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Sharona Hoffman

Case Western Reserve University School of Law, sharona.hoffman@case.edu

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The Drugs Stop Here: A Public Health Framework to Address the Drug Shortage Crisis

SHARONA HOFFMAN*

INTRODUCTION

I serve on the ethics committee of a prominent Cleveland hospital. During one meeting in the fall of 2011, our Chair announced that our first agenda item would be the drug shortages that the hospital was facing. These included anesthetic and chemotherapy agents needed by critically ill patients. While this issue was sadly familiar to committee members who were long-time hospital employees, others were stunned – how could such shortages plague premier hospitals in the twenty-first century in the wealthiest country in the world? How could even patients with comprehensive health insurance and abundant financial resources be denied adequate care because the medications they require are simply not available in the marketplace?

Unfortunately, our hospital is not alone. The drug shortage crisis has increasingly drawn the attention of the media and government authorities. In September of 2011, the FDA conducted a one-day Drug Shortage Workshop.¹ A front page New York Times story on January 1, 2012 focused on a national shortage of generic pills that treat attention deficit hyperactivity disorder (ADHD) and reported that it is affecting millions of patients.² A few weeks earlier, the Times published a story concerning the unavailability of Doxil, an important chemotherapy agent.³

Thus far, little has been written in the law review literature about the drug shortage crisis, and this article begins to fill this gap. It provides a thorough analysis of the origins and implications of the drug shortage problem and formulates a multi-layered approach to addressing it.

Part I of the Article describes the drug shortage problem. Part II analyzes the causes of the shortage crisis, including manufacturing difficulties, unanticipated demand, producers' economic calculations, and regulatory policies with unintended consequences. Part III explores the very serious impact that drug scarcity has on patients and health care providers.

Part IV argues that drug shortages result from a combination of market failures and regulatory constraints. However, because of the specialized nature of the health care market and the low price responsiveness that characterizes it, the problem cannot be fixed by the market alone without government involvement. The drug scarcity crisis should be considered a serious public health threat that requires vigorous government intervention under federal public health powers.

Part V assesses a large number of recommendations that have been offered by industry, government, and academic experts. While some suggestions are ill-advised,

* Professor of Law and Bioethics, Co-Director of Law-Medicine Center, Case Western Reserve University School of Law; B.A., Wellesley College; J.D., Harvard Law School; LL.M. in Health Law, University of Houston.

¹ Transcript of Food and Drug Administration Center for Drug Evaluation and Research Drug Shortage Workshop, September 26, 2011 [hereinafter FDA Workshop].

² Gardiner Harris, *F.D.A. Is Finding Attention Drugs in Short Supply*, N. Y. TIMES, Jan. 1, 2012, at A1.

³ Roni Caryn Rabin, *Drug Scarcity's Dire Cost, and Some Ways to Cope*, N.Y. TIMES, Dec. 13, 2011, at D1.

a selection of others should be adopted. The Article posits that public health policies and standards must serve multiple roles. They should deter both carelessness that leads to product contamination and strategic decisions to discontinue or suspend manufacturing when such decisions will cause shortages. At the same time, governmental rules should encourage production of vulnerable drugs. Accordingly, the Article proposes a blend of legislative, regulatory, and private-sector interventions that should realign manufacturers' incentives and significantly diminish the drug shortage phenomenon.

I. THE DRUG SHORTAGE PROBLEM

Serious drug shortages first emerged in 1999.⁴ The FDA defines drug shortages as occurring "when the total supply of all clinically interchangeable versions of a FDA-regulated drug is inadequate to meet the current or projected demand at the patient level."⁵ The problem has become increasingly acute in recent years.⁶ In 2005 there were 61 reported drug shortages.⁷ In 2010, the number increased to 178.⁸ Medical products other than drugs, such as biologics⁹ and devices, have also been subject to shortages but have garnered less attention from the media and policy-makers.¹⁰

Statistics may vary depending upon the focus of particular studies.¹¹ For example, the American Society of Health-System Pharmacists (ASHP) takes into account all instances in 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."¹² The Food and Drug Administration (FDA) focuses more narrowly on medically necessary drugs that are "used to treat or prevent a serious disease or medical condition ... [for which] there is no other

⁴ FDA Workshop, *supra* note 1, at 20.

⁵ CDER MANUAL OF POLICIES AND PROCEDURES MAPP 6003.1 at 2 (2006), available at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualsPoliciesProcedures/UCM079936.pdf>; *Prescription Drug Shortages: Examining a Public Health Concern and Potential Solutions*, Statement of Sandra Kweder, M.D. Before the Committee on Health, Education, Labor and Pensions, United States Senate, December 15, 2011, at <http://www.fda.gov/NewsEvents/Testimony/ucm282956.htm> [hereinafter Kweder Statement]. Dr. Kweder is the Deputy Director of the FDA's Office of New Drugs Center for Drug Evaluation and Research.

⁶ Kevin Haninger et al., *Economic Analysis of the Causes of Drug Shortages* 3 (Oct. 2011), available at <http://aspe.hhs.gov/sp/reports/2011/drugshortages/lib.pdf>; Joseph M. Hill & Cynthia Reilly, *Can the United States Ensure an Adequate Supply of Critical Medications?* 1 FDLI'S FOOD & DRUG POL'Y FORUM 1, 1 (August 24, 2011), available at <http://www.fdl.org/pubs/policyforum/> (noting that "the number of shortages has nearly tripled since 2006" and that the number of shortages in 2011 was expected to be larger than the 2010 figure).

⁷ U.S. Food and Drug Administration, *A Review of FDA's Approach to Medical Product Shortages* 3 (October 31, 2011) [hereinafter FDA Review], available at <http://www.fda.gov/downloads/AboutFDA/manuals/forms/reports/ucm277755.pdf>.

⁸ *Id.*; Jacelyn Kaiser, *Shortages of Cancer Drugs Put Patients, Trials at Risk*, 332 SCIENCE 523, 523 (2011) (noting that shortages "have tripled since 2006").

⁹ See U.S. Food and Drug Administration, *Biologic Product Shortages*, at <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Shortages/default.htm>. Biologics, unlike drugs are "derived from living sources (such as humans, animals, and microorganisms)" and include "blood, vaccines, allergens, tissues, and cellular and gene therapies." U.S. Food and Drug Administration, *About CBER*, at <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm123349.htm>.

¹⁰ FDA Workshop, *supra* note 1, at 41; C. Lee Ventola, *The Drug Shortage Crisis in the United States: Causes, Impact, and Management Strategies*, 36 P & T 740, 741 (2011) (indicating that the U.S. has suffered from shortages of medical supplies).

¹¹ *Id.* (explaining why the University of Utah's statistics are different from the FDA's).

¹² Erin R. Fox et al., *ASHP Guidelines on Managing Drug Product Shortages in Hospitals and Health Systems*, 66 AM. J. HEALTH-SYST. PHARM. 1399, 1400 (2009).

available source of that product or alternative drug that is judged by medical staff to be an adequate substitute.¹³ Thus, while the FDA identified 178 drug shortages in 2010, the ASHP reported the number as 211.¹⁴ Furthermore, according to the ASHP, as of September 2011, there had already been 210 medical product shortages in 2011.¹⁵

Certain drugs have been more vulnerable to shortages than others. When the FDA studied 127 drug shortages that were of long duration and had significant public health implications, it found that sterile injectables accounted for eighty percent of them.¹⁶ The three most common classes of drugs in shortage were “oncology drugs (28%), antibiotics (13%), and electrolyte/nutrition drugs (11%).”¹⁷ Many commentators have decried the alarming dearth of some chemotherapy drugs in recent years.¹⁸ Others have noted that heart drugs, pain medications, attention deficit hyperactivity disorder therapies, and anesthesia agents, have been in short supply as well.¹⁹

A recent survey found that forty-seven percent of hospitals with four-hundred or more beds experienced over thirty drug shortages in 2010.²⁰ Fifty percent of respondents were affected by seven drug shortages, and three shortages affected over eighty percent of respondents.²¹ Only one percent of respondents (four institutions) indicated that they were unaffected by drug shortages in 2010.²²

A second survey of 311 pharmacy experts from 228 hospitals and other health-care facilities, conducted by Premier Healthcare Alliance, yielded equally startling results.²³ Focusing on the period of July-December 2010, it found the following:

- 89 percent [of pharmacy experts] experienced shortages that may have caused a medication safety issue or error in patient care.
- 53 percent suggested occurrence 6+ times.

¹³ Fox et al., *supra* note 12 at 1405; U.S. Food and Drug Administration, *FDA and Manufacturers Work to Prevent Drug Shortages*, at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm257746.htm>.

¹⁴ Ventola, *supra* note 10, at 740.

¹⁵ *Id.*; FDA Workshop, *supra* note 1, at 42.

¹⁶ FDA Review, *supra* note 7, at 4.

¹⁷ *Id.*

¹⁸ Haninger et al., *supra* note 6, at 1; Mandy L. Gatesman & Thomas J. Smith, *The Shortage of Essential Chemotherapy Drugs in the United States*, 365 N. ENGL. J. MED. 1653, 1653 (2011); Steven Reinberg, *Cancer Drug Shortages Getting Worse, FDA Says*, HEALTHDAY (August 24, 2011), available at <http://yourlife.usatoday.com/health/story/2011-08-28/Cancer-drug-shortages-getting-worse-FDA-says/50148996/1>.

¹⁹ Ventola, *supra* note 10, at 740 (listing heart drugs, pain medications, intravenous electrolytes, leucovorin, propofol, morphine, hydromorphone, furosemide, amino acids, and technetium-99m); Valerie Jensen & Bob A. Rappaport, *The Reality of Drug Shortages – The Case of the Injectable Agent Propofol*, 363 N. ENGL. J. MED. 806, 806 (2010) (discussing the critical shortage of propofol, “a fast-onset, short-acting sedative-hypnotic agent used for the induction and maintenance of anesthesia or sedation.”); Hill & Reilly, *supra* note 6, at 1 (listing “anti-cancer drugs, anesthetics, and nutritional therapies”); Harris, *supra* note 2, at A1 (discussing the shortage of generic drugs to treat attention deficit hyperactivity disorder); Bruce A. Chabner, *Drug Shortages – A Critical Challenge for the Generic-Drug Market*, 365 N. ENGL. J. MED. 2147, 2147–48 (2011) (“The list of generic drugs in short supply across all medical specialties is astounding and includes antibiotics, anesthetic agents, antihypertensive medications, and common electrolyte solutions and vitamins.”).

²⁰ Rola Kaakeh et al., *Impact of Drug Shortages on U.S. Health Systems*, 68 AM. J. HEALTH-SYST. PHARM. 1811, 1814 (2011). The survey was completed by 353 directors of pharmacy. *Id.* at 1811.

²¹ *Id.* at 1815.

²² *Id.*

²³ Coleen Cherici et al., *Navigating Drug Shortages in American Healthcare: A Premier Healthcare Alliance Analysis 3* (March 2011), available at <http://www.premierinc.com/about/news/11-mar/drug-shortage-white-paper-3-28-11.pdf> (surveying pharmacy experts from hospitals as well as “infusion, oncology and surgery centers; outpatient and retail pharmacies; and long-term care facilities”).

- 80 percent experienced shortages that resulted in a delay or cancellation of a patient care intervention.
 - 34 percent suggested occurrence 6+ times.
- 98 percent experienced shortages that resulted in an increase in costs.
 - 88 percent suggested occurrence 6+ times.
 - 41 percent suggested occurrence 21+ times.²⁴

The drug shortage phenomenon is serious and pervasive. It is becoming an inescapable reality for many health care providers and millions of American patients.

II. CAUSES OF DRUG SHORTAGES

Numerous factors explain the medical product shortage phenomenon. According to the University of Utah Drug Information Service, 23% of shortages are caused by manufacturing problems, 13% are rooted in supply and demand changes, 6% occur because manufacturers discontinue production, 3% result from the unavailability of raw materials, and 55% of shortages are of unknown origin.²⁵ Information about drug shortage causes is often lacking because the FDA is not authorized to require manufacturers to explain shortages and must rely on voluntary reporting.²⁶ This Part will loosely classify the causes of drug shortages as: manufacturing difficulties, unanticipated demand, manufacturers' economic calculations, and regulatory policies with unintended consequences.

A. Manufacturing Hurdles

Some manufacturers suffer disruptions stemming from the unavailability of raw or bulk materials.²⁷ According to one estimate, the U.S. imports approximately eighty percent of raw materials used in pharmaceutical products.²⁸ Consequently, supplies can be impacted by a variety of occurrences abroad, such as armed conflict, political unrest, animal diseases, and adverse environmental conditions.²⁹ American manufacturers can also experience difficulties at their U.S. facilities because of faulty equipment or human errors that lead to production delays, voluntary recalls, or FDA enforcement actions.³⁰ In the past, for example, injectables were found to contain contaminants such as glass shards, metal filings, and fungus, and these impurities ultimately led to shortages.³¹

Natural disasters both within and outside of the United States can also affect product availability. Hurricanes, earthquakes, floods, and other catastrophes can

²⁴ *Id.*

²⁵ Ventola, *supra* note 10, at 741; Erin R. Fox, *Drug Shortage Update Current Status & Significant Trends*, at <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM274565.pdf>.

²⁶ U.S. Food and Drug Administration, *Current Drug Shortages*, at <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm>.

²⁷ Fox et al., *supra* note 12, at 1400; FDA Review, *supra* note 7, at 4 (indicating that "active pharmaceutical ingredient shortages" accounted for 10% of reported shortages).

²⁸ Fox et al., *supra* note 12, at 1400.

²⁹ *Id.*

³⁰ Fox et al., *supra* note 12, at 1400; FDA Review, *supra* note 7, at 4 (indicating that "problems at the manufacturing facility" accounted for 43% of reported shortages); Robert Steinbrook, *Drug Shortages and Public Health*, 361 N. ENGL. J. MED. 1525, 1525 (2009) (discussing the "viral contamination of a Genzyme Manufacturing plant in Massachusetts" that caused shortages of drugs for Gaucher's disease and Fabry's disease).

³¹ FDA Review, *supra* note 7, at 4.

damage production facilities, causing temporary or permanent shut-downs. Increased need for particular drugs in order to treat disaster victims in one location can also lead to scarcity in other regions.³² For example, drug shortages occurred in the aftermaths of the 1998 hurricane George that hit manufacturing facilities in Puerto Rico and the 2005 hurricanes Katrina and Rita.³³

If a manufacturer is one of only a few suppliers or the primary supplier, even a temporary suspension of production can have a devastating market effect. Unfortunately, some segments of the pharmaceutical market are not characterized by robust competition. For example, the top three manufacturers of generic injectables produce seventy-one percent of product volume, and commonly, a single manufacturer produces ninety percent or more of an individual sterile injectable drug.³⁴ Many vaccines in the U.S. are manufactured by only one source.³⁵ In some cases, mergers within the industry shrink the number of suppliers,³⁶ as do small profit margins, discussed in more detail below.³⁷

B. *Unanticipated Demand*

Demand can increase unexpectedly because of new usage recommendations made by government authorities or by other experts who generate clinical practice guidelines.³⁸ A pediatric flu vaccine shortage in 2006 resulted from the Centers for Disease Control and Prevention's new recommendation that children as young as 6 months be vaccinated.³⁹ Disease outbreaks may also raise demand unexpectedly and thus generate shortages.⁴⁰

Flexibility to meet demand changes is often limited because suppliers engage in "just-in-time" production and inventory practices that may exacerbate shortages.⁴¹ Limiting supply to meet only anticipated demand reduces vendors' storage costs and manufacturers' risk of being left with unsold product. However, "just in time" practices leave no surplus to create a cushion in case of shortages.⁴²

C. *Economic Calculations*

At times, manufacturers reduce or discontinue production because a medical product is not lucrative enough. Sterile injectable drugs are complicated to manufacture and often require dedicated manufacturing lines.⁴³ Consequently, companies at times conclude that manufacturing such drugs requires them to absorb excessive financial and opportunity costs and decide to abandon the product line.

³² Fox et al., *supra* note 12, at 1402; Ventola, *supra* note 10, at 742.

³³ Ventola, *supra* note 10, at 742.

³⁴ FDA Review, *supra* note 7, at 4; *see also*, Kwyder Statement, *supra* note 5 (stating that "[i]n 2010, the top five generic sterile injectable manufacturers accounted for 80 percent of the sterile injectables sold in the U.S. market by volume.").

³⁵ Fox et al., note 24, at 1401.

³⁶ *Id.*; Valerie Jensen et al., *FDA's Role in Responding to Drug Shortages*, 59 AM. J. HEALTH-SYST. PHARM. 1423, 1424 (2002).

³⁷ *See infra* Part II.C.

³⁸ Fox et al., *supra* note 12, at 1401.

³⁹ Ventola, *supra* note 10, at 742.

⁴⁰ *Id.*

⁴¹ *Id.*

⁴² *Id.*; FDA Review, *supra* note 7, at 4; Hill & Reilly, *supra* note 6, at 2.

⁴³ FDA Review, *supra* note 7, at 4.

Shortages of generic injectables have been particularly common, and this phenomenon has been attributable to high manufacturing costs and low profit margins.⁴⁴ For example, in 2008, the FDA approved the oncology drug levoleucovorin. The medication was no more effective than its generic form, leucovorin, and was fifty-eight times as expensive, but its use became increasingly widespread.⁴⁵ A shortage of the less costly leucovorin was reported eight months after the brand-name's approval because manufacturers were no longer interested in producing it.⁴⁶ Similarly, in 2000, several vaccines, including those against diphtheria and tetanus, were in shortage because a manufacturer with low revenues discontinued production.⁴⁷

Patent expiration has also been identified as a noteworthy cause of recent shortages.⁴⁸ Since 2008, a large number of chemotherapy patents have expired.⁴⁹ When a drug's patent expires and generic drugs or other competing medications become available, the drug's price is likely to decrease. Lower revenues can drive manufacturers to change course and invest their resources in more profitable products.⁵⁰

Manufacturers of generic drugs may prefer to sell their goods abroad in order to earn greater profits.⁵¹ In Europe, for example, generic drugs are sold at higher prices than in the U.S.⁵² Manufacturers' diversion of supplies to foreign countries further contributes to shortages in the U.S.

In the health care market, manufacturers are constrained in their ability to employ traditional techniques to reduce demand, increase profits, or quickly bolster supplies. The market is characterized by low "price responsiveness."⁵³ Producers of goods and services in other industries who wish to curtail supplies can diminish consumer demand by raising prices.⁵⁴ By contrast, patient demand is often unaffected by price changes because medically necessary drugs are critical to patients' welfare or even survival. Moreover, suppliers are often powerless to raise prices in the short term because health insurers typically pre-negotiate reimbursement rates so that suppliers cannot alter prices during the contract term.⁵⁵

At the same time, when demand rises in light of changed practice guidelines, manufacturers cannot always quickly increase supply because of the rigorous industry and regulatory standards that manufacturers must meet.⁵⁶ The need for costly specialized equipment and complicated production processes may thwart quick acceleration of production, and new alternative products can take years to move through the clinical testing and FDA approval process.⁵⁷ In addition, manufacturers are often loath to build excess production capacity, also known as "redundancy," in order to meet unanticipated demand increases, because doing so is costly and

⁴⁴ Hill & Reilly, *supra* note 6, at 4; Ventola, *supra* note 10, at 742.

⁴⁵ Gatesman & Smith, *supra* note 18, at 1653-54.

⁴⁶ *Id.*

⁴⁷ Ventola, *supra* note 10, at 742.

⁴⁸ Jensen & Rappaport, *supra* note 19, at 806.

⁴⁹ Haninger et al., *supra* note 6, at 1.

⁵⁰ Jensen & Rappaport, *supra* note 19, at 806.

⁵¹ Chabner, *supra* note 19, at 2149.

⁵² Gatesman & Smith, *supra* note 18, at 1655.

⁵³ Haninger et al., *supra* note 6, at 3-4.

⁵⁴ *Id.* See *supra* note 13 and accompanying text for definition of medically necessary products.

⁵⁵ Haninger et al., *supra* note 6, at 4.

⁵⁶ *Id.*

⁵⁷ U.S. Department of Health & Human Services, *Statement by Sherry Glied Ph.D. Assistant Secretary for Planning and Evaluation U.S. Department of Health and Human Services (HHS) on Prescription Drug Shortages: Examining a Public Health Concern and Potential Solutions before Committee on Health, Education, Labor and Pensions United States Senate* (December 15, 2011), at <http://www.hhs.gov/asl/testify/2011/12/20111215c.html> [hereinafter Glied Statement].

earnings are speculative. Manufacturers prefer to invest their resources in producing therapies for which there is existing demand and that are likely to generate more immediate and certain profits.⁵⁸

D. Unintended Consequences of Regulatory Policies

Ironically, federal regulatory agencies also have a hand in contributing to shortages. The Drug Enforcement Administration (DEA) sets quotas for the manufacturing of particular drugs in order to control supplies and combat drug abuse.⁵⁹ For example, the DEA subjects manufacturers of ADHD drugs to quotas because of concern that these drugs will be abused by non-disabled students seeking to enhance their concentration or by individuals who find that the medications' effect is a cocaine-like high.⁶⁰ Manufacturers who are constrained by a quota may opt to produce a large amount of more expensive, higher-profit ADHD pills, and consequently produce too few of their cheaper, generic counterparts that are often favored by patients.⁶¹

The FDA's Unapproved Drug Initiative, launched in 2006, also created incentives for some generic drug manufacturers to discontinue production. The initiative targets drugs that were introduced to the market before the FDA obtained drug approval authority in 1938 and aims to subject them to scrutiny under a formal approval process.⁶² Because filing a New Drug Application can be a time-consuming and burdensome process, some manufacturers may opt to cease production of these older, often generic drugs rather than seek FDA approval.⁶³

The Medicare reimbursement structure is an additional cause of shortages of chemotherapy agents because it incentivizes physicians to administer costly brand-name drugs rather than generics.⁶⁴ Under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), oncologist reimbursement is set at the average sales price paid during the preceding two quarters plus six percent.⁶⁵ Physicians who choose more expensive drugs thus receive a higher dollar amount than those who choose generics. To illustrate, six percent of Abraxane, whose price is \$5,824, will yield a much higher payment for an oncologist than six percent of paclitaxel, which sells for \$312.⁶⁶ Lower demand for a generic chemotherapy drug may motivate manufacturers to abandon production so that patients and physicians who prefer the generic are unable to obtain it.

A Department of Health and Human Services study that reviewed Medicare Part B volume of service data confirmed the association between sale volumes and shortages. It found that 44 drugs with declining sales in 2006-2008 were in

⁵⁸ Haninger et al., *supra* note 6, at 4.

⁵⁹ Hill & Reilly, *supra* note 6, at 4.

⁶⁰ Harris, *supra* note 2, at A17.

⁶¹ *Id.*

⁶² U.S. Food and Drug Administration, *Unapproved Drugs Initiative*, at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/ucm118990.htm>; Ventola, *supra* note 10, at 749.

⁶³ Ventola, *supra* note 10, at 749; Cherici et al., *supra* note 23, at 2.

⁶⁴ Gatesman & Smith, *supra* note 18, at 1654.

⁶⁵ *Id.*; Mireille Jacobson et al., *How Medicare's Payment Cuts for Cancer Chemotherapy Drugs Changed Patterns of Treatment*, 29 HEALTH AFF. 1391, 1392 (2010); Centers for Medicare and Medicaid Services, *2012 ASP Drug Pricing Files*, at https://www.cms.gov/McrPartBDrugAvgSalesPrice/01a17_2012ASPFiles.asp (stating that payment amounts "are 106 percent of the Average Sales Price (ASP) calculated from data submitted by drug manufacturers" with "quarter to quarter price changes").

⁶⁶ Gatesman & Smith, *supra* note 18, at 1654.

shortage in subsequent years, and 28 drugs with increased sales in 2006-2008 were never involved in a shortage.⁶⁷ The study also found that the prices of the 44 drugs in shortage had steadily decreased, while the prices of the 28 drugs whose supply was adequate did not change significantly.⁶⁸

III. IMPACT OF DRUG SHORTAGES

Drug shortages can have devastating consequences for patients and health care providers. They can endanger patients, significantly increase health care expenditures, and imperil medical research, among other consequences.

A. Poor Treatment Outcomes

Drug shortages often endanger the lives of patients. When health care providers cannot obtain needed drugs, they must ration care, delay treatment, and cancel procedures.⁶⁹ Cancer patients may have to be triaged so that those with the best prognosis are given priority for scarce chemotherapy drugs, and others do not receive the medication of choice and may not survive.⁷⁰

In September of 2011, the FDA held a Drug Shortage Workshop.⁷¹ Michael Cohen of the Institute for Safe Medication Practices described an instance in which a patient died because he could not obtain Amikacin to treat an infection that was resistant to other antibiotics.⁷² Mr. Cohen also noted nine deaths that occurred in Alabama because patients were given parenteral nutrition infusions that were contaminated with bacteria when a pharmacy facing a shortage used an unfamiliar ingredient.⁷³ He further stated that patients have awakened during surgery because their anesthesiologists were forced to use agents to which they were unaccustomed.⁷⁴ Other speakers recounted additional problems resulting from anesthetic substitutions, including longer recovery periods, agitation, delirium, and more frequent post-operative nausea and vomiting.⁷⁵

Thus, even when clinicians find adequate substitutes, drug shortages can lead to poor treatment outcomes or medical errors.⁷⁶ In one survey, twenty-five percent of respondents indicated that an error had occurred at their facility because of a shortage.⁷⁷ Clinicians who are inexperienced with an alternative product may administer it incorrectly or provide a patient with the wrong dosage.⁷⁸

⁶⁷ Haninger et al., *supra* note 6, at 7-8.

⁶⁸ *Id.* at 8.

⁶⁹ Ventola, *supra* note 10, at 750.

⁷⁰ *Id.* at 750-51; Susan Jenks, *Efforts Underway to Curb Drug Shortages*, 103 J. NAT'L CANCER INST. 914, 914 (2011) ("In recent weeks, shortages in cytarabine injections raised the specter ... of denying leukemia patients a chemotherapy drug carrying their best hope for survival").

⁷¹ FDA Workshop, *supra* note 1.

⁷² *Id.* at 110.

⁷³ *Id.* at 115. Parenteral nutrition is given intravenously using customized, sterile formulas and a central IV line when a patient cannot eat and digest normally. *Id.* at 88-89. See also, Ventola, *supra* note 10, at 751 (describing the same incident).

⁷⁴ FDA Workshop, *supra* note 1, at 110.

⁷⁵ *Id.* at 142, 248.

⁷⁶ Maryn McKenna, *Hospital Pharmacists Scrambling Amid Vast Drug Shortages*, 57 ANNALS OF EMERGENCY MED. 13A, 13A-14A (2011) (describing medical errors including "a 20-fold overdose of dexmedetomidine because the staff were not familiar with dosing for the alternative drug").

⁷⁷ Gatesman & Smith, *supra* note 18, at 1653.

⁷⁸ *Id.*

At the FDA Workshop, several patients provided poignant accounts of their personal encounters with drug shortages.⁷⁹ Jay Cuetara, a cancer patient, described his reaction when he learned that he would not be able to receive chemotherapy as scheduled because injectable 5-FU was unavailable: "At that point, I was dumb-founded. The question I then asked myself was how in the United States of America could critical lifesaving or life-prolonging drugs be in short supply?" Sarah Bataka, a muscular dystrophy patient who requires intravenous electrolytes recalled suffering extreme anxiety when she learned of an imminent shortage:

In April of this year, I got the worst possible news. I was told by my home infusion pharmacy that their supply of IV magnesium sulfate, a key ingredient in my IV bags and one without [which] I cannot survive, was dwindling and that they only had enough to fill my IV bags for a few more week[s]. To give you some idea of the impact this news had on [sic] me, please consider what it would feel like to you if someone told you there would only be enough air supply left for you for three weeks of breathing.⁸⁰

The number of deaths associated with drug shortages has not been tracked.⁸¹ The figure would be difficult to determine because of uncertainty as to whether particular patients died of their underlying disease or because of departures from standard therapy.⁸² There is no doubt, however, that drug shortages are significantly impacting treatment outcomes and costing patient lives.

B. Increased Healthcare Costs

A recent survey that was sent to health system pharmacy directors attempted to quantify the cost of drug shortages.⁸³ The survey found that the estimated annual labor cost associated with drug shortages was \$216 million.⁸⁴ Pharmacists and pharmacy technicians spent eight or nine hours a week managing drug shortages by gathering, communicating, and processing information; identifying alternatives; and managing inventory.⁸⁵ According to Scott Knoer, the Chief Pharmacy Officer of the Cleveland Clinic, the Clinic employs a full-time pharmacist for the sole purpose of addressing drug shortages and recalls.⁸⁶

In response to drug shortages, some vendors engage in the creation of "gray markets" and price gouging.⁸⁷ Distributors buy up the remaining supply of a product and then sell it to health care providers at ten to one-thousand times the ordinary price.⁸⁸ According to one source, in the case of cancer drugs, gray market vendors have charged markups of up to 3000%.⁸⁹

⁷⁹ *Id.* at 83-101.

⁸⁰ *Id.* at 103. Fortunately, the patient's pharmacy was able to obtain additional supplies of IV magnesium sulfate, which she was still receiving at the time of her testimony. However, the patient remained concerned about how she would fare in the future. *Id.* at 105.

⁸¹ Ventola, *supra* note 10, at 751.

⁸² *Id.*; Jenks, *supra* note 62, at 914.

⁸³ Kaukeh et al., *supra* note 20, at 1812.

⁸⁴ *Id.* at 1814.

⁸⁵ *Id.*

⁸⁶ FDA Workshop, *supra* note 1, at 329.

⁸⁷ Fox et al., *supra* note 12, at 1401.

⁸⁸ Ventola, *supra* note 10, at 750.

⁸⁹ Gatesman & Smith, *supra* note 18, at 1653. *See also*, FDA Workshop, *supra* note 1, at 265 (describing a markup of 4,500 percent in which a blood pressure medication that is normally priced at \$25.90 was offered for \$1200).

The pharmacy directors' survey estimated that U.S. hospitals spent at least \$200 million on the purchase of more costly alternatives when supplies of cheaper drugs dwindled.⁹⁰ These costs are likely attributable both to the replacement of generic drugs with brand-name medications and to gray market markups. Thus, drug shortages are estimated to cost U.S. hospitals a combined total of over \$415 million annually.⁹¹

C. Adverse Impact on Medical Research

Drug shortages can compromise the integrity of clinical trials and other research endeavors. The success of clinical studies depends on careful compliance with research protocols. Unavailability of study drugs can cause enrollment to be postponed, research projects to be suspended or canceled, or research outcomes to be skewed.⁹² Reportedly, adult and pediatric cancer studies are in fact being hindered by drug shortages.⁹³

Also at issue is comparative effectiveness research (CER), which has been promoted in recent federal legislation.⁹⁴ In 2009, Congress allocated \$1.1 billion in funding for CER, as part of the American Reinvestment and Recovery Act.⁹⁵ The Patient Protection and Affordable Care Act of 2010 (PPACA) embraced CER as an important health care reform initiative and established the Patient-Centered Outcomes Research Institute to oversee CER in the United States.⁹⁶ CER is defined as "research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of 2 or more medical treatments, services, and items...."⁹⁷ The goal of such research is to generate improved patient outcomes while maximizing the value derived from health care expenditures. CER, however, will be unproductive if the research is hindered by shortages or if manufacturers opt to discontinue production of drugs that are found to be both effective and inexpensive because suppliers seek a larger profit margin.

D. Other Consequences

Drug shortages have further implications for physicians and patients. Doctors face the unenviable task of having to explain to patients that they cannot provide them with a needed drug or must replace a drug that has previously worked well. Patients may consequently lose trust in their doctors or switch to different practices.⁹⁸ In other cases, facilities may have to turn new patients away because they do not have enough medication to treat their existing patients and, therefore, cannot accept additional ones.

⁹⁰ Cherici et al., *supra* note 23, at 7.

⁹¹ FDA Workshop, *supra* note 1, at 264.

⁹² *Id.* at 752; Kaiser, *supra* note 8, at 523 ("Shortages can also complicate clinical trials").

⁹³ FDA Workshop, *supra* note 1, at 123; Kweder statement, *supra* note 5.

⁹⁴ Sherona Hoffman & Andy Podgurski, *Improving Health Care Outcomes through Personalized Comparisons of Treatment Effectiveness Based on Electronic Health Records*, 39 J. L. MED. & ETHICS 425, 425 (2011).

⁹⁵ American Recovery and Reinvestment Act of 2009, tit. VIII, Pub. L. No. 111-5, 123 Stat. 115, 177-78 (2009).

⁹⁶ Patient Protection and Affordable Care Act of 2010, Pub. L. No. 111-148, §6301, 124 Stat. 119 (2010), codified at 42 U.S.C. § 1320e (2006).

⁹⁷ 42 U.S.C. §1320e(a)(2)(A) (2006).

⁹⁸ Ventola, *supra* note 10, at 752 (discussing strained professional relationships).

Additionally, insurers may refuse to cover a treatment that has been substituted for a drug in shortage because the alternate medication does not constitute standard therapy.⁹⁹ For patients who cannot pay out-of-pocket, an insurer's unfavorable decision can be a death sentence.

IV. DRUG SHORTAGES AS A PUBLIC HEALTH CRISIS

The drug shortage crisis is rooted in a combination of market failures and regulatory constraints. The problem cannot be corrected without governmental intervention, which would be justified by federal public health powers and a long history of federal initiatives to address serious public health threats.

A. *Regulatory Constraints and Market Failures*

Drug shortages arise because of both market failures and regulatory failures. First, government regulations in several arenas may inadvertently contribute to shortages. The FDA's thorough drug approval process and enforcement actions in response to manufacturing problems that endanger patients can delay, slow, or suspend production.¹⁰⁰ The Medicare reimbursement scheme has also been blamed by many commentators for skewing drug purchasing incentives in ways that lead to shortages of less costly generic medications.¹⁰¹ DEA quotas for controlled substances may further exacerbate the scarcity problem.¹⁰²

Much of the drug shortage crisis, however, is due to the limits of government involvement rather than to its excesses. The FDA cannot require manufacturers to produce drugs that are in short supply.¹⁰³ Thus, it cannot stop drug manufacturers from making decisions in their own best interest even when these conflict with patients' interests. Because cheaper generic drugs are not necessarily the least expensive drugs to produce,¹⁰⁴ manufacturers at times opt to minimize or discontinue production when generics do not generate sufficient income. Such decisions can be made despite robust demand for the products on the part of clinicians and patients.

Furthermore, the health care market is relatively inflexible and constrained in its ability to react effectively to supply and demand changes. Inadequate supplies do not necessarily reduce demand for drugs because patients cannot control what illnesses they suffer and what treatments they require. Manufacturers are also often powerless to raise prices in order to influence demand because of pre-negotiated terms with private and public insurers.¹⁰⁵ New manufacturers cannot quickly enter the market to increase supply because of strict regulatory requirements.¹⁰⁶ Finally, clinicians often cannot find equally effective alternatives because some drugs are produced by a single source, or substitutes have unacceptable side-effects for particular patients.¹⁰⁷

⁹⁹ FDA Workshop, *supra* note 1, at 248.

¹⁰⁰ See U.S. Food and Drug Administration, *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective*, at <http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm>.

¹⁰¹ See *supra* notes 58-60 and accompanying text.

¹⁰² See *supra* note 53-55 and accompanying text.

¹⁰³ Ventola, *supra* note 10, at 752; Jensen & Rappaport, *supra* note 19, at 807.

¹⁰⁴ See *supra* note 39 and accompanying text.

¹⁰⁵ See *supra* note 49 and accompanying text.

¹⁰⁶ U.S. Food and Drug Administration, *supra* note 91.

¹⁰⁷ See *supra* note 30 and accompanying text; FDA Workshop, *supra* note 1, at 82-87 (providing an account of a patient who suffered excruciating side effects from a substitute chemotherapy agent).

The unique nature of the health care market often makes it impossible for industry to rectify market problems through traditional supply and demand mechanisms and without the support of government involvement. In addition, the safety-critical nature of most medical treatments makes regulatory oversight vital to public health and welfare.

B. *Public Health Powers*

The federal government has considerable authority to address public health concerns.¹⁰⁸ Under Article 1, Section 8 of the Constitution, the federal government has the power to tax, spend, and regulate commerce among the various states.¹⁰⁹ Taxes and tax credits may be used as incentives to promote public health goals.¹¹⁰ Budget resources are routinely allocated to benefit public health.¹¹¹ And the government, through regulatory measures, oversees numerous private sector activities that affect public health.¹¹² The production and marketing of drugs and medical devices has been subject to rigorous federal regulation for nearly seventy-five years under the Food, Drug, and Cosmetics Act of 1938 (FDCA).¹¹³

The federal government has undertaken extensive initiatives in the area of public health emergencies.¹¹⁴ It has enacted numerous laws designed to facilitate disaster response activities and minimize casualties. Examples are the Emergency Management Assistance Compact,¹¹⁵ Section 1135 of the Social Security Act,¹¹⁶ the Public Readiness and Emergency Preparedness Act,¹¹⁷ and the Project BioShield Act of 2004.¹¹⁸ The drug shortage crisis can be compared to a public health emergency because of its large-scale public health implications. None of the traditional emergency preparedness laws would be applicable because they are generally tailored to natural disasters and pandemics.¹¹⁹ Nevertheless, these laws set important precedents for vigorous government action to address public health threats.

C. *Initial Public Health Responses to Shortages*

The federal government has not adopted a hands-off approach to drug shortages. The FDA has made the most of its existing powers and implemented several response measures. In addition, President Obama issued an executive order urging

¹⁰⁸ LAWRENCE O. GOSTIN, *PUBLIC HEALTH LAW: POWER, DUTY, RESTRAINT* 35 (2000)

¹⁰⁹ U.S. CONST. art. 1, §8, cl. 1, 3.

¹¹⁰ GOSTIN, *supra* note 99, at 35-38.

¹¹¹ *Id.* at 38-40.

¹¹² *Id.* at 35, 40-41.

¹¹³ 21 U.S.C. §§ 301-399 (2006).

¹¹⁴ Sharona Hoffman, *Responders' Responsibility: Liability and Immunity in Public Health Emergencies*, 96 *Geo. L. J.* 1941-46 (2008).

¹¹⁵ H.R.J. Res. 193, 104th Cong., §, 110 Stat. 3877 (1996) (establishing a mutual aid agreement that has been enacted by all states that is triggered by a governor's declaration of emergency and request for assistance).

¹¹⁶ Pub. L. No. 107-188, § 143(a), 116 Stat. 594, 627-29 (2002) (codified at 42 U.S.C. § 1320b-5 (2006) (authorizing the Secretary of Health and Human Services to waive or modify certain legal requirements that apply to health care providers furnishing goods and services in an emergency area).

¹¹⁷ 42 U.S.C.A. § 247d-6d (2006) (addressing immunity from liability relating to the administration and use of covered emergency countermeasures).

¹¹⁸ Pub. L. No. 108-276, 118 Stat. 835 (2004) (codified at 42 U.S.C.A. § 247d-6a (2006 & West Supp. 2011) (providing that during a declared emergency, the Secretary of Health and Human Services may authorize the emergency use of a product that is not yet "approved, licensed, or cleared for commercial distribution").

¹¹⁹ See Hoffman, *supra* note 106, at 1922, 1941-42, and 1945-46.

federal authorities to stretch their existing powers to their limits. These measures are effective first steps, but they are inadequate to fully resolve the crisis.

The FDA asserts that it helped prevent thirty-eight shortages in 2010 and ninety-nine shortages as of October 31, 2011.¹²⁰ In order to decrease the number of future shortages or end current ones quickly, the FDA has expedited its review of submissions related to new manufacturing sites, suppliers, and specification changes.¹²¹ The FDA also urged companies to increase production and worked with manufacturers to mitigate the dangers of safety problems.¹²² For example, when a manufacturing change led to the formation of crystals in vials of cytarabine, the FDA worked with the manufacturer to discover that the crystals could be dissolved through warming and permitted manufacturers to ship the product with special instructions for clinicians.¹²³ When foreign particles were found in sodium phosphate, an electrolyte used in IV nutrition therapy, the FDA verified that the contaminants could be removed with filters and permitted the supplier to ship the product so long as it provided instructions concerning the need for filtering.¹²⁴ On rare occasion, the FDA may also allow a drug or its equivalent to be imported from a foreign country until the shortage is resolved in the U.S.¹²⁵

On October 31, 2011, President Obama issued Executive Order 13588 entitled "Reducing Prescription Drug Shortages."¹²⁶ The order directed the FDA "to use all appropriate administrative tools" to require manufacturers to provide adequate notice of their intention to discontinue manufacturing drugs in cases that could result in shortages of medications that support or sustain life or "prevent debilitating disease."¹²⁷ Furthermore, the order instructed the FDA to bolster its efforts to expedite reviews of "new drug suppliers, manufacturing sites, and manufacturing changes" when such efforts may positively impact shortages.¹²⁸ Finally, President Obama directed the FDA to report to the Department of Justice (DOJ) any findings that market participants are stockpiling scarce drugs and selling them "at exorbitant prices."¹²⁹ While gray market sales are not themselves illegal, the DOJ and other regulatory authorities are to take appropriate enforcement actions against any parties found to have engaged in unlawful behavior, such as by violating antitrust laws or FDA regulations.¹³⁰

Still, national shortages persist to the great detriment of patients.¹³¹ The shortage crisis constitutes a serious public health threat that merits a much more aggressive federal government response.

V. RECOMMENDATIONS

There is no single solution that can resolve the drug shortage crisis. In partnership with industry, regulatory authorities must undertake a multi-faceted approach to

¹²⁰ FDA Review, *supra* note 7, at 4. See also, Kweder Statement, *supra* note 5 (asserting that by December 15th, the FDA had prevented 195 shortages in 2011).

¹²¹ FDA Review, *supra* note 7, at 4. See also, Jensen et al., *supra* note 32, at 1424-25.

¹²² FDA Review, *supra* note 7, at 4. See also, Jensen et al., *supra* note 32, at 1424-25.

¹²³ Kweder Statement, *supra* note 5.

¹²⁴ *Id.*

¹²⁵ Jensen et al., *supra* note 32, at 1425; Jensen & Rappaport, *supra* note 19, at 807 (noting that in response to a propofol shortage, the FDA "temporarily allowed the importation into the United States of the unapproved drug Fresenius Propoven 1%, a propofol product approved in other countries").

¹²⁶ Exec. Order No. 13,588, 76 Fed. Reg. 68295 (Nov. 3, 2011).

¹²⁷ *Id.* at § 2.

¹²⁸ *Id.* at § 3.

¹²⁹ *Id.* at § 4.

¹³⁰ *Id.*

¹³¹ See *supra* Parts I and III.

attack the problem. A blend of carrots and sticks should be used to achieve several goals: manufacturers must be incentivized to reach production levels that meet demand in the health care marketplace, and they must be deterred from intentional or negligent conduct that could lead to shortages.

This Part critiques a variety of solutions that have been proposed by industry, government, and academic experts. They include: 1) bills that would require advance notification for anticipated shortages; 2) amendment of the Hatch-Waxman Act; 3) creation of a national stockpile; 4) regulatory changes to the Medicare reimbursement system and DEA quotas; and 5) use of other financial incentives such as tax benefits, reduction in user fees, liability protection, and failure-to-supply contract clauses.

A. Legislative Mandate Requiring Advance Notification for Anticipated Shortages

In most instances, manufacturers are not required to notify the FDA of imminent shortages.¹³² Currently, the agency can require a six-month advance notification only in cases in which *sole* manufacturers of drugs that are "life-supporting," "life-sustaining," or used to prevent debilitating diseases plan to discontinue production.¹³³ In all other instances, absent voluntary reporting by industry, the FDA may remain ignorant of a shortage until it receives complaints from doctors who are grappling with it.

Proposed legislation is designed to ensure that the FDA consistently receives advance notice of all shortages that can be anticipated. The "Preserving Access to Life-Saving Medications Act of 2011" was introduced as bi-partisan legislation in 2011 by Senator Amy Klobuchar and Representative Diane DeGette.¹³⁴ The House and Senate bills would amend Section 506(c) of the FDCA.¹³⁵ They generally would require drug manufacturers to inform the FDA of known production discontinuances or disruptions six months in advance or as soon as they become aware of the possibility of a shortage if six months notice cannot be given.¹³⁶ The legislation also provides for the imposition of civil penalties on manufacturers that fail to comply with the notice requirements.¹³⁷ Furthermore, the proposed legislation instructs the FDA to do all of the following: 1) distribute information about shortages to providers and patient organizations; 2) prioritize inspection of facilities involved in the production of drugs that have been subject to shortages; 3) "implement evidence-based criteria" to identify drugs vulnerable to scarcity; and 4) collaborate with manufacturers to establish contingency plans for addressing shortages of these vulnerable drugs.¹³⁸

In order to protect manufacturers' interests, the bills establish a confidentiality mandate. They provide that disclosures concerning planned manufacturing discontinuations or interruptions will be treated as trade secrets or confidential information.¹³⁹

¹³² Jensen et al., *supra* note 32, at 1424.

¹³³ 21 U.S.C. §356c (2006).

¹³⁴ H.R. 2245, 112th Cong. (2011) and S. 296, 112th Cong. (2011) at <http://www.govtrack.us/congress/billtext.xpd?bill=h112-2245>; <http://www.govtrack.us/congress/billtext.xpd?bill=s112-296>.

¹³⁵ 21 U.S.C. §356c (2006).

¹³⁶ H.R. 2245 at §506C(b)(1)-(5); S. 296 at §2(a)(2)-(5). The bills also establish exceptions to the standard notification requirements.

¹³⁷ H.R. 2245 at §506C(b)(7); S. 296 at §2(a)(6).

¹³⁸ H.R. 2245 at §506C(c); S. 296 at §§2(d) and (3).

¹³⁹ H.R. 2245 at §506C(b)(6); S. 296 at §2(b).

The proposed legislation's future is uncertain. The Senate and House bills were referred to committee in February and June of 2011 respectively, but neither has progressed beyond that point.¹⁴⁰ Moreover, the Republican majority in the House of Representatives is unlikely to support the bill because of opposition from the pharmaceutical industry and philosophical objections to more stringent regulatory requirements.¹⁴¹

The stalled legislative process is unfortunate because the law would constitute a positive step in combating the drug shortage problem. The legislation would significantly bolster and extend President Obama's executive order, which allows the FDA only to use currently appropriate tools to induce manufacturers to disclose anticipated shortages. Absent new legislation, the FDA does not have an adequate statutory disclosure mandate at its disposal. Advance notice would enable the FDA to work with industry to find alternate manufacturers who are willing to increase supplies or commence production and to expedite review of relevant submissions to help avoid drug scarcity. The FDA could also identify alternatives and prepare informational and training materials that could be distributed to clinicians in case the shortage materializes. Finally, if the FDA reliably determined which drugs are vulnerable to shortages because of particularly complex manufacturing processes or extremely low profit margins, it could more strategically intervene to prevent shortages. The financial incentives described in Part V.D below could be especially valuable in this regard.

Some have expressed concern that early notice legislation would promote hoarding and gray market activities.¹⁴² Those hoping to profit from drug scarcity may try hard to find sources that will leak information about shortages as early as possible. The legislation addresses these fears through its confidentiality mandate, which is designed to keep the public from learning about anticipated shortages at the time they are disclosed to the FDA.¹⁴³ If the legislation is enacted, both manufacturers and the FDA would need to be committed to maintaining confidentiality and to preventing leaks.

While the proposed statute would constitute a constructive step towards overcoming the drug shortage problem, it is far from a comprehensive solution. It addresses planned production cessations or interruptions but not unanticipated manufacturing problems.

One improvement would be a requirement that manufacturers report all shortages, including unanticipated ones, to the FDA and provide explanations of their causes. This information would enable the FDA to build a database and analyze the reasons for various shortages in order to formulate solutions or to recommend appropriate courses of action to other parties. Currently, experts are constrained by a dearth of data and, more often than not, are unable to ascertain why shortages occur.¹⁴⁴ Rigorous reporting requirements should arm policy-makers with knowledge they can use to attack the problem more effectively.

An additional limitation is that the proposed legislation explicitly leaves the FDA powerless to force manufacturers to produce drugs or to revoke decisions

¹⁴⁰ <http://www.govtrack.us/congress/bill.xpd?bill=s112-296>; <http://www.govtrack.us/congress/bill.xpd?bill=h112-2245>.

¹⁴¹ Ventola, *supra* note 10, at 755; Stephen Barlas, *Severe Drug Shortages Impose Heavy Costs on Hospital Pharmacies: Senate Bill Might Help . . . or Not*, 36 P&T 242, 242 (2011).

¹⁴² Barlas, *supra* note 131, at 302.

¹⁴³ See *supra* note 129 and accompanying text.

¹⁴⁴ See *supra* note 25 and accompanying text (stating that 55% of shortages are of unknown origin).

to suspend or discontinue production.¹⁴⁵ Therefore, in many cases, the legislation will not allow the FDA to achieve an expeditious and permanent resolution to a shortage problem. Producers that have decided a particular drug is not sufficiently profitable¹⁴⁶ may often be immune to pressure from the FDA.¹⁴⁷

B. Hatch-Waxman Act Amendments

The Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act in honor of its two Congressional sponsors, is a 1984 amendment to the FDCA.¹⁴⁸ It enables manufacturers to file Abbreviated New Drug Applications (ANDA) with simplified requirements for generic medications.¹⁴⁹ Some have suggested that the Hatch-Waxman Act be revised to require manufacturers to include projections concerning demand for their product and plans for meeting this demand and that the FDA be authorized to revoke marketing licenses if minimal production goals are unmet.¹⁵⁰ Thus, generic drug manufacturers would be required to have redundancy capacity so that problems with particular sites, equipment, or a portion of the supply would not create catastrophic shortages.¹⁵¹

Furthermore, at least one expert has recommended that ANDA licensees who have consistently met market demand be awarded priority for any future ANDA submissions.¹⁵² In addition, the FDA could consider drug shortages as a factor in assessing ANDA filings and deem them to weigh against approval.¹⁵³

The Hatch-Waxman proposal would constitute a very aggressive intervention. By empowering the FDA to require redundancy and to revoke the licenses of companies whose production rate was inadequate, the legislation would depart significantly from current federal policy that prohibits the FDA from controlling manufacturers' decisions concerning quantity or continuation of production.¹⁵⁴ Such a proposal would likely meet vigorous industry resistance and may be unrealistic.

In addition, manufacturers may not be able to project demand for their product because of multiple factors that are outside their control. For example, producers cannot anticipate changes in clinical practice guidelines, natural disasters, or difficulties experienced by competitors that decrease their output and increase demand for supplies from other manufacturers.¹⁵⁵ Moreover, arguably, depriving manufacturers of the liberty to reduce or discontinue production in the face of adverse financial conditions may be counterproductive and further discourage companies from entering the generic drug market in the first place.

¹⁴⁵ H.R. 2245 at §506C(e)(4)(b).

¹⁴⁶ See *supra* Part II.C.

¹⁴⁷ But see Ventola, *supra* note 10, at 753 (stating that in the face of shortages, the "FDA has been fairly successful in influencing manufacturers to increase production" and that "[s]ome companies have even produced drugs at a loss, because they recognized a critical need for them).

¹⁴⁸ 21 U.S.C. §355(j). See generally, Gerald J. Messinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 *Food & Drug L. J.* 187 (1999).

¹⁴⁹ 21 U.S.C. §355(j)(2)

¹⁵⁰ Chabner, *supra* note 19, at 2148.

¹⁵¹ *Id.* See also, American Society of Health-System Pharmacists et al., *Drug Shortages Summit November 5, 2010 Summary Report 4* (2011) at <http://www.ashp.org/drugshortages/summitreport> (suggesting that the FDA "[r]equire manufacturing redundancies (e.g., multiple manufacturing sites for a sole product or multiple [active pharmaceutical ingredients] API sources, when available) as part of ... [its] approval process").

¹⁵² Chabner, *supra* note 19, at 2148.

¹⁵³ *Id.* at 2146-49.

¹⁵⁴ See *supra* notes 95 and 134 and accompanying text.

¹⁵⁵ See *supra* Part II (discussing causes of shortages).

Nevertheless, the proposal contains several laudable recommendations. The FDA would be well-advised to require applicants to indicate whether and how they will create redundancy in manufacturing capacity to avoid shortages in case of unplanned manufacturing difficulties. Redundancy would not be mandated but could be considered as a factor favoring approval. In addition, a past history of causing an avoidable shortage could be taken into account as a negative indicator if the manufacturer seeks approval of a new drug. Such a policy would aim to deter both carelessness that leads to product contamination and strategic decisions concerning product discontinuations or suspensions. These changes in policy could be incorporated into the FDCA through amendment and need not be restricted to generic drugs.

C. Creation of A National Stockpile

A national stockpile of medically necessary treatments is an option that has been considered by several commentators.¹⁵⁶ This approach would follow a precedent set for purposes of emergency preparedness. The Centers for Disease Control and Prevention has created a Strategic National Stockpile (SNS) that includes large quantities of medicine and medical supplies likely to be needed during a public health emergency.¹⁵⁷ SNS supplies are to be delivered to the states, which in turn are to quickly deliver them to local communities in accordance with emergency preparedness plans.¹⁵⁸

Several obstacles stand in the way of building a national stockpile of drugs that are vulnerable to shortage. First, in some cases, it would necessitate collection of supplies that are already scarce and currently needed in clinics rather than in storage.¹⁵⁹ Second, constructing and maintaining a national stockpile would require very significant financial and human resources and is logistically complex.¹⁶⁰ Finally, drugs have a limited shelf-life and must be replaced periodically. This means that staff will need to track the expiration dates of all supplies, and many drugs will go to waste if shortages do not materialize and they are not used in time.¹⁶¹ In light of shrinking federal resources and intense concern about the deficit, a national stockpile initiative is inadvisable at this time.

D. Regulatory Changes

Administrative agencies should utilize their regulatory powers to combat the drug shortage crisis. This section considers potential changes to the Medicare reimburse-

¹⁵⁶ American Society of Health-System Pharmacists et al., *supra* note 140, at 7; Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S. C. L. Rev. 741, 765-66 (2003).

¹⁵⁷ Centers for Disease Control and Prevention Office of Public Health Preparedness and Response, *Strategic National Stockpile (SNS)*, at <http://www.cdc.gov/phpr/stockpile/stockpile.htm> [hereinafter CDC OPHPR].

¹⁵⁸ *Id.*

¹⁵⁹ American Society of Health-System Pharmacists et al., *supra* note 140, at 7.

¹⁶⁰ Noah, *supra* note 144, at 766; CDC OPHPR, *supra* note 145.

¹⁶¹ CDC OPHPR, *supra* note 145 (stating that "[t]he SNS Program ensures that the medical material stock is rotated and kept within potency shelf-life limits. This involves quarterly quality assurance/quality control checks (QA/QC's) on all 12-hour Push Packages, annual 100% inventory of all 12-hour Push Package items, and inspections of environmental conditions, security, and overall package maintenance"); Ventola, *supra* note 10, at 756 (arguing against stockpiling by individual health care facilities).

ment system and DEA quota requirements. Regulatory policies should encourage manufacturers to produce generic drugs that are often favored by patients because they are both effective and inexpensive.

1. *Revise Medicare Reimbursement System*

Several commentators assert that the Medicare reimbursement system must be altered so that prescribers do not have financial incentives to make treatment choices that are likely to lead to shortages.¹⁶² Medicare payments of six percent above the average sales price may induce oncologists to select expensive brand-name drugs in order to maximize the yield of the six percent markup.¹⁶³ Minimal purchases of generics by physicians treating the elderly population may discourage manufacturers from producing generic drugs that would be the best choice for non-Medicare patients.

The current reimbursement system was established in order to contain Medicare costs, and budgetary savings remain a crucial necessity. Before 2003, Medicare paid ninety-five percent of the average wholesale price (AWP) for chemotherapy drugs, a price set by manufacturers without regulatory pricing constraints. In reality, oncologists typically paid only between sixty-six and eighty-seven percent of the AWP, which translated into an annual overpayment of approximately \$1.6 billion by Medicare.¹⁶⁴

There is an inevitable tension between public programs' cost containment goals and providers' need to ensure the profitability of their practices. The Centers for Medicare and Medicaid Services, however, should continue to revisit its reimbursement policies, and, to the extent possible, revise them to avoid creating perverse incentives for clinicians. One possible solution is a payment system based on disease-management fees rather than on chemotherapy sales.¹⁶⁵ The severity of the problem could also perhaps be diminished through a greater shift to fixed physician salaries.¹⁶⁶ Fixed salaries would remove individual physicians' incentive to select particular drugs in order to maximize Medicare reimbursement, though doctors may nonetheless face institutional pressure to do so. There is also some concern that the prospect of earnings based on salary alone would make the practice of oncology less profitable and appealing to talented medical students.¹⁶⁷

2. *Alter DEA Quotas*

The DEA should establish a mechanism to increase production quotas for controlled substances found to be in short supply or vulnerable to shortage, such as the attention deficit hyperactivity medications that were reportedly scarce in 2011.¹⁶⁸ The Justice Department has already noted that the quota regulations "have not

¹⁶² Bronwyn Mixter, *Sen. Hatch Developing Bill to Address 'Growing Crisis' of Medicine Shortages*, 19 HEALTH CARE POL'Y REP. 1880, 1880 (2011); Gatesman & Smith, *supra* note 18, at 1655; Chabner, *supra* note 19, at 2149.

¹⁶³ See *supra* notes 58-60 and accompanying text.

¹⁶⁴ Gatesman & Smith, *supra* note 18, at 1654; Renee Twombly, *Medicare Cost Containment Strategy Targets Several Oncology Drugs*, 96 J. NAT'L CANCER INST. 1268, 1268 (2004).

¹⁶⁵ Gatesman & Smith, *supra* note 18, at 1655.

¹⁶⁶ *Id.* (noting that "Kaiser Permanente, Veterans Affairs, and most academic centers" already pay their physicians salaries).

¹⁶⁷ *Id.*

¹⁶⁸ See *supra* notes 2, 53-55 and accompanying text; Hill & Reilly, *supra* note 6, at 4.

been reviewed or revised since they were first implemented in the early 1970's.¹⁶⁹ It plans to re-evaluate the quota regulations under its Retrospective Analysis of Existing Rules.¹⁷⁰

E. *Influence Manufacturer Conduct through Taxes, User Fees, and Other Incentives*

Policy-makers should consider several other strategies to address the drug shortage crisis. Under our free-enterprise system, manufacturers are at liberty to decide which goods to produce, and the government cannot dictate that they supply particular products.¹⁷¹ Consequently, appropriate incentives and disincentives must be in place to ensure that manufacturers voluntarily choose to produce sufficient supplies of drugs.

The federal government could establish tax incentives to reward manufacturers for producing drugs that are in short supply or that are identified by the FDA as vulnerable to shortage.¹⁷² An FDA initiative designed to ascertain which drugs are vulnerable, such as that proposed in the "Preserving Access to Life-Savings Medications Act of 2011," would facilitate implementation of a tax incentive program.

The FDA could also build incentives into its fee programs. The Prescription Drug User Fee Act (PDUFA) was first enacted in 1992 and is renewed every five years.¹⁷³ It authorizes the FDA to collect fees from manufacturers of certain drugs and biological products, which are used to expedite the drug approval process.¹⁷⁴ The FDA is contemplating adding a generic user fee program to the PDUFA's 2012 reauthorization.¹⁷⁵ The goal of the program would be to generate funds that would enable the FDA to reduce approval time from thirty months to ten months.¹⁷⁶ Bringing new generic drugs to market more quickly could itself eliminate some shortages, and the prospect of a short approval process may encourage some members of industry to undertake production of generics.¹⁷⁷ The fees themselves could be used as an added inducement mechanism. The FDA could award fee reductions or exemptions in select cases in which producers will increase the supply of vulnerable or scarce drugs.¹⁷⁸ This would be consistent with PDUFA's current policy of exempting applications for "orphan drugs" that treat rare diseases in order to incentivize their production.¹⁷⁹

A different suggestion was made by Professor Lars Noah in a 2003 article. Professor Noah recommended that Congress enact legislation to reduce manufacturers' liability exposure, which theoretically might drive suppliers out of the

¹⁶⁹ Department of Justice, *Final Plan for Retrospective Review of Existing Regulations Pursuant to Executive Order 13563*, at 14 (August 22, 2011), available at <http://www.justice.gov/open/doj-rr-final-plan.pdf>.

¹⁷⁰ *Id.*

¹⁷¹ See *supra* note 95 and accompanying text.

¹⁷² Hill & Reilly, *supra* note 6, at 4; Mixer, *supra* note 150 at 1880.

¹⁷³ Pub. L. No. 102-571, 106 Stat. 4491 (1992) (codified primarily at 21 U.S.C.A. §§ 379g, 379h); U.S. Food and Drug Administration, *The Prescription Drug User Fee Act*, at <http://www.fda.gov/Food/Industry/UserFees/PrescriptionDrugUserFee/default.htm>.

¹⁷⁴ 21 U.S.C. § 379h(g) (2006), U.S. Food and Drug Administration, *supra* note 161.

¹⁷⁵ Meeting notice, 76 Fed. Reg. 76738 (2011) (announcing "a public meeting to discuss proposed recommendations for enactment of a Generic Drug User Fee Act (GDUFA)").

¹⁷⁶ Kweder Statement, *supra* note 5.

¹⁷⁷ *Id.*

¹⁷⁸ Hill & Reilly, *supra* note 6, at 4.

¹⁷⁹ 21 U.S.C. § 379h(a)(1)(F).

market and generate shortages.¹⁸⁰ Congress has included liability protection for health care providers in various emergency preparedness initiatives,¹⁸¹ and I have argued in previous work for more extensive provider immunity in the specialized context of declared public health emergencies.¹⁸² However, recent literature does not suggest that the current wave of shortages is attributable to concerns about liability.¹⁸³ Consequently, legislation altering tort liability would not be justified at this time. If liability concerns emerge as a major cause of drug shortages in the future, policy-makers could consider narrowly-tailored protections in response to the circumstances at issue.

Private parties may also be able to contribute to shortage prevention through contract terms. Providers may include strong failure-to-supply requirements in their contracts in order to deter manufacturer conduct that leads to shortages.¹⁸⁴ Failure-to-supply clauses require manufacturers to provide reimbursement for the difference between the agreed-upon sale price and the price at which the provider ultimately purchased the drug from another source.¹⁸⁵ Such provisions have been successfully used by some health care entities to recoup significant costs.¹⁸⁶

VI. CONCLUSION

The drug shortage crisis is ongoing and serious. It jeopardizes the lives of untold numbers of patients and causes anxiety and misery for patients and health care providers alike. The crisis has not escaped attention at the highest levels of government, including Congress and the President of the United States. Commentators and policy-makers have not lacked for ideas as to how to address the problem, but measures implemented thus far have not been adequately comprehensive and potent to avert further scarcity.

This Article argues that the drug shortage crisis should be treated as a public health threat that justifies forceful intervention. Because of the low level of price responsiveness in the health care market,¹⁸⁷ the marketplace alone cannot correct the drug shortage problem.

The crisis requires a multi-faceted offensive involving legislative, regulatory, and private sector changes. Public health policies and standards must serve multiple roles: they should deter both carelessness that leads to product contamination and purposeful decisions to discontinue or suspend manufacturing when such decisions will cause shortages, and at the same time, they should encourage production of vulnerable drugs.

To that end, the article recommends that the "Preserving Access to Life-Saving Medications Act of 2011"¹⁸⁸ be passed at the earliest opportunity. Congress should add a provision requiring manufacturers to report all drug shortages along with

¹⁸⁰ Noah, *supra* note 144, at 767-70 (suggesting implementation of a model based on the workers' compensation system or a "regulatory compliance defense.").

¹⁸¹ Hoffman, *supra* note 105, at 1941-46.

¹⁸² *Id.* at 1959-67.

¹⁸³ See *supra* Part II.

¹⁸⁴ Haninger et al., *supra* note 6, at 15; Glied Statement, *supra* note 51.

¹⁸⁵ Glied Statement, *supra* note 51 (noting that "failure-to-supply clauses, however, provide no reimbursement if there are no alternative sources for the drug, do not reimburse for resources expended looking for other sources, and are of limited duration.").

¹⁸⁶ Alven Weil, *Failure-to-Supply Pharmacy Program Saves Hospitals More than \$3.5 Million by Attacking Drug Shortage Problems*, at <http://www.premierinc.com/about/news/10-dec/fts120910.jsp>.

¹⁸⁷ See *supra* notes 48-52 and accompanying text.

explanations of their causes so that the problem can be better analyzed and understood. The FDA should ask applicants for drug approval to indicate whether they will create redundancy in manufacturing capacity to avoid shortages, and if so, how. The agency should regard such plans favorably during its application review process. Furthermore, the FDA could consider a past history of causing an avoidable shortage as an adverse indicator if the manufacturer seeks approval of a new drug. Additional components of the drug shortage solution are changes to the Medicare reimbursement system and DEA quotas for scarce controlled substances. Shortages should also be deterred through financial incentives for production of vulnerable or scarce drugs, including tax benefits, user fee adjustments, and failure-to-supply clauses. These recommendations are not necessarily exhaustive, and others should be carefully considered as they emerge.

Excessively aggressive approaches that are hostile to manufacturers and undermine their interests should be rejected. Although it is ironic that inexpensive drugs that are preferred by patients are often the ones in short supply,¹⁸⁸ manufacturers cannot be expected to produce generic drugs if those drugs will be unprofitable for them. Policy-makers must make every effort to formulate balanced solutions that take the welfare of all stakeholders into account. As emphasized by Jay Cuetara, a cancer patient who experienced a drug shortage during his illness, health care providers, industry and the government must work together to ensure that patients "have access to the best critical drug at the right time and every time it's needed."¹⁸⁹

¹⁸⁸ FDA Workshop, *supra* note 1, at 99.

¹⁸⁹ *Id.* at 101.