide FDA with six months' notice before discontinuing production. Because IFR is superseded by the Food Drug Administration Safety and Innovation Act (FDASIA), this Article does not substantively address the IFR.

<sup>207</sup> *President Obama Signs the FDA Safety and Innovation Act*, NVCA TODAY (July 27, 2012, 3:29 PM), <http://nvcatoday.nvca.org/index.php/life-sciences-policy-updates/president-obama-signs-the-fda-safety-and-innovation-act.html>.

<sup>208</sup> FDASIA, Pub. L. No. 112-144, § 1001(a), 126 Stat. 993, 1099 (2012).

<sup>209</sup> *Id.* §§ 1001-08, 126 Stat. at 1099-1108.

<sup>210</sup> *Id.* § 1001(a)-(c), 126 Stat. at 1099.

<sup>211</sup> Food, Drugs, and Cosmetics Act § 506C(a)-(b), 21 U.S.C. § 356c(a)-(b) (2006).

<sup>212</sup> FDASIA § 1001(a)-(c), 126 Stat. at 1099; 21 U.S.C. § 356c(a)-(b).

<sup>213</sup> 21 U.S.C. § 356c(a)-(b).

The Act requires all manufacturers to alert the FDA of a permanent discontinuance or a production interruption that is likely to lead to a meaningful disruption in the availability of that drug in the United States.<sup>214</sup> Manufacturers must also include in the notice the reasons for the disruption.<sup>215</sup> Historically, manufacturers alerted the Agency only of permanent drug discontinuances. Manufacturers are now required to give the FDA six months’ notice before permanently discontinuing a drug.<sup>216</sup> The FDASIA extends this requirement to product interruptions that could lead to a meaningful disruption in the supply of the drug within the United States.<sup>217</sup> The Act defines meaningful disruption as a more than negligible change in production that affects the manufacturer’s ability “to fill orders or meet expected demand.”<sup>218</sup>

The FDASIA requires the FDA to issue letters of noncompliance to manufacturers who fail to notify the Agency of a product discontinuance or interruption within a specified time frame.<sup>219</sup> The Act also authorizes the FDA to investigate, and make available, instances of noncompliance.<sup>220</sup>

In addition to increasing manufacturer notification requirements, the FDASIA also expands the Agency’s notification responsibilities to the public. The FDA is required to create a process for entities to communicate information regarding shortages to the Agency.<sup>221</sup> The FDA is also responsible for maintaining a publicly available list of drugs currently in shortage.<sup>222</sup> Finally, in terms of expanding FDA reporting requirements, the Act formalizes existing Agency practices aimed at preventing shortages. It is now mandatory for the FDA to consider the potential impact a warning letter may have on the supply of a drug before taking enforcement action.<sup>223</sup> An appropriate FDA center must vet any Agency enforcement action that could have an adverse impact on a drug’s supply center.<sup>224</sup>

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<sup>214</sup> FDASIA § 1001(a)(2), 126 Stat. at 1099.

<sup>215</sup> *Id.*

<sup>216</sup> 21 U.S.C. § 356c(a)(3).

<sup>217</sup> FDASIA § 1001(b), 126 Stat. at 1099.

<sup>218</sup> *Id.* § 1001(h)(3)(A), 126 Stat. at 1101.

<sup>219</sup> *Id.* § 1001(f), 126 Stat. at 1100.

<sup>220</sup> *Id.* § 1001(g), 126 Stat. at 1100.

<sup>221</sup> *Id.* § 1003(a)(1)(B)(iii), (d), 126 Stat. at 1103–04.

<sup>222</sup> *Id.* § 1004(c), 126 Stat. at 1105.

<sup>223</sup> *Id.* § 1003(b), 126 Stat. at 1104.

<sup>224</sup> *Id.* § 1003(a)(1)(D), 126 Stat. at 1103–04.

*b. Strategic Plan*

Perhaps in tacit recognition that the FDASIA may be insufficient to prevent future shortages, the Act creates two mechanisms for continuing drug shortage research and strategic planning. First, as mentioned above, the Act requires that the Agency establish a task force to develop and implement a strategic plan to prevent and mitigate shortages.<sup>225</sup> Part of the strategic plan must analyze whether a Qualified Manufacturing Partner Program is necessary.<sup>226</sup> Manufacturers in the program would have the ability and “capacity to quickly supply drugs in, or anticipated to be in, shortage.”<sup>227</sup> Under the program, the FDA is also tasked with determining if incentives would help encourage manufacturers to participate.<sup>228</sup> The second mechanism the FDASIA creates to continue drug shortage research is its requirement for the Comptroller General to examine the causes of drug shortages.<sup>229</sup> The Comptroller General must submit recommendations to Congress regarding how to prevent or alleviate shortages by January 9, 2014.<sup>230</sup>

*B. Current Regulatory Solutions to the Drug Shortage Crisis*

*1. FDA Proposed Rule Implementing FDASIA*

The proposed rule would amend FDA regulations to implement the FDASIA drug shortage notice provisions. It contains broad definitions of several key terms which give maximum effect to the FDASIA notice requirements. For example, the proposed rule refers to a product as “a specific strength, dosage form, or route of administration.”<sup>231</sup> Under this rule, if a manufacturer experiences disruption that relates to only one strength of a particular drug, it would have to notify the FDA, even if other strengths are available.<sup>232</sup> The FDASIA already requires manufacturers to alert the Agency of manufacturing interruptions that are likely to lead to a “meaningful

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<sup>225</sup> *Id.* § 1003(a), 126 Stat. at 1103–04.

<sup>226</sup> *Id.* § 1003(a)(1)(B)(v), 126 Stat. at 1103.

<sup>227</sup> *Id.* § 1003(a)(1)(C)(i)(I), 126 Stat. at 1103.

<sup>228</sup> *Id.* § 1003(a)(1)(C)(ii), 126 Stat. at 1103.

<sup>229</sup> *Id.* § 1008, 126 Stat. at 1107–08.

<sup>230</sup> *Id.* § 1008(d), 126 Stat. at 1008. As of the writing of this Article, the Comptroller Report was not available.

<sup>231</sup> Discontinuance or Interruption, *supra* note 17, at 65,912.

<sup>232</sup> *Id.*

disruption in the supply of that drug in the United States.”<sup>233</sup> The proposed rule would require manufacturers to report interruptions that will likely lead to a meaningful disruption in their *own* supply.<sup>234</sup> In other words, it requires manufacturers to notify the FDA even if the manufacturer has such a small market share that its disruption is unlikely to affect the market as a whole.<sup>235</sup>

Consistent with the FDASIA’s intent, these notification requirements expand the FDA’s access to information regarding drug discontinuances and interruptions. According to the FDA, this information will allow the Agency time to work with manufacturers to resolve production disruptions or find alternative producers.<sup>236</sup> It is unclear whether the Agency has the capacity to analyze and react to the volume of notifications the proposed rule will likely generate. The Agency acknowledges that six months’ advanced notice of a manufacturing interruption is purely aspirational.<sup>237</sup> The proposed rule notes that often only a few days advance notice is practicable.<sup>238</sup> Further, the FDA acknowledges that, in some cases, notice may even postdate the production disruption.<sup>239</sup> In the proposed rule, the FDA expresses concern regarding the expanded definition of the types of drugs subject to notice requirements.<sup>240</sup> Perhaps mindful of its limited resources, the FDA seeks public comment on whether the definitions may have the effect of “unintentionally broaden[ing] the scope of reporting to such an extent that the Agency is ‘over-notified’ . . . .”<sup>241</sup>

Interestingly, the FDA’s ability to enforce the notice requirements is limited to issuing public noncompliance letters.<sup>242</sup> Generally, the FDA’s ability to publicize violations is one of its most powerful enforcement tools. In the past, the Agency has used this “name and shame” approach and published noncompliance letters of companies who failed to conduct federally required parenteral studies.<sup>243</sup>

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<sup>233</sup> FDASIA § 1001(a)(2), 126 Stat. at 1099.

<sup>234</sup> Discontinuance or Interruption, *supra* note 17, at 65,912.

<sup>235</sup> *Id.*

<sup>236</sup> *FDA Announces Actions to Combat Drug Shortages*, JAVMA NEWS (Dec. 4, 2013), <https://www.avma.org/News/JAVMANews/Pages/131215i.aspx>.

<sup>237</sup> Discontinuance or Interruption, *supra* note 17, at 65,914.

<sup>238</sup> *See id.*

<sup>239</sup> *Id.*

<sup>240</sup> *Id.*

<sup>241</sup> *Id.*

<sup>242</sup> *See id.*

<sup>243</sup> Alexander Gaffney, *Focusing on Pediatric Study Commitments, FDA Prepares to Name and Shame Noncompliant Companies*, REG. AFF. PROF. SOC’Y (Aug. 26, 2013),

Stronger enforcement provisions were included in draft legislation. Both the House of Representatives and Senate drug shortage bills contained fines for noncompliance.<sup>244</sup> The House of Representative bill authorized the FDA to levy fines up to \$10,000 a day.<sup>245</sup> No such provisions were included in the FDASIA. Perhaps they were omitted because fines or other punitive measures have the potential to exacerbate shortages. There would always be the risk that a manufacturer subject to a large fine could decide to simply shut down a facility rather than remediate it.

## 2. FDA Drug Shortage Task Force

As mentioned above, one of the ways the FDASIA tries to mitigate and prevent drug shortages is by requiring the FDA to create a task force to develop a Strategic Plan.<sup>246</sup> Released in October of 2013, the Strategic Plan outlines ways to improve the FDA's response to manufacturer shortage notifications.<sup>247</sup> Task Force recommendations include: (1) streamlining FDA internal processes, (2) clarifying roles and responsibilities of manufacturers, (3) improving communications with the public and healthcare providers regarding actual or potential shortages, and (4) collaborating with manufacturers on remediation efforts.<sup>248</sup>

The FDA identifies deficiencies in product and manufacturing facilities as the leading causes of drug shortages.<sup>249</sup> The Strategic Plan includes a blueprint of Agency actions to strengthen its effort to address shortages. As part of the plan, the FDA will create an Office of Pharmaceutical Quality.<sup>250</sup> The Agency will develop a risk-based approach to detect manufacturing problems that could result in shortages.<sup>251</sup> According to the plan, the FDA will also increase collaborations with industry and other stakeholders.<sup>252</sup> With this joint

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<http://www.raps.org/focus-online/news/news-article-view/article/3989/focusing-on-pediatric-study-commitments-fda-prepares-to-name-and-shame-noncompl.aspx>.

<sup>244</sup> Preserving Access to Life-Saving Medications Act of 2011, H.R. 2245, 112th Cong. § 506C(b)(7) (2011); S. 296, 112th Cong. § 2(a)(6) (2011).

<sup>245</sup> Preserving Access to Life-Saving Medications Act of 2011, H.R. 2245, 112th Cong. § 506C(b)(7) (2011).

<sup>246</sup> FDASIA, Pub. L. No. 112-144, § 1003, 126 Stat. 993, 1103 (2012).

<sup>247</sup> FDA 2013 PLAN, *supra* note 14, at 3.

<sup>248</sup> *Id.* at 18-19.

<sup>249</sup> *Id.* at 11.

<sup>250</sup> *Id.* at 20.

<sup>251</sup> *Id.* at 21.

<sup>252</sup> *Id.*

effort, the task force believes the FDA can gain a better understanding of shortages and strategies to prevent them.<sup>253</sup>

Notwithstanding these measures, the Strategic Plan notes that “shortages cannot be resolved until one or more manufacturers commit to fill in for lost production.”<sup>254</sup> The Strategic Plan recommends manufacturers consider building redundant manufacturing capacity or increasing inventory levels to lower the risks of shortages.<sup>255</sup> The task force notes that the FDA lacks the authority to require or regulate such practices, but it recognizes that the Agency is exploring ways to develop positive incentives to improve prioritizing manufacturing quality.<sup>256</sup>

The Strategic Plan seems to represent a nascent proposal rather than a fully developed approach to mitigating and preventing shortages. Two years ago, the FDASIA directed the FDA to create a plan to improve intra-agency and interagency communication.<sup>257</sup> The Strategic Plan indicates that the FDA is still “implementing” such a proposed office in the Office of Pharmaceutical Quality, but the Agency expects it to begin in January 2015.<sup>258</sup> The FDA was also instructed to explore whether a qualified manufacturing partner program would help mitigate future drug shortages.<sup>259</sup> In response to the FDA’s request for public comments, the Agency received substantial industry input specifically addressing the viability of such a partner program.<sup>260</sup> In addition, the Agency had access to a potential model in the Biomedical Advanced Research and Development Authority (BARDA) program, the partnership and data used to mitigate Doxil shortages.<sup>261</sup> Nevertheless, the task force states

<sup>253</sup> *Id.* at 23–24.

<sup>254</sup> *Id.* at 38.

<sup>255</sup> *Id.* at 6.

<sup>256</sup> *Id.* at 22–23.

<sup>257</sup> FDASIA, Pub. L. No. 112–144, § 1003(a)(1)(B)(i), 126 Stat. 993, 1103 (2012).

<sup>258</sup> FDA 2013 PLAN, *supra* note 14, at 20. The Office of Pharmaceutical Quality “creates a single unit dedicated to product quality . . . [and] is expected to provide better alignment among all drug functions . . . including review, inspection, and research.” *Office of Pharmaceutical Quality*, FDA, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm418347.htm> (last updated Oct. 16, 2014).

<sup>259</sup> FDASIA § 1003(a)(1)(B)(v).

<sup>260</sup> See *Food and Drug Administration Drug Shortages Task Force and Strategic Plan; Request for Comments*, FED. REG. (Feb. 7, 2013), <https://www.federalregister.gov/articles/2013/02/12/2013-03198/food-and-drug-administration-drug-shortages-task-force-and-strategic-plan-request-for-comments> [hereinafter *Request for Comments*] (noting that the FDA received 127 comments).

<sup>261</sup> *Id.*

that it still needs more industry input on feasibility.<sup>262</sup> As a result, the Strategic Plan contains no information regarding whether it will actually create such a partnership program.

In crafting the Strategic Plan, the FDA also requested public comment regarding how manufacturers use quality metrics to monitor production and select contract manufacturers.<sup>263</sup> In response, manufacturers and trade associations submitted comments describing several different industry standards and quality assurance approaches.<sup>264</sup> This input provided the task force a range of reporting material that purchasers and manufacturers identified as helpful in assessing quality. However, the task force does not appear to consider these or any other system to standardize and consolidate quality reporting information. Rather, the Strategic Plan indicates that purchasers should rely on already published data.<sup>265</sup> The FDA eschews its responsibility to create useful quality metrics by stating “buyers ultimately decide how or whether they will use this data when they make purchasing decisions.”<sup>266</sup> The Strategic Plan makes no reference to increasing the availability of quality information to the public or presenting the already available information in a more usable format for purchasers.

The Strategic Plan does make passing reference to shortage-related issues it considers outside of the FDA’s direct control. On the issue of manufacturing incentives, the Strategic Plan indicates that the FDA’s “ability to offer financial or other economic means to promote innovation in quality manufacturing is limited.”<sup>267</sup> This inert statement misses the point. No one expects the Agency to mete out cash rewards for quality improvements. As evident in several industry responses, the FDA has the ability to offer several valuable noneconomic incentives. For example, the Agency could offer expedited “review of new facilities for companies that have exhibited exemplary manufacturing quality standards . . . .”<sup>268</sup> The Agency could expedite product reviews for manufacturers who voluntarily

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<sup>262</sup> FDA 2013 PLAN, *supra* note 14, at 5.

<sup>263</sup> *Request for Comments*, *supra* note 260.

<sup>264</sup> *Id.*

<sup>265</sup> FDA 2013 PLAN, *supra* note 14, at 22.

<sup>266</sup> *Id.*

<sup>267</sup> *Id.*

<sup>268</sup> Jennifer M. Thomas, *FDA Issues Proposed Rule and Strategic Plan to Address Drug Shortages*, FDA LAW BLOG (Nov. 5, 2013), [http://www.fdalawblog.net/fda\\_law\\_blog\\_hyman\\_phelps/2013/11/fda-issues-proposed-rule-and-strategic-plan-to-address-drug-shortages.html](http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2013/11/fda-issues-proposed-rule-and-strategic-plan-to-address-drug-shortages.html).



invest in state of the art production technologies. Yet, the Strategic Plan does not analyze, or include, any quality-based incentives.

Despite some shortcomings, the Strategic Plan could have a positive effect on mitigating shortages. As enacted, however, it is questionable whether the task force will have sufficient time to entrench itself within the market and regulatory system sufficiently to have any lasting effect. Pursuant to FD&C section 506D(f), the structure and purpose of the task force ends in 2017.<sup>269</sup> This sunset provision means that even if the Strategic Plan’s initiatives begin to succeed, the task force will cease operations at the end of five years.<sup>270</sup> Given the severity of the drug shortages, however, such a short time frame does not give the task force much time to assert itself before losing its mandate.

### C. Current Industry Solution to the Drug Shortage Crisis

The Generic Pharmaceutical Association (GPhA) and a subset of member companies have collaborated with the FDA to develop and implement a program to address potential drug shortages.<sup>271</sup> Under the Accelerated Recovery Initiative (ARI), generic companies share manufacturing information about drugs in short supply with the FDA and a third party.<sup>272</sup>

The ARI consists of voluntary confidential communications among the FDA, IMS Health, and stakeholders involved in the manufacturing and distribution of generic drugs currently in shortage.<sup>273</sup> The goal of the initiative is to use real-time supply and

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<sup>269</sup> See Food, Drugs, and Cosmetics Act § 506D(f), 21 U.S.C. § 356d(f) (2012), amended by FDASIA, Pub. L. No. 112–144, § 1003(f), 126 Stat. 993, 1104 (2012).

<sup>270</sup> *Id.*

<sup>271</sup> *GPhA Receives Positive FTC Advisory Opinion on the Accelerated Recovery Initiative*, GENERIC PHARMACEUTICAL ASS’N, <http://www.gphaonline.org/gpha-media/press/gpha-receives-positive-ftc-advisory-opinion-on-the-accelerated-recovery-initiative> (last visited Oct. 15, 2014) [hereinafter *FTC Advisory Opinion*].

<sup>272</sup> Thomas Sullivan, *FTC Approves Accelerated Recovery Initiative to Reduce Drug Shortages*, POL’Y & MED. (Sept. 5, 2012), <http://www.policymed.com/2012/09/ftc-approves-accelerated-recovery-initiative-to-reduce-drug-shortages.html> [hereinafter *FTC Approves Accelerated Recovery Initiative*].

<sup>273</sup> *Id.* IMS Health is an information and technology company that collects, analyzes, and connects healthcare data on diseases, treatments, results, and costs to enable its clients to operate more efficiently. *About IMS Health*, IMS HEALTH, <http://www.imshealth.com/portal/site/imshealth/menuitem.051a1939316f851e170417041ad8c22a/?vgnnextoid=7311e590cb4dc310VgnVCM100000a48d2ca2RCRD&vgnnextfmt=default> (last visited Oct. 28, 2014). IMS Health is the independent third party ARI uses to collect and impart data from the stakeholders to the FDA. *FTC Approves Accelerated Recovery Initiative*, *supra* note 272.

distribution information to expedite Agency efforts to mitigate shortages.<sup>274</sup> The multi-stakeholder approach also will use manufacturers' production and release forecasts to assist Agency staff in preventing shortages.<sup>275</sup> The FDA and GPhA are also currently working to identify four to eight generic sterile injectables that have at least two manufacturers to cooperate in meeting market production needs.<sup>276</sup>

A key element of the ARI is the agreement among drug manufacturers to pool competitively sensitive production information about shortage drugs. To avoid antitrust concerns, the GPhA requested review by the Federal Trade Commission (FTC).<sup>277</sup> The FTC concluded that safeguards built into the process are sufficient to prevent collusion and unfair competition among the participants.<sup>278</sup> For example, the ARI requires that an independent third party gather and transmit the data from the stakeholders to the FDA.<sup>279</sup> "[N]o other party . . . will have access to this information or any analysis derived therefrom."<sup>280</sup> The initiative also requires ARI participants to sign a binding commitment not to use the program for anticompetitive ends.<sup>281</sup>

#### *D. Things Left Unsaid: Additional Deficiencies in the Current Approach*

The measures discussed above attempt to mitigate drug shortages through advanced agency notification, increased industry communication regarding drug supply levels, and task force efforts aimed at increasing manufacturing quality. These are positive steps; however, they focus on the symptoms, rather than the causes, of drug shortages. The underlying cause for generic manufacturers' decision to stop producing certain categories of drugs lies in simple economics. Advanced notification requirements or increased industry communications will not replenish drugs in situations in which slim

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<sup>274</sup> *FTC Approves Accelerated Recovery Initiative*, *supra* note 272.

<sup>275</sup> *Id.*

<sup>276</sup> *Id.*

<sup>277</sup> *FTC Staff Issues Advisory Opinion Regarding Generic Pharmaceutical Association's Proposed Initiative to Address Drug Shortages*, FED. TRADE COMM'N (Aug. 8, 2012), <http://www.ftc.gov/news-events/press-releases/2012/08/ftc-staff-issues-advisory-opinion-regarding-generic>.

<sup>278</sup> *Id.*

<sup>279</sup> *FTC Approves Accelerated Recovery Initiative*, *supra* note 272.

<sup>280</sup> *Id.*

<sup>281</sup> *Id.*

profits and market imbalances have resulted in manufacturers leaving the market. Until there is increased elasticity of demand or supply, shortages will continue. Yet, the solutions implemented thus far fail to acknowledge this fact.

Admittedly, the FDA’s ability to end shortages is constrained. The Agency does not have the legal authority to compel manufacturers to produce drugs.<sup>282</sup> Nor does the FDA possess the manufacturing ability to produce drugs itself. The FDASIA, the proposed rule, and the Strategic Plan fail to address the imbalance of market forces in the current system. To date, no legislation has been passed that offers a solution to the root causes of manufacturers’ inability or unwillingness to meet current drug demands. What follows is a multiparty approach that addresses the economic underpinnings of drug shortages. The next Part offers legislative, regulatory, and private industry solutions aimed at motivating generic manufacturers to produce safe, adequate quantities of affordable generics that are currently in short supply.

#### IV

#### MULTIPRONGED APPROACH TO END DRUG SHORTAGES

##### *A. Regulatory Solutions*

##### *1. Manufacturer Incentives*

It is difficult to conceive of a viable approach to ending shortages without manufacturer incentives. The task force acknowledges that incentives are a key element in its prevention strategies.<sup>283</sup> However, the Strategic Plan contains no Agency-specific proposals.<sup>284</sup> Instead, the drafters encourage unnamed “others” to explore means to incentivize manufacturing innovation and quality.<sup>285</sup> Setting aside the Agency’s self-imposed limitations, there are several incentives the FDA could offer that would have an economic impact on manufacturers’ willingness to both remain in and enter the market to produce critical, lifesaving drugs.

The Agency could offer targeted financial incentives in exchange for generic manufacturers building extra capacity into their facilities. Infrastructure redundancy measures might include manufacturers

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<sup>282</sup> FDA 2013 PLAN, *supra* note 14, at 23.

<sup>283</sup> *See id.* at 22.

<sup>284</sup> *See generally id.*

<sup>285</sup> *Id.* at 22.

establishing and maintaining alternate production lines or facilities.<sup>286</sup> Manufacturers who create risk-management programs that include extra manufacturing capacity dedicated to prevent shortages could be eligible for tax rebates.<sup>287</sup> In return for increased manufacturing capacity, the FDA could additionally waive user fee requirements and streamline the approval process for redundant facilities at single-source manufacturers.<sup>288</sup> The Agency could also offer tax rebates offered for programs that identify and maintain alternate active pharmaceutical ingredient (API) suppliers.

Improving quality in the manufacturing process is another core element in preventing shortages. Currently, the drug's price is the primary consideration in purchasing decisions.<sup>289</sup> This can lead manufacturers to prioritize reducing costs over quality. This type of manufacturing approach can contribute to shortages. Agency incentives that encourage better manufacturing processes could help reorient the industry. Agency actions could include reduced oversight for manufacturers who maintain good compliance histories and effective risk remediation plans.<sup>290</sup> Reduced oversight could include downgrading filing categories for site transfers and assay improvements.<sup>291</sup> The FDA could consider granting additional exclusivity for products in the same therapeutic areas as the drugs in shortage to manufacturers who consistently maintain high-quality manufacturing standards.<sup>292</sup>

The FDA could also consider implementing a scoring system to encourage manufacturers to focus on quality. The FDA could post on its website the names of manufacturing facilities who received high-

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<sup>286</sup> See Letter from Richard Johnson, President, Parenteral Drug Ass'n, to Div. of Docket Mgmt., FDA 4 (Mar. 13, 2013) [hereinafter Letter from Richard Johnson], available at <http://www.pda.org/docs/default-source/website-document-library/scientific-and-regulatory-affairs/regulatory-comments-resources/2013/fdas-draft-drug-shortages-strategic-plan-march-13-2013.pdf?sfvrsn=6>.

<sup>287</sup> *Id.* at 5.

<sup>288</sup> See *id.* at 4; see also Letter from Cancer Leadership Council, to Leslie Kux, Assistant Comm'r for Policy, FDA (Mar. 14, 2013), available at [http://www.lymphoma.org/atf/cf/%7Baaf3b4e5-2c43-404c-afe5-fd903c87b254%7D/LEADERSHIP\\_COUNCIL\\_DRUGSHORTAGE\\_STRATEGICPLAN.PDF](http://www.lymphoma.org/atf/cf/%7Baaf3b4e5-2c43-404c-afe5-fd903c87b254%7D/LEADERSHIP_COUNCIL_DRUGSHORTAGE_STRATEGICPLAN.PDF).

<sup>289</sup> See U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 63, at 5; see, e.g., Letter from Blair Childs, Senior Vice President, Pub. Affairs, Premier, to Margaret Hamburg, Comm'r, Food & Drug Admin. (Mar. 14, 2013) [hereinafter Premier Letter], available at <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-0124-0129>.

<sup>290</sup> Premier Letter, *supra* note 289, at 4.

<sup>291</sup> Letter from Richard Johnson, *supra* note 286, at 4.

<sup>292</sup> See Premier Letter, *supra* note 289, at 4.

quality scores during Agency inspections. This FDA “stamp of approval” could favorably influence the supplier selection. It could also improve the market value of these publicly held companies. Another approach would offer incentives to manufacturers who successfully adopt the Pharmaceutical Quality Manufacturing Guidelines contained in the International Conference on Harmonization (ICH).<sup>293</sup> The ICH provisions cover risk-management as well as maintaining quality in the pharmaceutical sector.<sup>294</sup> The Agency could also award these manufacturers with the FDA “stamp of approval.” In addition, the existing Good Manufacturing Practice regulations provide a framework for manufacturers to produce safe, pure, and high quality drugs.<sup>295</sup>

Finally, the FDA could consider financial incentives patterned after the Orphan Drug Act. Under that Act, the Agency offers tax credits for clinical research and a seven-year period of exclusive marketing to developers of drugs for rare diseases.<sup>296</sup> Since the Act’s passage in 1983, the FDA has approved more than 1000 orphan products for rare diseases.<sup>297</sup> Prior to this incentive-based Act, only a handful of orphan drugs were on the market.<sup>298</sup> As noted by Abbey Meyers, then-president of the National Organization for Rare Disorders, “[t]he act has been very successful in attracting companies.”<sup>299</sup> A similar tax-based incentive could help attract new entrants to the market by countering the low profit margins manufacturers associate with producing certain critical drugs.

## 2. Improved FDA Communication

A primary goal of the FDASIA is averting drug shortages through improved communication and notification.<sup>300</sup> A critical component to

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<sup>293</sup> FDA, PHARMACEUTICAL CGMPs FOR THE 21ST CENTURY—A RISK-BASED APPROACH 9 (2004), available at <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswers/CurrentGoodManufacturingPracticescGMPforDrugs/UCM176374.pdf>.

<sup>294</sup> *Id.* at 14.

<sup>295</sup> See generally CURRENT GOOD MANUFACTURING PRACTICES, *supra* note 68.

<sup>296</sup> Orphan Drug Act, 21 C.F.R. § 316 (2014); OFFICE OF INSPECTOR GEN., ORPHAN DRUG ACT: IMPLEMENTATION AND IMPACT 1 (2001) [hereinafter ORPHAN DRUG ACT IMPACT], available at <http://oig.hhs.gov/oei/reports/oei-09-00-00380.pdf>.

<sup>297</sup> ORPHAN DRUG ACT IMPACT, *supra* note 296, at 1.

<sup>298</sup> 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>.

<sup>299</sup> *Id.*

<sup>300</sup> See FDASIA, § 1003(a)(1)(B)(iii), (d), 126 Stat. 993, 1103–04 (2012).

achieving that goal is the Agency's ability to quickly disseminate information. The FDA should maintain a real-time map that allows healthcare providers to see where critical drugs can be found and in what quantities.<sup>301</sup> The FDA's website should include timelines regarding how long the Agency expects a shortage to last.<sup>302</sup> The expected duration of the shortage would help manufacturers provide guidance to hospitals regarding appropriate steps to take to minimize the impact of the shortage.<sup>303</sup> The FDA website should also post the compliance status of manufacturing sites and products.<sup>304</sup>

The FDA maintains an index of all drug shortages.<sup>305</sup> This system relies on manufacturer-supplied information regarding current drug supply levels.<sup>306</sup> While helpful in providing the public information regarding drug availability, the system could be improved. The Agency should consider creating a template for manufacturers to submit drug index information.<sup>307</sup> A streamlined approach would increase efficiency and ensure that the information is submitted in a uniform format by the reporting manufacturers.<sup>308</sup>

There reportedly have been more than 2000 generic applications in the queue for FDA approval.<sup>309</sup> The median wait-time is thirty months.<sup>310</sup> It is critical that the FDA devote the necessary resources to expedite approvals and eliminate this backlog. Shorter approval times allow more lifesaving medications into the market. Reducing the thirty-month approval timeframe would also give the Agency more generic options within the six-month manufacturer notice period of an anticipated drug shortage.<sup>311</sup> Increasing the number of FDA-

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<sup>301</sup> Letter from Thomas K. McInerney, President, Am. Acad. of Pediatrics, to Margaret Hamburg, Comm'r, FDA (Mar. 13, 2013), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-0124-0125>.

<sup>302</sup> See Premier Letter, *supra* note 289, at 5.

<sup>303</sup> *Id.*

<sup>304</sup> Letter from Richard Johnson, *supra* note 286, at 3.

<sup>305</sup> *Current and Resolved Drug Shortages*, *supra* note 23.

<sup>306</sup> See *id.*

<sup>307</sup> Letter from David R. Gaugh, Senior Vice President for Sci. & Regulatory Affairs, Generic Pharmaceutical Ass'n, to Div. of Dockets Mgmt., Food & Drug Admin. (Mar. 14, 2013), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-0124-0087>.

<sup>308</sup> *Id.*

<sup>309</sup> Link, Hagerty & Kantarjian, *supra* note 100, at 694.

<sup>310</sup> *Id.*

<sup>311</sup> *Id.*

approved entrants would also reduce the presence and influence of gray market suppliers.<sup>312</sup>

### 3. *Quality Metrics*

Opacity in the pharmaceutical drug production process limits purchasers’ information about manufacturing quality.<sup>313</sup> Purchasers often base their knowledge on press reports or personal experiences.<sup>314</sup> As a result, they may be “unaware of potential variation in pharmaceutical product quality and assume products are manufactured to high standards.”<sup>315</sup> In this environment, price is often the sole determinant in deciding which generic drug to purchase.<sup>316</sup> These facts, and the FDA’s goal of increasing manufacturing quality, require the task force to revisit its approach to quality metrics.

The Strategic Plan cannot adequately address production quality concerns without including some type of metrics for purchasers. Access to quality metrics—such as the number and level of recalls, inspection irregularities, and production line maintenance reports—would help purchasers and prescribers balance price with quality.<sup>317</sup> Manufacturing quality metrics should be as readily available to purchasers as price when ordering sterile injectables. Changing the purchasing dynamics would encourage manufacturers to focus on quality.<sup>318</sup> Nursing homes, restaurants, and other settings have successfully used this approach when it is difficult to observe or interpret quality.<sup>319</sup>

As noted previously, quality metrics should also be available to manufacturers choosing a contract provider. The FDA solicited and received several industry examples regarding useful metrics to evaluate contract manufacturers.<sup>320</sup> Identified metrics include employee turnover rates, inspection history, ability to meet the contract giver’s quality system requirements, facility maintenance

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<sup>312</sup> *Id.*

<sup>313</sup> Woodcock & Wosinska, *supra* note 71.

<sup>314</sup> Letter from Richard Johnson, *supra* note 286, at 2.

<sup>315</sup> *Id.*

<sup>316</sup> See Woodcock & Wosinska, *supra* note 71.

<sup>317</sup> Letter from David R. Gaugh, *supra* note 307.

<sup>318</sup> *Id.*

<sup>319</sup> *Id.*

<sup>320</sup> *Request for Comments*, *supra* note 260; GAO DRUG SHORTAGES, *supra* note 22, at 74–83.

reports, and the availability of alternate suppliers.<sup>321</sup> These metrics have high industry acceptance as reliable ways to assess manufacturing quality.

The Agency also solicited and received comments on metrics the industry relies on to assess internal quality. According to comments submitted by Pharmaceutical Manufacturers of America (PhRMA) and the GPhA, pharmaceutical companies regularly monitor error rates to assess quality.<sup>322</sup> “[H]igh error rates are considered evidence of poor process control, poor training of operators, lax oversight by supervisors, poorly maintained equipment and facilities, or poor product and process characterization . . . .”<sup>323</sup> Comments submitted by the Parenteral Drug Association (PAD) note that yield analysis, inspection outcomes, and contingency plans for act-of-God situations, such as pandemics, are commonly used quality metrics.<sup>324</sup> PAD comments also state that companies use similar metrics when selecting contract manufacturers.<sup>325</sup>

Based on these industry suggestions, the FDA should adopt standard nationwide metrics to assess all manufacturing quality. To increase transparency, the FDA could then use these metrics to issue quarterly trend analyses on how manufacturers have performed.<sup>326</sup> The FDA should also provide manufacturers a clear policy statement on what the Agency reviews during facility inspections.<sup>327</sup> Finally, the FDA should consider revising its Form 483 facility inspection report; a more user-friendly format would allow non-manufacturers to better assess the level of concern the FDA has regarding a facility.<sup>328</sup>

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<sup>321</sup> Letter from Richard Johnson, *supra* note 286, at 3.

<sup>322</sup> Letter from David R. Gaugh, *supra* note 307; Letter from Alice E. Till, Vice President, Sci. Policy and Tech. Affairs, PhRMA, to Div. of Dockets Mgmt., FDA 2 (Feb. 12, 2013), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-0124-0106>.

<sup>323</sup> Biopharm Int'l, *FDA Seeks Metrics to Define Drug Quality*, ASQ (Oct. 15, 2013), <http://asq.org/qualitynews/qnt/execute/displaySetup?newsID=17124>.

<sup>324</sup> Letter from Richard Johnson, *supra* note 286, at 1–2.

<sup>325</sup> *Id.* at 3.

<sup>326</sup> *See id.*

<sup>327</sup> Premier Letter, *supra* note 289, at 3.

<sup>328</sup> *Id.* A Form 483 “notifies the company’s management of objectionable conditions. At the conclusion of an inspection, the FDA Form 483 is presented and discussed with the company’s senior management.” *FDA Form 483 Frequently Asked Questions*, FDA, <http://www.fda.gov/ICECI/Inspections/ucm256377.htm> (last updated Mar. 13, 2012).



#### 4. *International Imports*

The FDA has approved a limited number of imports from Europe to help mitigate shortages.<sup>329</sup> In 2010, the Agency permitted import of the unapproved anesthetic agent Propofol to address shortages.<sup>330</sup> The task force should expand the scope of the Strategic Plan to include a mechanism that allows for the timely import of approved drugs from foreign markets.<sup>331</sup> International imports are referenced in the Strategic Plan’s appendix.<sup>332</sup> However, foreign markets are an underdeveloped aspect of the task force’s approach to mitigate shortages. The FDA could also consider adapting the tentative approval process the Agency has used to approve anti-HIV medications for purchase.<sup>333</sup> For more than a decade, the FDA has approved foreign drugs as part of the President’s Emergency Plan for AIDS Relief.<sup>334</sup> This plan allows for “the review and approval of high-quality medical products made in foreign countries and . . . develop[s] mechanisms to allow the purchase and domestic use of products when domestic shortages . . . occur.”<sup>335</sup>

### *B. Congressional Solutions*

#### *1. Hatch-Waxman Act Revisions*

Revising certain Hatch-Waxman Act requirements for generic manufacturers may help address the shortage crisis. In general terms, the Hatch-Waxman Act established a streamlined approval process for generic drugs.<sup>336</sup> Under the Hatch-Waxman Act, generic

<sup>329</sup> *Questions and Answers on the Propofol Shortage*, PROPOFOL SHORTAGE QA, [http://www.ipqpubs.com/wp-content/uploads/2010/05/Propofol\\_Shortage\\_QA.pdf](http://www.ipqpubs.com/wp-content/uploads/2010/05/Propofol_Shortage_QA.pdf) (last visited Oct. 15, 2014).

<sup>330</sup> *Id.*

<sup>331</sup> *See id.*

<sup>332</sup> FDA 2013 PLAN, *supra* note 14, at 39.

<sup>333</sup> Press Release, FDA, FDA Gives Tentative Approval to New Generic AIDS Drug in Association with the President’s Emergency Plan for AIDS Relief (May 18, 2006), available at <http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119230.htm>.

<sup>334</sup> *Id.*

<sup>335</sup> Letter from Mark Harrington & Coco Jervis, Treatment Action Grp., FDA to Drug Shortages Task Force and Strategic Plan 2 (Mar. 14, 2013), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-0124-0116>.

<sup>336</sup> 21 U.S.C. § 355(j) (2012); see generally Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 FOOD & DRUG L.J. 187 (1999) (describing the drafting, function, and revisions of the Hatch-Waxman Act).

manufacturers file Abbreviated New Drug Applications (ANDA) with the FDA to receive marketing approval.<sup>337</sup> Congress could amend the Hatch-Waxman Act's ANDA process to require manufacturers to include current product demand projections and their plans for fulfilling those demands.<sup>338</sup> Borrowing from the legislative approach used for patented drugs, the amendment could also require that manufacturers build redundancy into their production facilities.<sup>339</sup> This proposal could diminish the impact of production disruptions on overall market supply, but such an amendment would likely face legislative opposition.

The Eleventh Circuit and the D.C. Circuit both recently affirmed that the FDA does not have the authority to regulate or control manufacturer decisions regarding production.<sup>340</sup> In addition, accurate production forecasts may be difficult given the limited control manufacturers have over the supply of raw materials used in their medications.<sup>341</sup> Approximately eighty percent of the raw materials used in manufacturing drugs are imported.<sup>342</sup> Many of these imports are from countries where political instability or problems with product contamination are common.<sup>343</sup> Industry stakeholders would similarly oppose legislation that penalizes manufacturers for not meeting product goals due to events that were outside their control.

A slightly different approach would grant the FDA authority to revoke market approval if a manufacturer consistently fails to meet stated production levels.<sup>344</sup> This too would likely face fierce opposition. Legislation authorizing the FDA to require manufacturers to include redundancy capabilities and revoke market approval of drugs in short supply seems to run counter to the FDASIA's intent.

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<sup>337</sup> Mossinghoff, *supra* note 336, at 188, 190.

<sup>338</sup> See Chabner, *supra* note 121, at 2148; Hoffman, *supra* note 26, at 16.

<sup>339</sup> Hoffman, *supra* note 26, at 16.

<sup>340</sup> *Lacognata v. Hospira, Inc.*, 521 F. App'x 866 (11th Cir. June 7, 2013) (unpublished), *aff'g* No. 8:12-cv-822-T-30TGW, 2012 WL 6962884 (M.D. Fla. July 2, 2012); see also *Carik v. U.S. Dep't of Health & Human Servs.*, No. 12-272, at \*5 (D.D.C. Nov. 27, 2013).

<sup>341</sup> See *Hospital Drug Shortages*, PREMIER (Mar. 2012), <https://legacy.premierinc.com/about/advocacy/iss/Position%20Papers/Hospital-Drug-Shortages-Premier-Policy-Paper-March2012.pdf>.

<sup>342</sup> *Id.*

<sup>343</sup> *Id.*

<sup>344</sup> Hoffman, *supra* note 26, at 16.

## 2. Medicare Modernization Act

Some politicians view the MMA’s reimbursement system as one of the primary economic causes of drug shortages.<sup>345</sup> In 2012, members of Congress introduced the Patient Access to Drugs in Shortage Act, which aimed to increase generic injectable production by recalibrating the Medicare rate to more accurately reflect the value of those drugs.<sup>346</sup> The legislation proposed amending the Social Security Act to exempt generic sterile injectables with three or fewer active manufacturers from the ASP-based reimbursement pricing method.<sup>347</sup> The proposed legislation died in committee.<sup>348</sup> However, its approach of eliminating disincentives to production posed by the Medicare reimbursement system may be a necessary component to any long-term approach to end drug shortages. To date, no other potential solution directly addresses manufacturers’ profit margin concerns.

An alternate solution is to establish a minimum price for generics based on comparable brand-name drugs.<sup>349</sup> If a brand-name drug costs \$70,000 per year, the generic version could be priced at 5% to 10%, or \$3500 to \$7000 per year.<sup>350</sup> Another suggestion is to establish a payment system based on disease-management fees rather than drug sales.<sup>351</sup> These more robust reimbursement rates could provide the economic incentive for generic drug manufacturers to enter and remain in the market.

Enacting such a proposal, however, would be challenging. In fact, a past proposal aimed at reducing the deficit recommended the opposite. A joint committee considered reducing the Medicare Part B drug reimbursement formula from ASP +6% to ASP +3%.<sup>352</sup> The MMA’s reimbursement system illustrates the classic tension between

<sup>345</sup> See Emanuel, *supra* note 107.

<sup>346</sup> Patient Access to Drugs in Shortage Act of 2012, H.R. 6611, 112th Cong. (2012); see *The Patient Access to Drugs in Shortage Act*, POL’Y & MED. (Dec. 20, 2012), <http://www.policymed.com/2012/12/the-patient-access-to-drugs-in-shortage-act.html> [hereinafter *Patient Access*].

<sup>347</sup> *Patient Access*, *supra* note 346.

<sup>348</sup> H.R. 6611 (112th): *Patient Access to Drugs in Shortage Act of 2012*, GOVTRACK.US, <https://www.govtrack.us/congress/bills/112/hr6611> (last visited Nov. 8, 2014).

<sup>349</sup> Link, Hagerty & Kantarjian, *supra* note 100, at 693–94.

<sup>350</sup> *Id.*

<sup>351</sup> Hoffman, *supra* note 26, at 18.

<sup>352</sup> *Special Action Alert: Tell Congress to Oppose Medicare Cuts to Cancer-Fighting Drugs!*, US ONCOLOGY NETWORK (Nov. 10, 2011), <https://ex.democracymed.com/CB13278093BDCEAE05CA9FC1F62FC3D4C5EC6424/799bd1ed-e4e6-4ae3-a48f-ef549b94c160.pdf>.

a public program's goal of cost containment and manufacturers' need to maintain profit margins sufficient to justify continued production.<sup>353</sup>

### 3. GPOs and Safe Harbor Provisions

Over the past two decades, GPOs' effect on competition and innovation has been the subject of inquiry. As previously discussed, some have theorized that GPO anticompetitive business practices are a major contributor to current shortages.<sup>354</sup> Numerous Senate Antitrust Subcommittee hearings and GAO investigations have scrutinized the GPO contract practices.<sup>355</sup> In 2005, members of Congress introduced a draft discussion bill to eliminate GPO contract administration fees by repealing the Medicare anti-kickback safe harbor provisions.<sup>356</sup> Supporters of the bill argued that GPO administrative fees create a "pay to play" mechanism that inhibits free market competition.<sup>357</sup> The bill died in subcommittee.<sup>358</sup> Two years ago, Congress asked the GAO to investigate GPO business practices.<sup>359</sup> Specifically, lawmakers were concerned that GPO contract provisions limit competition among manufacturers and contribute to drug shortages.<sup>360</sup> It appears, however, that the GAO has taken no action on this request.

GPOs' role in the healthcare supply system remains controversial. To assess accurately whether substantive changes should be made to

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<sup>353</sup> Hoffman, *supra* note 26, at 18.

<sup>354</sup> Blair & Durrance, *supra* note 154.

<sup>355</sup> See generally Letter from Herb Kohl, Charles E. Grassley & Tom Coburn, Senators, to the Gov't Accountability Office (Mar. 30, 2012) [hereinafter Kohl, Grassley & Coburn Letter], available at <http://www.gao.gov/assets/590/589778.pdf>; GROUP PURCHASING ORGANIZATIONS, *supra* note 150; *Group Purchasing Organizations: Services Provided to Customers and Initiatives Regarding Their Business Practices*, GAO (Aug. 2010), <http://www.gao.gov/products/GAO-10-738>.

<sup>356</sup> Patricia Earl & Phillip L. Zweig, *Connecting the Dots: How Anticompetitive Contracting Practices, Kickbacks, and Self-Dealing by Hospital Group Purchasing Organizations (GPOs) Caused the U.S. Drug Shortage*, CARE & COST (Feb. 14, 2012), <http://careandcost.com/2012/02/14/connecting-the-dots-how-anticompetitive-contracting-practices-kickbacks-and-self-dealing-by-hospital-group-purchasing-organizations-gpos-caused-the-u-s-drug-shortage/>.

<sup>357</sup> See *id.*

<sup>358</sup> *Id.*

<sup>359</sup> Press Release, Markey, Top Democrats Call for GAO Investigation into Link Between Drug Shortages and Increased Reliance on Compounding Pharmacies (Nov. 15, 2012), available at <http://www.psanes.org/Portals/0/docs/Drug%20Shortages/Markey%20Press%20Release%2011-15-2012.pdf>.

<sup>360</sup> *Id.*

safe harbor provisions to ensure competition and innovation among generic manufacturers, more information is needed. One approach is to use various governmental agency tools to compel the necessary information. The Executive Branch could direct the Department of Justice and the FTC to investigate GPO business practices.<sup>361</sup> These agencies can subpoena documents, compel testimony, and seize property. Additionally, they have the authority to prosecute if they find anticompetition violations.

In 2004, Congress asked the GAO to investigate the impact of GPO administrative fees on generic manufacturers’ ability to upgrade their facilities and conduct quality control.<sup>362</sup> A 2012 GAO report notes the DHHS Office of Inspector General (OIG) has the authority to compel production of this information.<sup>363</sup> For more than ten years, the OIG has failed to regularly obtain the information.<sup>364</sup> The FDA should prevail upon the DHHS to demand that GPOs immediately produce the data and to continue to do so on a consistent basis. The DHHS should also make the information available to the public on the OIG website.

The FTC could also exercise its antitrust enforcement authority to investigate GPO antitrust allegations. Shortly after the Executive Order directing the FDA to end drug shortages, five U.S. senators also made a request to FTC Chairman Jonathan Leibowitz to examine the healthcare delivery system’s effect on patients’ access to drugs.<sup>365</sup> The FTC has not made any public statement regarding the investigation. The Executive Branch could consider directing the FTC to make its findings public. To the extent appropriate, the FTC should also exercise its authority to “halt anticompetitive contracting practices” that are involved in GPO business practices.<sup>366</sup>

### *C. Industry Solutions*

Ending drug shortages requires a multiparty approach. Congress and the FDA play significant roles in addressing shortages. Their

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<sup>361</sup> Kohl, Grassley & Coburn Letter, *supra* note 355, at 3 n.8.

<sup>362</sup> *See id.* at 3.

<sup>363</sup> *Id.* at 3, 7.

<sup>364</sup> *See id.* at 3, 8.

<sup>365</sup> Exec. Order No. 13,588, 3 C.F.R. 281 (2011); Letter from Barbara Boxer, Charles E. Grassley, Richard J. Durbin, Herb Kohl & Tom Harkin, Senators, to Jonathan Leibowitz, Chairman, FTC (Nov. 9, 2011), *available at* <http://www.puncturemovie.com/wp-content/themes/Romix/pdfs/herb-kohl-11-9-11.pdf>.

<sup>366</sup> Earl & Zweig, *supra* note 356.

efforts will fail, however, unless generic manufacturers agree to increase drug production. The Strategic Plan highlights the Agency's need to collaborate with manufacturers to develop new strategies as a key feature to address shortages.

One potential solution involves manufacturers collaborating with the FDA to establish voluntary production and quality levels in exchange for customized incentive packages. The FDA cannot compel manufacturers to meet certain capacity levels,<sup>367</sup> nor can the Agency prevent a manufacturer from exiting the market to pursue other more profitable production lines. However, in return for facilities building in extra capacity to meet pre-set production levels, the FDA can provide a variety of economic and noneconomic incentives that manufacturers could select to suit their individual business needs.<sup>368</sup>

This approach is appealing because, unlike other solutions, it offers a flexible approach for manufacturers to create their own incentives. Generic manufacturers have different priorities depending on whether they are considering entering the market or whether they are already producing a drug in shortage. As a result, some incentives will be more attractive than others based on manufacturers' individual business plans and strategies. Manufacturers in the final stages of drug development may value a voucher for expedited FDA product review over a tax rebate.

In exchange for a customized incentive package, manufacturers would commit to increasing capacity while maintaining quality. While the FDA could offer this option on an individual manufacturer basis, an industry-wide approach is preferable. As discussed previously, one manufacturer building redundancy into its operations results in higher production costs compared to others in the market.<sup>369</sup> To avoid that production cost differential, all manufacturers would need to commit to infrastructure improvements sufficient to meet the established capacity levels. In addition to ending shortages, this approach eliminates the downstream effects of gray market suppliers and price gouging.

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<sup>367</sup> See *supra* text accompanying note 282.

<sup>368</sup> See *supra* text accompanying notes 287–88.

<sup>369</sup> See *supra* Part II.A–B.

## CONCLUSION

While there are several causes to drug shortages, the common effect is the risk to patient care. The number and frequency of shortages has risen dramatically over the past five years. The repercussions of shortages adversely affect hospitals and other healthcare providers' ability to treat patients. The unavailability of certain drugs has required healthcare providers to cancel interventions, administer less effective second-line alternatives, and purchase drugs through the gray market.

To date, administrative, legislative, and industry approaches to address shortages have focused on the symptoms. The FDA's revised manufacturer notice requirements and the multi-stakeholder ARI initiative to share drug production information may aid in addressing shortages. However, these measures will not address the root cause.

The solution to ending shortages lies in removing the economic and regulatory obstacles that prevent manufacturers from achieving profit margins sufficient to produce certain needed medicines. Legislative action to restructure the MMA's reimbursement system is necessary. Government agencies should conduct a thorough investigation of GPO contract activities. If appropriate based on the findings, Congress should repeal the safe harbor provisions to ensure free-market competition among manufacturers. Manufacturers should build on the multiparty industry collaboration that created the ARI to approach the FDA about working together to develop customized incentive packages in exchange for manufacturer commitments to meet certain production and quality levels. The appeal of this approach is that it has the potential to provide what has been largely absent—willing manufacturers.

The U.S. government spends trillions of dollars each year subsidizing healthcare so more people can receive medical treatment. Advancements in chemotherapy and other drugs allow physicians to treat and cure several types of diseases that would have been fatal a few years ago. The most pernicious aspect of drug shortages is that they jeopardize, and in some cases eliminate, patients' access to those lifesaving drugs. This Article proposes solutions to ensure patients have access to the right medicine at the right time.

