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## Drug Shortages: The Problem Of Inadequate Profits

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**DRUG SHORTAGES: THE PROBLEM OF  
INADEQUATE PROFITS**

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## **ABSTRACT**

Drug shortages are a growing problem in the United States. The scope and severity of drug shortages has caught the public eye and prodded the FDA into action. Among the potential causes of drug shortages are Medicare Part B reimbursement policies, the 340B federal drug rebate program, market consolidation and competition in the pharmaceutical industry, regulatory overreach by the FDA and manufacturing and supply problems at production plants. What these causes have in common is that they can all be understood as dampening profits for manufacturers in one way or another. Some causes effectively impose price caps which prevent manufacturers from charging a free-market price for their products. Other causes create cost floors which stymie cost-cutting efforts by manufacturers. Whether by elevating costs or reducing prices, these contributors dampen profits, and without profits, incentives to produce evaporate. Pulling these conclusions together, it becomes clear that the best approach to drug shortages is to make drug manufacture more attractive by removing price caps and reducing cost floors. Whether through tax subsidies, Medicare Part B and 340B drug rebate reform, or relaxed regulatory requirements, the most promising approach is one that makes drug manufacture more profitable.

## I. THE PROBLEM OF DRUG SHORTAGES

In recent years, drug shortages have become a critical problem in the United States. Various American news outlets have reported on the shortages of vital life-saving drugs<sup>1</sup>. In particular, cancer patients have been especially hard-hit by the disproportionate amount of shortages afflicting oncology medication<sup>2</sup>. Through its reporting mechanism to monitor drug supplies, the Food and Drug Administration<sup>3</sup> has recorded a marked increase in shortages. Non-governmental organizations such as the American Society of Health System Pharmacists have also recorded an increase in the number of shortages.

As a result of the media blitz and startling statistics, drug shortages have become a focal point of several Senate and House Committee meetings in recent months. The severity of the crisis was highlighted by Senator Max Baucus at a Senate Finance Committee hearing on drug shortages:

The types of patients affected by a drug shortage show the seriousness of the problem. We read heartbreaking stories of drug shortages forcing cancer patients to forgo critical treatment. We hear stories about emergency room providers forced to use makeshift drugs when conventional drugs are in

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<sup>1</sup> See, e.g., Jennifer Corbett Dooren, *Hospitals Cut Doses Amid Drug Shortage*, Wall St. J., Dec. 15, 2011 (“Hospitals are grappling with a shortage of nutrition drugs and disinfectant products that has led doctors to cut doses and ration supplies, prompting patients at a handful of facilities to get sick.”); Gardiner Harris, *U.S. Scrambling to Ease Shortage of Vital Medicine*, N.Y. Times, Aug. 19, 2011 (“Federal officials and lawmakers, along with the drug industry and doctors’ groups, are rushing to find remedies for critical shortages of drugs to treat a number of life-threatening illnesses, including bacterial infection and several forms of cancer.”); Rob Stein, *Shortages of Key Drugs Endanger Patients*, Wash. Post, May 1, 2011 (“Doctors, hospitals and federal regulators are struggling to cope with an unprecedented surge in drug shortages in the United States that is endangering cancer patients, heart attack victims, accident survivors and a host of other ill people.”).

<sup>2</sup> See Dep’t of Health & Human Services, Assistant Sec’y for Planning and Evaluation, *Economic Analysis of the Causes of Drug Shortages*, at 1 (2011) (“Currently, class-wide shortages are affecting the sterile injectables segment of the industry, particularly sterile injectable oncology products.”).

<sup>3</sup> The Food and Drug Administration (FDA) is an executive agency empowered to regulate food, drugs and medical devices (among other products) in the United States. The FDA has a heavy hand in American markets, regulating approximately \$1.5 trillion worth of consumer products each year. See Eve E. Slater, *Today’s FDA*, 352 New Eng. J. Med. 293, 293 (2005). In the area of drugs, the FDA generally requires pre-market approval in order to market pharmaceutical products in the United States. This pre-market approval takes the form of clinical testing to establish the safety and efficacy of new drugs.

short supply. This compromises care in a place where even a minute's delay can mean the difference between life and death.<sup>4</sup>

The White House also joined the fray of concerned parties when President Obama issued an executive order in October 2011 directing the FDA to mitigate shortages:

Shortages of pharmaceutical drugs pose a serious and growing threat to public health. While a very small number of drugs in the United States experience a shortage in any given year, the number of prescription drug shortages in the United States nearly tripled between 2005 and 2010, and shortages are becoming more severe as well as more frequent. The affected medicines include cancer treatments, anesthesia drugs, and other drugs that are critical to the treatment and prevention of serious diseases and life threatening conditions.<sup>5</sup>

Much of the discussion on drug shortages has focused on its causes. Frequently cited are manufacturing problems, whether due to the difficulty of securing raw materials or unexpected production breakdowns. Regulatory burdens and the associated compliance costs are also commonly cited. More recently, Medicare prescription drug programs have been implicated, to the extent that below-market reimbursement policies make these drugs unprofitable. Less frequently cited are prescribing patterns of doctors (primarily oncologists) that tend to disfavor certain lower-priced generic drugs. The increased costs of business due to liability suits – whether due to product defects or price gouging – has also sometimes come up as a potential contributor.

The discourse about these commonly-cited causes tends to miss the mark because it is too narrowly focused. Academics and bureaucrats spend much time trying to pinpoint the “primary” contributor or the “main” cause. What is ignored is that all of these factors are symptoms of the underlying problem: Insufficient profits. According to basic economics, a product that can be readily produced will be in short supply if the profits are too low. In the drug shortages debate,

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<sup>4</sup> *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Sen. Max Baucus, Chairman, S. Comm. on Fin.).

<sup>5</sup> Exec. Order No. 13,588, 76 Fed. Reg. 68,295 (Nov. 3, 2011).

whether the alleged contributors increase the production costs or reduce sales revenue, the ultimate effect is to reduce profits for drug manufacturers. When profits in one line of production are too low, economically rational manufacturers will direct their capital to other lines of production. As a result, any proposed solution to the drug shortages problem that does not ultimately promote profitability is unlikely to have much long-lasting effect.

The proposal in this paper is to attack the problem of insufficient profits on two fronts: (1) Decreasing costs; and (2) increasing revenue. First, by decreasing costs of production and regulatory compliance, all else being equal, manufacturers of low-margin generics will see increased profits. Second, by removing price controls from drugs, manufacturers will be free to set prices that will maximize their profits and make drug production more lucrative. Revenue can also be increased via higher demand and larger market share for manufacturers, though this type of intervention is not as effective for pharmaceuticals that have relatively inelastic demand.

In terms of structure, this paper will begin with statistics showing the extent of the drug shortages problem. It will then discuss potential causes of drug shortages – the usual suspects – and commonly-cited fixes to these causes. The purpose of this paper is to highlight the potential inadequacy of many of the proposed solutions to the drug shortages problem. In particular, the flaw with most of the current “fixes” is that they often ignore that the root cause is likely inadequate profits for generics manufacturers. The paper will finish with several proposed tweaks to the current market environment that would incentivize drug production. These tweaks rely heavily on a free-market approach to supply disruptions. Among the suggestions are overhauls of the Medicare drug reimbursement formulas, more streamlined FDA regulatory procedures and tax subsidies to incentivize new production lines or existing drug manufacture. The drug shortage problem is highly concentrated, and many of these proposed changes would

be especially effective for generic sterile injectables. Though none of the tweaks is likely to be enough on its own, judging from the experience of vaccine shortages. the combination of small fixes is likely to have a real impact.

## II. SCOPE AND CONSEQUENCES OF DRUG SHORTAGES

### *1. Magnitude of the problem*

A drug shortage means that for a particular pharmaceutical medication, there is insufficient supply to meet currently existing demand<sup>6</sup>. In the United States, two organizations collect the most commonly-cited information on drug shortages: The American Society of Health-System Pharmacists (ASHP) and the FDA.

The ASHP has recorded data since 2001, receiving its data from the University of Utah Drug Information Service. According to the ASHP statistics, there were 267 national shortages in 2011, up from 211 in 2010. The figure for last year is over four times higher than the lowest recorded figure (just 58 shortages in 2004) in the ASHP records. The FDA has collected data on drug shortages since 2004. It reported 200 shortages as of September 30, 2011, its most recent measure of shortages in 2011. This figure is up from 178 in 2010 and more than triple the lowest recorded figure (only 56 shortages in 2006). In sum, using either the ASHP or FDA statistics, the number of drug shortages has been increasing annually since 2006.

<b>Year</b>	<b>ASHP/Utah Figures</b>	<b>FDA Figures</b>
<b>2001</b>	120	N/A
<b>2002</b>	88	N/A

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<sup>6</sup> *Examining the Increase in Drug Shortages: Hearing Before the H. Comm. on Energy & Commerce, 112th Cong. (Sept. 23, 2011) (statement of Dr. Howard K. Koh, Assistant Sec'y of Health, Dep't of Health & Human Services) ("The Food and Drug Administration 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")*.

<b>2003</b>	73	N/A
<b>2004</b>	58	58
<b>2005</b>	74	61
<b>2006</b>	70	56
<b>2007</b>	129	90
<b>2008</b>	129	110
<b>2009</b>	166	157
<b>2010</b>	211	178
<b>2011</b>	267	200 (as of Sept. 30/11)

**Table 1: Recorded Drug Shortages**

The figures cited by the ASHP and FDA differ because these organizations use slightly different definitions of “drug shortage”. The ASHP and FDA also poll different links in the drug supply chain. The FDA data is provided voluntarily by drug manufacturers; by contrast, the ASHP receives its data from health care organizations such as hospital pharmacies – i.e. the data comes from buyers experiencing shortages. Despite these differences in methodology, the data from the ASHP and FDA both exhibit a worsening problem of drug shortages in the past decade.

Interestingly, the drugs most prone to shortages tend to be generics and sterile injectable drugs. The combined class of products – generic injectables – makes up over 80% of the shortages problem<sup>7</sup>; almost half of the total generic injectable market is on the shortages list<sup>8</sup>. In terms of treatment areas, drug shortages tend to be concentrated in five disease areas: oncology, anti-infectives, cardiovascular, central nervous system and pain management, with oncology drugs making up the highest share of the shortages list at sixteen percent<sup>9</sup>. Graphs from the IMS Institute for Healthcare Informatics demonstrate the striking propensity for shortages of generics and sterile injectables.

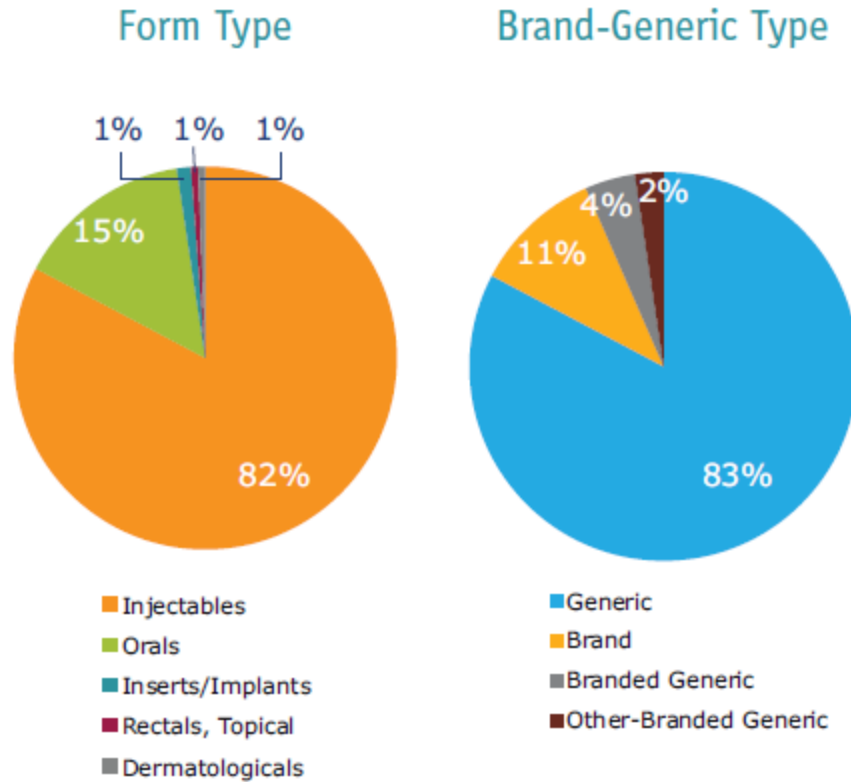
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<sup>7</sup> See *Drug Shortages: A Closer Look At Products, Suppliers And Volume Volatility*, IMS Institute for Healthcare Informatics 4 (2011).

<sup>8</sup> *Id.* at 3.

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





Source: IMS National Sales Perspectives, Sep 2006 – Aug 2011

**Figure 1: Characteristics of Current Drug Shortages**

Another feature of the problem is that most of the drugs in short supply have fewer than four unique suppliers. This scenario is demonstrated by Figure 2 below, which plots the number of suppliers for drugs in short supply as of August 2011. Over 50% of the drugs are supplied by only one or two manufacturers<sup>10</sup>. Two-thirds of the drugs have three or fewer suppliers<sup>11</sup>. Having only a few manufacturers for each product likely has detrimental consequences: Drugs that are not in short supply are far more likely to have multiple suppliers<sup>12</sup>. Besides the number of suppliers, another feature of the drug production industry is that there is a lot of fluctuation in *which* particular firms supply a product. There is a lot of flux in the manufacturing market, with

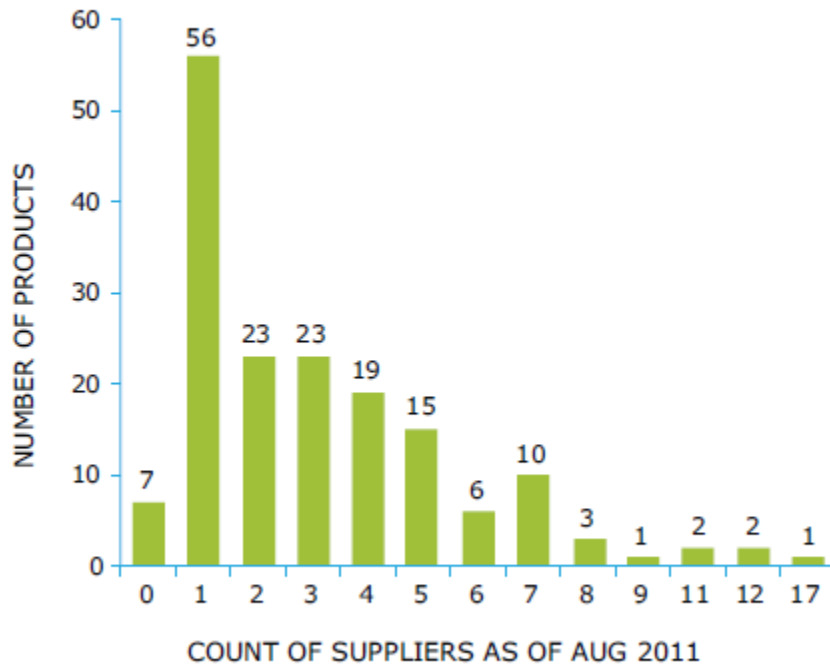
<sup>10</sup> *Id.* at 9.

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

<sup>12</sup> *Id.*

many players entering and leaving the market for a particular drug. The overall trend is that an increasing number of suppliers have left the markets for good<sup>13</sup>.

### Number of Products by Supplier Count



Source: IMS National Sales Perspectives, Sep 2006 – Aug 2011

Figure 2: Number of Suppliers for Drugs Experiencing Shortages

#### 2. Consequences of the problem

Although a tiny minority of all drugs used in the United States experience shortages in a given year<sup>14</sup>, the short supply of affected drugs still has a significant adverse impact on patients and health care providers. Drug shortages impose significant labor costs in the healthcare sector, estimated at \$216 million annually for pharmacists, pharmacy technicians, physicians and

<sup>13</sup> *Id.*

<sup>14</sup> See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 3 (typically only about 0.5% of all drugs used in the United States experience a shortage in any given year).

nurses<sup>15</sup> to manage shortages. Drug shortages also have a detrimental impact on patients, who are often forced to use less desirable, more expensive alternatives with the resulting potential for poor patient outcomes<sup>16</sup>. A study by the Institute for Safe Medication Practices in September 2011 found that its respondents experienced over one thousand adverse drug events (including medication errors and adverse drug reactions) due to shortages<sup>17</sup>. A survey by the American Hospital Association in July 2011 found that 82% of the hospital respondents had experienced delayed treatment due to shortages, and over half could not provide patients with the recommended therapy. Shortages disproportionately affect generics in the sterile injectable market, and sterile injectable drugs are often used for life-threatening diseases and conditions such as cancer, intravenous feeding, surgery and emergency medicine.

Patients who need drugs that are in short supply have only two options: Paying more, or using less. However, quite often, patients do not have the option to just “pay more”; as will be discussed later in this paper, government price controls on many of the affected drugs make it impossible for a patient to induce manufacturers to produce more of a life-saving drug by paying more. The result is that for most patients, the only option is to “use less” when it comes to vital life-saving medication. Using less often means that doctors and pharmacists have to resort to less-effective, more-expensive alternatives that increase the potential for patient harm.

A salient example of the costs of drug shortages is the case of propofol, a sterile injectable generic used in general anesthesia . Between 2009 and 2010, the supply of propofol

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<sup>15</sup> See Rola Kaakeh et al., *Impact of Drug Shortages on U.S. Health Systems*, 68 Am. J. of Health-Sys. Pharmacy 1811, 1811-19 (2011).

<sup>16</sup> See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 2(citing the results of a survey of hospitals that found that a majority “reported problems with drug shortages, including the use of less desirable, often more expensive alternatives and the potential for medication errors and poor patient outcomes”).

<sup>17</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Kasey Thompson, Vice President, American Society of Health-System Pharmacists).

had become critically low due to recalls stemming from possible contamination at manufacturing plants<sup>18</sup>. An endoscopy clinic in Nevada tried to manage the shortage by extending its current supply and administering propofol vials intended for use by a single patient to multiple patients<sup>19</sup>. Administering single-use vials to multiple patients is contrary to the safe-use information on the propofol label<sup>20</sup>. The consequence of this desperate attempt to stem the impact of a shortage was severe: The propofol vials were contaminated from improper use, resulting in an outbreak of hepatitis C at the clinic with approximately 40,000 were tested for potential infection<sup>21</sup>. In response to the propofol shortages, the FDA temporarily allowed emergency importation of an alternative version of the drug<sup>22</sup>. The case of propofol is only one of many serious adverse events due to drug shortages.

### III. CAUSES OF DRUG SHORTAGES

#### *1. Medicare Part B reimbursement policies*

A prominent villain in the drug shortages debate is the reimbursement mechanism of Medicare. Medicare is a federal health insurance program for seniors aged 65 and over, covering a large swath of the population (approximately 47 million Americans in 2010)<sup>23</sup>. In the drug shortages debate, a commonly-cited culprit<sup>24</sup> is the change in reimbursement policies caused by the Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA).

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<sup>18</sup> See Valerie Jensen, *The Reality of Drug Shortages: The Case of the Injectable Agent Propofol*, 363 *New Eng. J. Med.* 806 (2010).

<sup>19</sup> *Id.* at 807.

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

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

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

<sup>23</sup> See Kaiser Family Foundation, *Medicare Chartbook 3* (2010).

<sup>24</sup> See, e.g., Ezekiel J. Emanuel, *Shortchanging Cancer Patients*, *N.Y. Times*, Aug. 6, 2011 (opinion piece by Ezekiel Emanuel, a former White House advisor on health care reform, blaming the MMA for exacerbating drug shortages); *Drug Shortages: Why They Happen and What They Mean: Hearing Before*

Before discussing the MMA and its purported effect on drug shortages, it is important to describe its target, the Medicare Part B drug reimbursement program. Medicare Part B covers a limited number of physician-administered prescription drugs, such as outpatient sterile injectable drugs. As mentioned previously, sterile injectable drugs make up a disproportionate part of the drugs affected by supply shortages. The reimbursement policies of Medicare Part B determine to a large extent how much manufacturers receive for their products. These reimbursement prices are administratively determined by the Centers for Medicare & Medicaid Services (CMS)<sup>25</sup>.

The MMA adjusted the way reimbursements were calculated for drugs covered by Medicare Part B. Prior to its enactment, reimbursement was generally between 85-95% of the average wholesale price (AWP) paid to the manufacturer by wholesalers<sup>26</sup>. The AWP was entirely self-reported, making it easy for drug manufacturers to inflate the figures to receive more Medicare money<sup>27</sup>. This type of price gouging was at issue in multistate reimbursement fraud litigation<sup>28</sup> for false claims made prior to the enactment of the MMA.

Partly in response to such price gouging, the MMA changed its reimbursement formula to one based on the average sales price (ASP) paid to the manufacturer by all purchasers<sup>29</sup>. Under the new regime, manufacturers would provide CMS with the average sales price<sup>30</sup> (ASP) and

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*the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research); Mandy L. Gatesman & Thomas J. Smith, *The Shortage of Essential Chemotherapy Drugs in the United States*, 365 *New Eng. J. Med.* 1653, 1654 (2011).

<sup>25</sup> See Dep't of Health & Human Services, Office of Inspector Gen., *Monitoring Medicare Part B Drug Prices: A Comparison of Average Sales Price to Average Manufacturer Price*, at 1 (2006).

<sup>26</sup> *Id.* at 2.

<sup>27</sup> See Patrick Mullen, *The Arrival of Average Sales Price*, *Biotechnology Healthcare* 48-53 (June 2007).

<sup>28</sup> *In Re Pharm. Indus. Average Wholesale Price Litig.*, (D.Ma. 2007) (multidistrict litigation finding that drug manufacturers engaged in unfair and deceptive trade practices by inflating the AWP prices they reported to Medicare for reimbursement).

<sup>29</sup> See generally 42 U.S.C. § 1395w-3a(c)(1) (2011).

<sup>30</sup> ASP is “the manufacturer’s sales to all purchasers” divided by “the total number of such units of such drug or biological sold by the manufacturer.” 42 U.S.C. § 1395w-3a(c)(1) (2011).

volume of sales of each of their covered drugs on a quarterly basis. Medicare would pay manufacturers the ASP over the previous two quarters plus a 6% premium<sup>31</sup>.

This new reimbursement policy caps the amount manufacturers can charge for their products<sup>32</sup>, regardless of how much their production costs have changed. Because ASP is calculated based on prices from the previous two quarters (six months) of business, if production costs rise sharply in the meantime, suppliers cannot charge enough to recoup those losses<sup>33</sup>. There is some evidence that shortages are more common for drugs with lower average prices and hence lower reimbursement rates<sup>34</sup>. In addition, shortages disproportionately affect sterile injectables, drugs which are typically physician-administered and reimbursed under Medicare Part B<sup>35</sup>.

One criticism of this explanation is that it does not take into account that most drug purchases are funded by private insurance policies. That is, although Medicare Part B accounts for a large proportion of drug spending, private insurance is still a significant player. In such a case, even if Medicare reimbursement was too low, private reimbursement would be higher. The response to this criticism is that it assumes that private insurers set their prices independently of

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<sup>31</sup> See 42 U.S.C. § 1395w-3a(b)(1) (2011).

<sup>32</sup> For manufacturers participating in the Medicare Part B program, a reimbursement cap is a binding price for two reasons. First, the scale of the Medicare Part B program dwarfs that of private industry, which means that government reimbursement makes up a larger proportion of supplier revenues. Second, for administrative purposes, many private insurers adhere closely to government reimbursement rates. These two factors both contribute to making Medicare Part B the dominant player in pricing certain drugs. See Paul N. Van de Water, *Medicare Changes Can Complement Health Reform*, Center on Budget and Policy Priorities (2008).

<sup>33</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research) (Medicare Part B “makes it hard for manufacturers to take, and sustain price increases to reflect demand or – more importantly -- their rising cost of producing these goods.”)

<sup>34</sup> See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 8 (“Among the group of drugs that eventually experience a shortage, average prices decreased in every year leading up to a shortage.”)

<sup>35</sup> *Id.* at 5.

Medicare. In fact, however, private insurance prices often mirror Medicare prices<sup>36</sup> because private insurers tend to set their reimbursement rates as a percentage of Medicare reimbursement schedules.

Besides the actual pricing formula used by Medicare Part B, there is also the problem of the *method* of pricing. When computing the reimbursement figures for different drugs, CMS does not calculate ASP for a specific type of drug. Instead, CMS groups several drugs together into a category and computes the ASP for all of those drugs in that category<sup>37</sup>. This means that reimbursement is not directly based on ASP for a specific drug, but on the ASP for a specific *category* of drugs<sup>38</sup>. The resulting ASP is a rough approximation that penalizes higher-cost drugs in a certain category<sup>39</sup>. The reimbursement amount will reflect the production expenses of the lowest-cost manufacturer. The higher-cost manufacturer is forced to either participate in a “race to the bottom”, or else, to discontinue production altogether.

## ***2. The 340B federal drug rebate program***

Also cited as a contributor to drug shortages is the 340B Drug Pricing Program, a federally-run drug discounting scheme. The 340B program limits the cost of covered outpatient drugs to certain “covered entities” – federal grantees and federally-qualified health centers and hospitals<sup>40</sup>. Covered entities are typically government-sponsored or supported hospitals and

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<sup>36</sup> See, e.g., Cristina Boccuti & Marilyn Moon, *Comparing Medicare and Private Insurers: Growth Rates in Spending Over Three Decades*, 22 *Health Affairs* 230, 234; Van de Water, *supra* note 32, at 3.

<sup>37</sup> See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 4.

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

<sup>39</sup> Because average sales price will diverge from the actual sales price of a particular drug (that is the very definition of an average), the reimbursement amount will produce a windfall for low-cost medications at the expense of higher-cost drugs. See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research).

<sup>40</sup> 42 USC § 256B(a)(4) (2011).

clinics serving vulnerable populations<sup>41</sup>. Participation in the 340B program is mandatory for pharmaceutical firms whose drugs are covered by Medicare<sup>42</sup>. In addition to receiving deep discounts, covered entities can also generate additional revenue by seeking reimbursement through patients' insurance policies that exceed the price paid for the drugs<sup>43</sup>. Most drug manufacturers that participate in Medicare programs have participated in the 340B program since its inception<sup>44</sup>.

The 340B price ceiling is based on a statutory formula<sup>45</sup> that effectively caps the drug price at the average manufacturer price. The "average manufacturer price" is the average price paid to the manufacturer by wholesalers and retail community pharmacies<sup>46</sup>. The price ceiling may be even lower than the AMP, however; when the AMP increases more quickly than the inflation rate, the manufacturer must pay an additional rebate amount<sup>47</sup>.

Nearly a third of all U.S. hospitals participate as "covered entities" and force drug discounts from manufacturers<sup>48</sup>. The benefits to covered entities are clear: Qualified recipients typically save between 20 to 50% off the cost of pharmaceuticals and can pocket this difference by selling the drugs to patients at a higher price<sup>49</sup>. The result is a transfer of surplus from the manufacturers to the hospitals, reducing the profitability of drug production. Things are set to

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<sup>41</sup> See Gov't Accountability Office, *Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement* 1 (2011).

<sup>42</sup> See 42 U.S.C. § 256B(a) (2011).

<sup>43</sup> For example, a covered entity may receive Drug X for \$100 a unit under the 340B program for which they are reimbursed \$150 a unit from patients' insurance companies. The resulting \$50 a unit is pure profit to the covered entity, but it comes at the expense of the manufacturer. See *Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement*, *supra* note 41, at 2.

<sup>44</sup> *Id.* at 3.

<sup>45</sup> The price ceiling is determined by the "rebate percentage": a percentage amount equal to "the average total [Medicaid] rebate" divided by the "average manufacturer price". 42 U.S.C. §§ 256B(a)(2) (2011).

<sup>46</sup> 42 U.S.C. § 1396R-8(k).

<sup>47</sup> See *Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement*, *supra* note 41, at 11.

<sup>48</sup> *Id.* at 20.

<sup>49</sup> *Id.* at 2.



get worse since the passage of the Patient Protection and Affordable Care Act (ACA). The ACA expands the reach of the 340B program by expanding the list of covered entities and increasing the size of the required drug discounts<sup>50</sup>.

### ***3. Market consolidation and competition***

Another possible contributor to drug shortages is the increased merger and acquisition activity among drug manufacturers. As the argument goes, when manufacturers consolidate, there are fewer “niche” firms willing to produce less-lucrative generic drugs<sup>51</sup>. The resulting behemoths are more likely to focus their greatly-enlarged resources on producing more-lucrative pharmaceuticals.

The problem with this explanation is both evidentiary and theoretical. On the matter of evidence, the little data that exists on the issue suggests that there is little consolidation activity in the drug production industry<sup>52</sup>. Regarding theory, this explanation ignores that consolidation among manufacturers could just as likely *mitigate or prevent* shortages by reducing competition in an otherwise cutthroat industry. While it is true that most of the drugs in short supply are made by only one or two companies<sup>53</sup>, this fact does not explain why the few remaining firms would take advantage of their larger market share to create operational efficiencies. The resulting larger firms are uniquely placed to attain cost efficiencies by purchasing suppliers in bulk, for example.

### ***4. Regulatory overreach by the FDA***

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<sup>50</sup> See §§7101-7103 of the Patient Protection and Affordable Care Act.

<sup>51</sup> Letter from Senator Herb Kohl, U.S. Senate, to Chairman Jonathan Leibowitz, Federal Trade Commission (May 19, 2011) (Recommending that the FTC give close antitrust scrutiny to drug firm mergers because “as the number of drug manufacturers decline, there are fewer and fewer manufacturers of older and less profitable products.”).

<sup>52</sup> See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 6 (“We have identified fewer than a dozen mergers since 2005, largely relatively small in nature, contradicting the idea that there has been a lot of recent consolidation. As merger and acquisition activity does not appear to have grown in the last 5 years, it does not appear to be a factor in the recent surge of sterile injectable drug shortages.”).

<sup>53</sup> See IMS Institute for Healthcare Informatics, *supra* note 7, at 9.

The expense of regulatory compliance also potentially contributes to drug shortages. Regulatory compliance can be broken down into two types relevant to the drug shortages discussion: (1) “Current good manufacturing practices<sup>54</sup>” (cGMPs) that increase the costs of existing drug production; and (2) regulatory requirements for amendments to abbreviated new drug applications (ANDA) that increase the costs of changes to existing manufacturing.

Current good manufacturing practices apply to all drug producers, whether branded or generic. They refer to FDA regulations regarding the design, monitoring, and control of drug manufacturing processes and facilities. Inability to comply with cGMP has been cited as a major contributor to drug shortages<sup>55</sup>. If a company does not comply with cGMP (as determined by the FDA during inspections), any drugs it makes are considered “adulterated” and subject to seizures and injunctions<sup>56</sup>.

The expense of complying with cGMPs may dissuade new entrants or force out current manufacturers of drugs in short supply. New entrants already face large start-up costs before they can enter the market for a new drug. The additional compliance burden of cGMPs may tip the balance in favor of staying out of the new market. In addition, cGMPs may also act to force existing manufacturers out of the market. In the generics market that is particularly prone to shortages, profitability is very sensitive to small increases in costs<sup>57</sup>. Compliance costs are

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<sup>54</sup> According to the FDA website, cGMPs are regulations that establish systems to assure proper design, monitoring and control of manufacturing processes and facilities. The goal of cGMP regulations is to establish strong quality control systems and robust operating procedures.

<sup>55</sup> See American Society of Health-System Pharmacists, *Drug Shortages Summit 5* (Nov. 5, 2010) (“Manufacturing-related causes that contribute to drug shortages are multifactorial. Inability to fully comply with [cGMPs], which results in production stoppages or recalls, was considered a major cause.”);

<sup>56</sup> A drug is “adulterated” if it is “not operated or administered in conformity with current good manufacturing practice.” 21 USC § 351(a)(2)(B) (2011).

<sup>57</sup> See Michael P. Link et al., *Chemotherapy Drug Shortages in the United States: Genesis and Potential Solutions*, 30 J. Clinical Oncology 692, 693 (2012) (nothing that the vast majority of shortages have been concentrated in sterile injectables, which are relatively inexpensive to purchase and suffer from low profit margins).

especially high for sterile injectables, the category of drugs that are uniquely vulnerable to supply disruptions.

Under the Hatch-Waxman Act<sup>58</sup>, generic drugs do not have to go through full-scale clinical testing if they can prove that they have the same quality, strength, purity and stability as brand-name drugs<sup>59</sup>. To submit an abbreviated new drug application (ANDA), drug manufacturers must prove bioequivalence<sup>60</sup>. Although the ANDA approval process produces huge cost savings by avoiding wasteful and duplicative clinical testing, other regulatory requirements impose substantial costs on generics production. In particular, changes to the ANDA generally require FDA approval, which is an expensive and time-consuming endeavor for all but the most efficient firms<sup>61</sup>.

For drug production, many types of manufacturing changes require amendments to the ANDA<sup>62</sup>. Section 506A of the FDCA lists the notice and approval requirements for such changes to an approved manufacturing process. Changes to (1) components and composition, (2) manufacturing sites, (3) manufacturing process, (4) specifications, (5) container closure system, and (6) labeling, as well as (7) miscellaneous changes may all qualify as “postapproval changes” to the ANDA<sup>63</sup>. The specific reporting requirements depend based on whether the changes qualify as “major”, “moderate” or “minor”<sup>64</sup>.

Increased competition in the generics industry means that manufacturers are forced to price close to cost. A small price advantage in the cost of supplies, for example, could be the

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<sup>58</sup> See Drug Price Competition and Patent Term Restoration Act of 1984 (colloquially known as the Hatch-Waxman Act).

<sup>59</sup> See 21 C.F.R. (S) 314(a) (2011).

<sup>60</sup> A generic must perform in the same manner as the innovator drug to qualify as bioequivalence. See *id.*

<sup>61</sup> See Dep't of Health & Human Services, Food and Drug Administration, *Changes to an Approved NDA or ANDA*, at 1 (2004).

<sup>62</sup> See 21 C.F.R. (S) 314.70(a) (2011).

<sup>63</sup> See *Changes to an Approved NDA or ANDA*, *supra* note 61, at 1.

<sup>64</sup> See *id.* at 3-4.

tipping point that makes the generics production profitable or prohibitive. If the manufacturer finds that an alternative supply source would make production profitable, they may be unable to make the switch because of the costs of going through an ANDA amendment procedure<sup>65</sup>. As a result, generics manufacturers may find themselves “locked in” to bad supply chains or manufacturing procedures, simply because efficient switches are prohibitively expensive.

### ***5. Product liability litigation***

Litigation expenses are just another cost of doing business. In the pharmaceutical industry, lawsuits represent a sizeable share of expenses<sup>66</sup>. A study by the National Bureau of Economic Research found that product liability may reduce efficiency of drug manufacture by raising prices without encouraging firms to invest further in product safety<sup>67</sup>. The NBER study notes that the National Vaccine Injury Compensation Program, which shielded vaccine manufacturers from liability suits, was associated with a rapid decrease in prices for these drugs<sup>68</sup>.

It is unclear how relevant these findings are in the context of sterile injectables and other classes of drugs most prone to shortages. There is little information on the extent of product liability litigation for drugs in short supply, nor is there relevant information on the expected costs of the lawsuits. According to the NBER report, low marginal costs of production in drug and vaccine industries means that “even small legal costs can account for a significant fraction of

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<sup>65</sup> See *Drug Shortages Summit*, *supra* note 55, at 3 (“[R]egulatory barriers include the time for FDA review of Abbreviated New Drug Applications (ANDA) and supplemental applications, which are required for changes to FDA-approved drug products... Manufacturers described this approval process as lengthy and unpredictable, which limits their ability to develop reliable production schedules.”).

<sup>66</sup> See Tomas J. Philipson et al., *The Effects of Product Liability Exemption in the Presence of the FDA*, National Bureau of Economic Research 10 (2009) (“While estimates of the costs of liability for pharmaceuticals and devices are few, there are indications that these costs are substantial, especially when viewed as a share of marginal costs.”).

<sup>67</sup> See *id.* at 21.

<sup>68</sup> See *id.* at 30.

overall marginal costs<sup>69</sup>. Given the other contributors to shortages – such as price controls and strict regulatory requirements – it is unclear whether liability expenses are a significant contributor to increased costs.

### ***6. Prescribing patterns by doctors***

The prescribing habits of doctors have also been cited as a contributor to drug shortages<sup>70</sup>. Like any other economic actors, physicians may alter their work behavior to maximize their economic returns. When it comes to treating patients, economic incentives may lead doctors to favor certain treatments over others.

Oncologists in particular are especially vulnerable to these incentives given that they rely on drug sales for half their revenue<sup>71</sup>. Many cancer drugs are purchased by patients directly from their oncologist, rather than from a pharmacy. As mentioned previously, Medicare Part B only pays a 6% premium over the wholesale drug price. Since some of this 6% premium is shared with the manufacturer, oncologists are left with a small profit margin on the drugs they prescribe. Because the reimbursement is a percentage of the price of a drug, oncologists wishing to maximize their profits should favor branded drugs over lower-priced generics. Indeed, there is empirical evidence of this change in prescribing patterns<sup>72</sup>. In addition, Medicare Part B does not

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<sup>69</sup> *Id.* at 39.

<sup>70</sup> See, e.g., Gatesman & Smith, *supra* note 24, at 1655 (“oncologists need incentives to use generics”); Reed Abelson, *Drug Sales Bring Huge Profits, And Scrutiny, to Cancer Doctors*, N.Y. Times, Jan. 26, 2003 (“cancer specialists can make huge sums -- often the majority of their practice revenue -- from the difference between what they pay for the drugs and what they charge insurers and government programs”).

<sup>71</sup> See Gatesman & Smith, *supra* note 24, at 1654 (“In recent decades, oncology-drug prices have skyrocketed, and today more than half the revenue of an oncology office may come from chemotherapy sales, which boost oncologists’ salaries and support expanding hospital cancer centers.”).

<sup>72</sup> See Mireille Jacobson et al., *How Medicare’s Payment Cuts for Cancer Chemotherapy Drugs Changed Patterns of Treatment*, 29 *Health Affairs* 1394, 1394 (2010) (Statistical analysis showed that since Medicare Part B became based on ASP, “physicians switched from dispensing the drugs that experienced the largest cuts in profitability... to other high-margin drugs.”).

fully reimburse the cost of administering complex sterile injectables<sup>73</sup>. If the physician is not reimbursed for the services associated with sterile injectables and other oncological drugs, they may be less likely to prescribe these medications. By prescribing fewer of these drugs, the demand is depressed and manufacturers have less of an incentive to manufacture these pharmaceuticals.

### ***7. Production-related problems***

Another commonly-cited culprit in the drug shortages debate is the issue of production-related problems at drug manufacturers<sup>74</sup>. The leading reasons for shortages reported to the FDA are problems at the manufacturing facility, delays in manufacturing or shipping, and active pharmaceutical ingredient shortages<sup>75</sup>. The ASHP has found through its analysis that drug shortages are often the result of problems with the manufacturing process, loss of a manufacturing site, delays and capacity issues and shortages of raw materials<sup>76</sup>. Manufacturing difficulties may be particularly acute for sterile injectables, the types of drugs most prone to shortages. Sterile injectables require a complex production process and long lead time to bring up to speed. In addition, sterile injectables must be manufactured “just-in-time” because of their

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<sup>73</sup> *See id.*

<sup>74</sup> *See, e.g., Examining the Increase in Drug Shortages: Hearing Before the H. Comm. on Energy & Commerce*, 112th Cong. (Sept. 23, 2011) (statement of Dr. W. Charles Penley, American Society of Clinical Oncology) (“Companies that experience raw material or other manufacturing complications do not have the incentive to invest resources required to upgrade facilities or correct quality problems; it is not a good business decision”); Thomas M. Burton, *GAO Report Blames Drug Shortages on Manufacturing Problems*, Wall St. J., Dec. 14, 2011 (““Manufacturing problems were the primary cause of most shortages,” says an analysis by the Government Accountability Office.”); Dep’t of Health & Human Services, Food and Drug Administration, *A Review of FDA’s Approach to Medical Product Shortages* (2011).

<sup>75</sup> *See A Review of FDA’s Approach to Medical Product Shortages*, supra note 74, at 4 (“The leading primary reasons for the shortages reported to FDA were problems at the manufacturing facility (43%), delays in manufacturing or shipping (15%), and active pharmaceutical ingredient shortages (10%).”).

<sup>76</sup> *See Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Kasey Thompson, Vice President, American Society of Health-System Pharmacists).

relatively-short shelf life, making it more difficult to forecast the optimal production level<sup>77</sup>. One estimate is that 54% of shortages of sterile injectables are due to manufacturing problems<sup>78</sup>. Some of the most serious quality control problems have affected entire plants, resulting in shortages of many drugs.

Although it is tempting to view manufacturing problems as an independent cause of shortages, the more likely story is that manufacturing problems are just a consequence of another underlying cause. Most manufacturing problems would be avoidable if a firm simply invested adequate resources to improving its facilities and procedures; if so, then the question becomes why doesn't a firm spend more to improve its production processes? A plausible answer is that manufacturers shy away from expensive improvements because of inadequate incentives to invest. Put simply, if they are not making enough money on a certain product line, they will have little reason to invest to improve that line. If a manufacturer was making a generous profit on a drug, it would invest time and effort into making sure manufacturing went smoothly.

There is some evidence of the profit-dependence of manufacturing prowess. For one, supply disruptions are rare for branded (i.e. higher-priced) drugs with market exclusivity, even for difficult-to-manufacture sterile injectables<sup>79</sup>. Manufacturers have fewer problems with drugs that are shielded from competition, even if these pharmaceuticals have never before been mass-produced. In addition, drugs that are in short supply in one market are frequently available in

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<sup>77</sup> Many drugs hit by shortages have a limited shelf life which makes holding excess inventory expensive. The result is that drug manufacturers will try to keep their inventories as low as possible by erring on the side of undersupply. See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 4.

<sup>78</sup> See *id.*

<sup>79</sup> Although approximately half of the sterile injectable market is generic, a disproportionate amount of the sterile injectables in short supply are generics. That is, generic sterile injectables are more prone to shortages than their branded counterparts. See, e.g., IMS Institute for Healthcare Informatics, *supra* note 7, at 5 (“In terms of the type of product, 83% of products are multi-sourced generics without patent protection or other forms of market exclusivity”); *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 6 (“Sterile injectable oncology drugs include both generic and branded drugs. Approximately half the market is generic and the proportion of the market that is generic is rising.”).

another market<sup>80</sup>. If the drug shortages were due to problems with the manufacturing process, it does not explain why the shortages are confined to particular markets.

Another complication is that it is unclear to what extent manufacturing problems are simply a consequence of rigorous FDA regulation. As the section on Current Good Manufacturing Practices discusses, there has been a fairly recent tightening of regulatory requirements for generics and sterile injectable drugs. What may look like a manufacturing problem today may have been an acceptable practice yesterday. That is, it is hard to know how much of the recent upswing in manufacturing problems is due to something other than enhanced regulatory scrutiny by the FDA.

#### ***8. Group Purchasing Organization contracts***

A less-frequently cited contributor to shortages is the contracting process occurring between manufacturers and Group Purchasing Organizations (GPOs) for drug purchases<sup>81</sup>. Most hospitals and other healthcare organizations do not purchase pharmaceuticals directly from the manufacturer but do so through GPOs. Thus, prices are negotiated between the manufacturer and GPOs<sup>82</sup>. Most sterile injectable drugs are purchased through GPOs<sup>83</sup>. The terms of purchase are drawn up in GPO contracts which contain many provisions unique to the pharmaceutical industry. Relevant to this paper are what known as “failure to supply” clauses, which apply when

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<sup>80</sup> See Hagop M. Kantarjian, *Chemotherapy Drug Shortages: A Preventable Human Disaster*, 2 American Society of Clinical Oncology Post (drug shortages are a "uniquely American problem" because prices of generics are slightly higher in Europe than in the United States).

<sup>81</sup> See, e.g., *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research); *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 5.

<sup>82</sup> This is a slight simplification, because although GPOs negotiate prices with manufacturers, wholesalers actually take physical possession of the drugs. The wholesalers receive a cut from the manufacturer and sell these drugs to the GPO at the GPO negotiated price. However, for the purposes of this discussion, this difference is not significant because the relevant contract provisions are those that deal directly with the manufacturer. See *Economic Analysis of the Causes of Drug Shortages*, *supra* note 2, at 5.

<sup>83</sup> See *id.*



the manufacturer is unable (or unwilling) to deliver the drugs<sup>84</sup>. Failure to supply clauses require the manufacturer to pay the GPO the difference between the contract price and the acquisition price (for drugs acquired from other sources). However, these clauses offer no reimbursement if there are no alternate supplies for a drug.

It is unclear whether failure to supply clauses would tend to exacerbate or mitigate drug shortages. The FDA takes the position that strengthening failure to supply clauses would encourage manufacturers to hold excess inventory and keep manufacturing capacity online<sup>85</sup>. However, the FDA provides no evidence to support its point and it is just as plausible that tightening failure to supply clauses would exacerbate shortages. Such clauses represent an additional cost of doing business because manufacturers will have to include the expected penalties into their profit projections. No economically rational manufacturer will take on the risk of production problems without receiving some additional compensation. Higher costs must be offset by higher prices to maintain the same profit margin.

GPO contract may also contribute to shortages because of the way they arrange bulk purchase agreements with manufacturers by setting a fixed price for many types of drugs. In order to win GPO contracts, manufacturers may be willing to sell some drugs below-cost if doing so will allow them to sell other highly-profitable products<sup>86</sup>. The drugs that are sold below-cost are “loss leaders”; these are also the types of drugs especially susceptible to shortages. The problem with a “loss leader” approach to negotiating GPO contracts is that it manufacturers may prefer to discontinue production of a loss leader rather than its price. Perhaps by the terms of the contract, manufacturers cannot raise prices at all, so that the best option is to discontinue

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<sup>84</sup> *See id.*

<sup>85</sup> *See id.* at 15.

<sup>86</sup> *See Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research)

production. Even if manufacturers could raise prices, they may be reluctant to do so for fear of putting at risk future contracts with the GPO<sup>87</sup>. Either way, the result is that there is a perverse incentive for manufacturers to discontinue production of low-profit products.

#### **IV. CURRENT RESPONSES TO DRUG SHORTAGES**

##### ***1. Legislative fixes: Reporting requirements and regulatory fast-tracking***

Drug shortages have become a hot topic in Congress, with both Senate and House Committee hearings on the issue in 2011. The House Subcommittee on Health held a hearing on September 23<sup>rd</sup>, 2011 to examine the increase in drug shortages<sup>88</sup>. Chaired by Representative Joseph Pitts (R-PA), witnesses included representatives of drug manufacturers, oncology clinical directors and specialists as well as the assistant secretary for the Department of Health and Human Services. Representative Pitts limited the hearing to a discussion on industry and clinical experiences with drug shortages and learning what remedies the experts recommended. On December 7<sup>th</sup>, 2011, the Senate Committee on Finance met to discuss the causes and consequences of drug shortages.<sup>89</sup> Witness testimony came from representatives of the American Enterprise Institute and the American Society of Health-System Pharmacists, as well as an oncologist and medical professor. In his hearing statement, Senator Max Baucus (D-MT) told the committee that the early focus of the Senate was on stating the problem of drug shortages and investigating its likely causes. Lastly, another Senate hearing took place on December 15<sup>th</sup>,

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<sup>87</sup> *See id.*

<sup>88</sup> *See Examining the Increase in Drug Shortages: Hearing Before the H. Comm. on Energy & Commerce, 112th Cong. (Sept. 23, 2011).*

<sup>89</sup> *See Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin., 112th Cong. (Dec. 7, 2011).*

2011<sup>90</sup>. The Committee on Health, Education, Labor & Pensions, chaired by Senator Amy Klobuchar (D-MN), focused on the public health concerns related to drug shortages. Healthcare representatives from hospitals and the Department of Health and Human Services provided testimony.

Though some legislation pertaining to drug shortages has been introduced in Congress, the content of the proposed legislation reflects the misplaced concerns of the House and Senate hearings but offer little in terms of long-term fixes. Pending legislation would require drug manufacturers to give the FDA advance notification of expected shortages. Under current law, manufacturers do not have to report supply interruptions to the FDA unless the drug has been designated “medically necessary”. However, under existing law, the FDA lacks an enforcement mechanism to act against manufacturers who are required to report and fail to do so. The result is that effectively, there is no reporting regime.

In the Senate, S. 296 has been introduced by Senator Amy Klobuchar<sup>91</sup>. If enacted, S. 296 would require manufacturers to give the FDA six months advance notice (or as soon as possible for unplanned stoppages) of supply disruptions or production stoppages that could lead to shortages<sup>92</sup>. Senate bill 296 also gives the FDA teeth to enforce the notice requirement by imposing civil monetary penalties on manufacturers that fail to report<sup>93</sup>. A similar House bill, H.R. 2245, has been introduced in the House by Representative Diane DeGette<sup>94</sup>. The main difference between the House and Senate bills is that H.R. 2245 caps the monetary fines that can

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<sup>90</sup> See *Prescription Drug Shortages: Examining a Public Health Concern and Potential Solutions: Hearing Before the S. Comm. on Health, Educ., Labor & Pensions*, 112th Cong. (Dec. 15, 2011).

<sup>91</sup> See *Preserving Access to Life-Saving Medications Act*, S. 296, 112th Cong. (2011).

<sup>92</sup> Notice is required “at least 6 months prior to the date of such discontinuance or planned interruption or adjustment”. *Id.* at §2(a).

<sup>93</sup> See *id.*

<sup>94</sup> See *Preserving Access to Life-Saving Medications Act of 2011*, H.R. 2245, 112th Cong. (2011).

be imposed on intransigent manufacturers<sup>95</sup>. The precise size of the penalties in S. 296 is left to future rulemaking.

There are two problems with this proposed legislation. First, it does not *prevent* shortages; at best, it may give the FDA more time to deal with expected shortages. The proposed legislation would simply require by law what is now largely voluntary. The manufacturer does not have any obligations regarding drug *production* – the sole responsibility is one of *notification*<sup>96</sup> or contacting the FDA if there is a discontinuance, interruption or adjustment to a supply line. Knowing of supply disruptions may allow the FDA to inform affected parties in the supply chain (e.g. patients, doctors, hospitals), but it is unclear why this notice requirement could not be implemented by private contract instead. For example, the GPO and manufacturer contract could require advance notice of supply disruptions, and these private organizations and firms would be better placed to tailor reporting requirements to their needs.

Second, the legislation could actually exacerbate the problem of shortages by steering firms away from product lines that impose regulatory costs. If a company determines that it is no longer good business sense to produce a drug, under the proposed legislation, it will have a difficult time immediately shutting down production; rather, there are several legal hurdles that may encourage the firm to incur the attendant costs and wait six months before cutting off supplies. In addition, the stiff monetary penalties for failing to provide adequate notice may deter manufacturers from taking on risky ventures for fear of raising the ire of the FDA. Asking manufacturers to give at least six months of notice of supply disruptions is in effect asking

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<sup>95</sup> Civil monetary penalties are “not to exceed \$10,000 for each day on which the violation continues” to a maximum of \$1,800,000 “for all such violations adjudicated in a single proceeding”. *Id.* at §506C(b)

<sup>96</sup> *See, e.g.*, S. 296 §2(a)(2) (“A manufacturer of a drug described in paragraph (3) shall notify the Secretary of a discontinuance, interruption, or other adjustment of the manufacture of the drug that would likely result in a shortage of such drug.”) (emphasis added); H.R. 2245 §506C(b)(1) (“A manufacturer of a drug that is subject to section 503(b)(1) and marketed in interstate commerce shall notify the Secretary of a discontinuance or interruption in the manufacture of such drug.”) (emphasis added).

manufacturers to make predictions about demand in inherently unpredictable markets. If the penalty for failing to give adequate notice is high enough, manufacturers may decide to shut down otherwise-profitable production lines in order to avoid FDA discipline.

## ***2. Executive fixes: Directing the FDA to focus resources on the problem***

On October 31<sup>st</sup>, 2011, the White House issued Executive Order 13588 directing the FDA to take steps to reduce prescription drug shortages<sup>97</sup>. In the Order, President Obama identified drug shortages as posing “a serious and growing threat to public health” and directed the FDA to “take steps that will help to prevent and reduce current and future disruptions in the supply of lifesaving medicines”<sup>98</sup>.

The Order directed the FDA to (1) broaden reporting requirements; (2) expedite regulatory review; and (3) refer illicit activities to the Department of Justice. To broaden reporting, the FDA was directed to administer the reporting requirements in 21 U.S.C. §356C and require drug manufacturers to provide “adequate notice” of manufacturing disruptions<sup>99</sup>. The FDA was also advised to expedite regulatory review of new drug suppliers, manufacturing sites, and manufacturing changes “whenever it determines” that doing so could help mitigate shortages<sup>100</sup>. Lastly, the FDA was directed to refer to the DOJ any evidence of market participants stockpiling affected drugs or selling them at exorbitant prices<sup>101</sup>.

The Executive Order is unlikely to have much practical effect on drug shortages. The Order lacks the authority to make changes to Medicare reimbursement policies or drug manufacturing requirements. Directing the FDA to do whatever it can within its statutory limits

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<sup>97</sup> The Order was titled “Reducing Prescription Drug Shortages”. Exec. Order No. 13,588, 76 Fed. Reg. 68,295 (Nov. 3, 2011).

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

<sup>99</sup> *Id.*

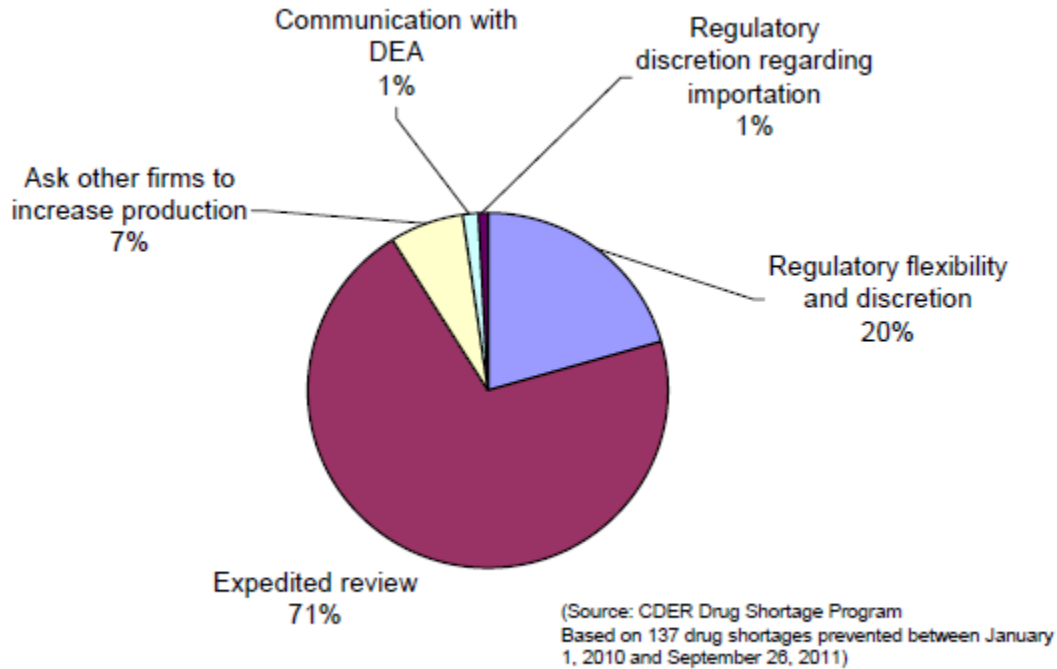
<sup>100</sup> *Id.*

<sup>101</sup> *Id.* (“The FDA shall communicate to the Department of Justice (DOJ) any findings that shortages have led market participants to stockpile the affected drugs or sell them at exorbitant prices.”).

is simply restating what the FDA has already been trying to do. At most, the Order may have value in attracting public attention to the drug shortages problem.

***3. FDA fixes: Expedited review of regulatory submissions, temporary importations of foreign drugs and broadened reporting of potential shortages***

The FDA has tried to alleviate shortages by three means<sup>102</sup>: (1) Temporary importation of unapproved foreign drugs; (2) expedited approvals of regulatory submissions (such as changes to manufacturing processes); and (3) broadened reporting of potential shortages. A visual of the FDA's responses is shown below.



**Figure 3: Primary FDA Action Taken Between 2010-2011 (Drug Shortages Prevented)**

The FDA has attempted to eliminate red tape by expediting approval of regulatory submissions and allowing temporary emergency importation of certain products. Importation is a quick-fix of limited applicability. Assuming that the drugs can even be sourced overseas (that is,

<sup>102</sup> See *A Review of FDA's Approach to Medical Product Shortages*, supra note 74, at 20.

that they are not in short supply themselves), there is a safety concern because foreign suppliers are not necessarily FDA-approved<sup>103</sup>. Reducing red tape is a laudable goal, though it is questionable whether the FDA has the right incentives to make this approach work. There is a trade-off between efficiency and safety for many regulations. If the FDA only gets attention for *failures* of regulation, it may have little incentive to relax red tape even if the overall social benefit is higher.

In terms of reporting requirements, the FDA can only require advance notification of production stoppages from sole-source manufacturers of certain life-supporting drugs<sup>104</sup>. More often than not, however, manufacturers fail to provide notification of actual or potential shortages<sup>105</sup>. In addition, the FDA does not have explicit enforcement authority under section 506C, making this provision toothless.

Besides these three approaches, the FDA has also tried to mitigate shortages by simply asking manufacturers of the same or similar products to increase production. According to its report on drug shortages, these requests have frequently been successful<sup>106</sup>. However, it is questionable whether manufacturers are complying with the FDA request out of basic business sense or something more nefarious. It is unlikely the FDA request was the trigger for a rational, business decision based on expected demand and price for a product. Rather, fear of running

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<sup>103</sup> *Examining the Increase in Drug Shortages: Hearing Before the H. Comm. on Energy & Commerce*, 112th Cong. (Sept. 23, 2011) (statement of Dr. Howard K. Koh, Assistant Sec'y of Health, Dep't of Health & Human Services) (“The product may already be in shortage abroad, and importation to the United States could exacerbate the shortage. In addition, while there may be foreign suppliers that possess or have access to a particular drug, these suppliers are not necessarily FDA-approved and may need to be inspected and their drug labels evaluated before a product can be imported into the United States.”).

<sup>104</sup> A manufacturer that is the “sole manufacturer of a drug” must notify the Secretary of a “discontinuance of the manufacture of the drug at least 6 months prior to the date of the discontinuance”. 21 U.S.C. § 356C(a) (2011).

<sup>105</sup> See *A Review of FDA's Approach to Medical Product Shortages*, supra note 74, at 19.

<sup>106</sup> According to FDA, in 2010 the agency was able to prevent 38 drug shortages in 2010 and 99 in 2011 when they were made aware of production interruptions ahead of time. See *id.* at 41.

afoul of the agency's good graces may provide a better explanation. Regulatory retribution can impose significant costs on firms, and for at least the short-run, manufacturers may prefer to stay in the FDA's good graces.

#### ***4. Market fixes: Development of grey markets to take advantage of shortages***

In its own sinister way, the market has dealt with drug shortages. Grey markets are market "fixes" in the sense that these are irregularities that tend to emerge when ordinary supply-demand mechanisms fail. Where customers are willing to pay more than the binding market price to purchase a product, non-traditional channels will inevitably emerge to satisfy that demand.

The grey market, sometimes known as a parallel market, is a supply channel through which a good is traded through distribution channels that are illegal, unofficial or unauthorized by the manufacturer. Two preconditions for grey markets are that grey marketers must have a source of supply and that the price differentials among the various markets must be great enough to make the transaction profitable<sup>107</sup>. In the context of drug shortages, both of these preconditions are satisfied. The drugs may be in short supply through *traditional* market channels (i.e. through the manufacturer/wholesaler/GPO/hospital supply chain), but may still be available in illicit outlets. Any link in the supply chain – whether manufacturer, hospital or patient – may participate in the grey market. The price differential is due to the price controls that limit the sales price of the drug in regular channels. Since many of the drugs in short supply are life-saving sterile injectables, the price they command on a truly free market may be exorbitant.

Not surprisingly, the advent of drug shortages been accompanied by a marked rise in the number of grey markets. A survey by the Premier Healthcare Alliance found that grey markets

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<sup>107</sup> See Dale F. Duhan & Mary Jane Sheffet, *Gray Markets and the Legal Status of Parallel Importation*, 52 J. Mktg. 75, 76 (1988).



were common for drugs that were back-ordered or otherwise unavailable. The average markup was 650% above the manufacturer's selling price, with the largest markups concentrated for drugs needed to treat the critically ill<sup>108</sup>. The concern with grey markets is that they put drug integrity at risk. Drugs often have strict storage and handling instructions passed to the buyers. In traditional market channels, these safety requirements can be strictly enforced. However, grey markets lack the same rigorous controls. Concerns about "drug speculation" via grey markets prompted an investigation by Representative Elijah Cummings (D-MD) of the House Committee on Oversight and Government Reform<sup>109</sup>. Launched in October 2011, the investigation focused on drug supply companies that charged prices many times higher than those authorized and negotiated with drug manufacturers. Whether the investigation has something other than symbolic value is questionable; when the free market price for a product is high enough, firms may find it irresistible to participate in the illicit channels.

## **V. INADEQUATE PROFITS AND DRUG SHORTAGES**

### ***1. The profit problem***

As discussed, there are many players in the drug shortages debate. The commonly-cited causes focus on different parts of the drug supply chain: Manufacturers, physicians, hospitals, as well as private and public insurers. Given the plethora of causes, how do we tackle the problem of drug shortages? The data available on the contributors is limited, and many of them may be

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<sup>108</sup> The average markup was 650%, but even higher markups (exceeding one or two thousand percent) were found in back-ordered critical care and oncology drugs. *See* Coleen Cherici, Buyer Beware: Drug Shortages and the Gray Market, Premier Healthcare Alliance 2 (2011).

<sup>109</sup> As part of the investigation, Representative Cummings sent document requests to five "grey market" drug companies suspected of charging exorbitant prices for drugs in short supply. *See* Potential Prescription Drug Price Gouging: Investigation by the H. Comm. on Oversight & Gov't Reform, 112th Cong. (Oct. 5, 2011).

interrelated such that one reinforces the other. Given this complexity, any proposed solution may seem likely to miss the mark or to have an insignificant impact, if at all.

Though the problem is complex, it is important not to confuse the consequences with the causes. From an economic perspective, there is one “ultimate cause” of drug shortages when you consider the economic incentives of the actors: Not enough profits. Supply is the result of a manufacturer’s desire to earn profits. If the drug industry were a true free market, drug manufacturers would be free to set the optimal price for their products based on forecasted demand. The profit motive reigns supreme and economically rational drug manufacturers would select a production level and product price to maximize profits. That is, assuming the manufacturers, physicians, hospitals, and private and public insurers are economically rational actors, their behavior is primarily profit-driven.

Economic analysis of drug shortages by the Department of Health and Human Services supports this point. This report found that shortages have been “concentrated in drugs where the volume of sales and drug prices were declining in the years preceding a shortage, suggesting that manufacturers are diverting capacity from shrinking lines of business to growing ones”<sup>110</sup>. This finding is elementary economics. Where the volume of sales is declining (which is possible even if demand remains high) and prices are also declining, the manufacture will see fewer profits. When deciding between a low-volume low-price drug and a high-volume-high-price alternative product, it is clear that an economically rational manufacturer would choose the latter.

Further support for the profit motive comes from the fact that the majority of drugs in short supply have three or fewer suppliers<sup>111</sup>. These suppliers are not the same across drugs;

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<sup>110</sup> *A Review of FDA's Approach to Medical Product Shortages*, supra note 74, at 12.

<sup>111</sup> See IMS Institute for Healthcare Informatics, supra note 7, at 9.

overall, many firms supply the drugs<sup>112</sup>. This data shows an interesting phenomenon. In the generic injectables market, though demand generally remains quite high, the supply of the critical life-saving drugs is staying the same, suggesting that the many potential suppliers are unwilling to shift gears and enter the market. This leads to the question, why are suppliers staying out of a (at first sight) lucrative market where there is strong demand for their products? From the perspective of economic analysis, the answer is simple: New entrants are staying out because of the insufficient profits<sup>113</sup>.

Many reports make a cursory mention of inadequate profits in their discussion of causes. However, profits are almost always treated as an “in addition to” factor. For example, the FDA report on drug shortages highlights manufacturing problems *and* low profits as potential contributors, as though these two causes were separable<sup>114</sup>. Another example is the Senate Committee statement by a representative of the ASHP that “many drug shortages are the result of quality issues in the manufacturing process”<sup>115</sup>. The correct approach is to see that manufacturing problems *are a result of* low profits. Firms will invest less in reliable but expensive production processes if their profits are too low.

## ***2. Price ceiling/cost floor model for a single competitor***

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<sup>112</sup> While over one hundred manufacturers supplied products on the drug shortages list, two-thirds of these drugs had three or fewer suppliers. *See id.*

<sup>113</sup> Generic manufacture is unattractive because many generics are sold for slim profit margins, if any. In some cases, the drugs are sold at a loss because of hikes in production and distribution expenses. See, e.g., *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research); *Examining the Increase in Drug Shortages: Hearing Before the H. Comm. on Energy & Commerce*, 112th Cong. (Sept. 23, 2011) (statement of Dr. W. Charles Penley, American Society of Clinical Oncology (“Shortages in cancer drugs are almost exclusively in generic sterile injectables, which are generally inexpensive drugs with a very low profit margin.”)).

<sup>114</sup> *See A Review of FDA's Approach to Medical Product Shortages*, supra note 74, at 3, 30.

<sup>115</sup> *See Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Kasey Thompson, Vice President, American Society of Health-System Pharmacists).

The best way to demonstrate how the causes of drug shortages are ultimately related to profits is via elementary economics diagrams as shown below. These are simple supply-demand curves which can be used in a fairly stylized example to discuss the impact of price ceilings and cost floors (i.e. price floors). Price ceilings are maximum prices that may be charged for goods. These maximums may be *de facto* or *de jure*: Charging lower prices may be illegal, or a regulatory scheme may make it uneconomical to charge less (e.g. Medicare Part B reimbursement policies). Price ceilings are thus the effective maximum price that manufacturers can charge for their products. According to the earlier discussion, the price ceiling is determined by the Medicare reimbursement policies as well as Group Purchasing Organization contracts. Before explaining the effect of price ceilings on quantity supplied (see Figure 4), it is important to highlight the *ideal* result – what would happen in a truly free market without government-imposed price controls. In Figure 4, this ideal scenario is represented by  $p^*$  and  $q^*$ , the intersection of the supply and demand curves. This point is known as the market equilibrium, which represents the natural resting point of quantity sold and purchase price.



**Figure 4: Effect of Price Ceilings on Supply**

Price ceilings result from a lack of patent protection and limited demand for generic injectable drugs, factors which reduce the market power of these manufacturers. Along with

effective price controls imposed by Medicare reimbursement policies, the price ceiling becomes even more intractable. The result of a price ceiling is that prices are inelastic and cannot easily reflect growing demand or rising costs.

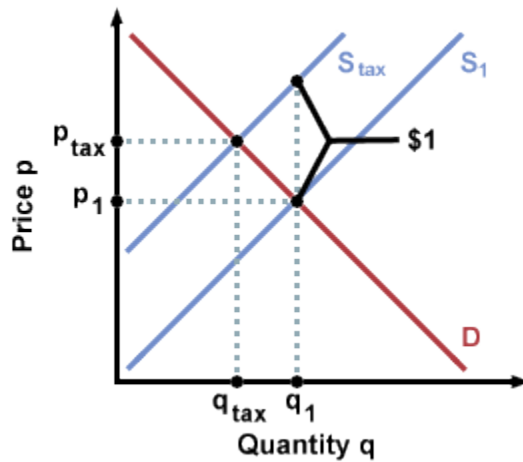
In an imperfect market where there is a price ceiling, the market equilibrium changes. In Figure 4, the price ceiling is marked by  $p_{\text{ceiling}}$ . The price ceiling could be an explicit maximum price set by law, or it could be an effective price control set by a contract with a consolidated, powerful buyer. Where there is a price ceiling, the supply-demand graph changes as follows: The demand increases to  $q_d$  because buyers are attracted by the low price. However, the price is artificially low. The amount the supplier is willing to sell plummets to  $q_s$ . Obviously,  $q_s$  is less than  $q_d$ , which means that there is a supply shortage in this market. So in this stylized example, price ceilings introduce shortages. In the case of drug markets, the demand curve may not be quite so flexible as in Figure 3. Demand is likely highly inelastic (that is, not susceptible to fluctuations even with large price changes) because patients will buy life-saving medications at almost any cost. Drugs that treat critical conditions are likely to have highly inelastic or fixed demand. In the context of Figure 4, this fact does not change much. As before, the supplier is only willing to sell quantity  $q_s$  of the drug while the buyer may be unaffected by the price ceiling because whatever the price, his demand does not markedly change.

There is some empirical evidence linking drug shortages to inadequate profits. A study by the National Bureau of Economic Research suggests that price controls stymie drug production by dampening profit margins and discouraging new entrants<sup>116</sup>. Economic analysis by the Department of Health and Human Services found that drugs that eventually experience a

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<sup>116</sup> See Jean O. Lanjouw, Patents, *Price Controls and Access to New Drugs: How Policy Affects Global Market Entry*, National Bureau of Economic Research 42 (2005) (“the standard argument regarding price regulation – that it will dissuade market entry – appears to have more relevance among the high-income countries. For these countries, extensive price control is always found to lower the probability of market entry”).

shortage have an average prices decrease in every year leading up to the shortage<sup>117</sup>. By contrast, there was an average price *increase* for drugs that never experienced a shortage in the relevant period. Though theoretically, lost revenue from capped prices could be recouped by increased market share, the relatively stable absolute demand for sterile injectables and other drugs in short supply makes purchasing demand inelastic and somewhat fixed.



**Figure 5: Effect of Cost Floors on Supply**

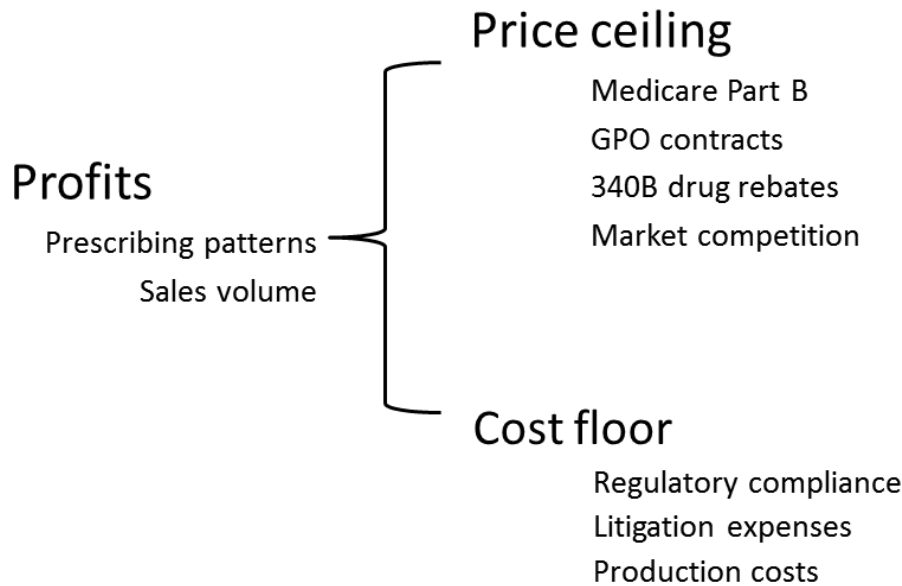
Cost floors, not to be confused with price floors<sup>118</sup>, also change the market equilibrium point, though in a subtly different manner. Cost floors are the minimum expenses necessary to produce a certain drug, taking into account marginal cost of production as well as the distributed fixed capital costs. Marginal costs of production includes the material and labor costs of producing one more unit of a good. Capital costs of production include construction costs and

<sup>117</sup> See, e.g., *A Review of FDA's Approach to Medical Product Shortages*, supra note 74, at 12; *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research) (“The mean price decrease over these periods leading up to the shortages averaged of as much as 27%.”).

<sup>118</sup> The term “cost floor”, as used in this paper, refers to average cost of production. This is not to be confused with the common economics term “price floor”. Price floors generally refer to government-mandated minimum *prices* for a certain commodity. Average cost (or the “cost floor” as used in this paper) is calculated by combining marginal cost and fixed cost and dividing this sum by the production quantity.

other fixed and generally one-time expenses incurred in setting up the production process. In the area of sterile injectables, capital costs can be quite high relative to marginal costs of production, due to the low quantity of sales of these medications and the complexity of their manufacture. As explained before, cost floors represent the minimum average cost associated with manufacturing a drug. An economically-rational manufacturer would seek to maximize its profits and hence, minimize its costs. However, costs can only be cut down to a certain point. Perhaps because of the minimum compliance costs associated with FDA regulations, or because of the minimum costs of active ingredients for pharmaceuticals, there comes a point where costs cannot be reduced through smart business sense. Therefore, a firm that wishes to maximize profits *must* sell at some price above this cost floor. This situation is represented by the supply line  $S_1$  in Figure 4. At this supply line, the quantity supplied will be  $q_1$ . If the cost floor is increased, however – if it becomes more expensive to do business – then the supply line will shift to the left of the supply curve. This situation is represented by the supply line  $S_{tax}$ . Although the shift is labeled as tax-induced in Figure 5, there are many ways for the cost floor to increase. For drug shortages, increasingly stringent FDA regulation and enforcement of production brings costs up. If the supply line shifts to the left but the demand line remains the same, the result is that fewer goods are supplied. The quantity supplied becomes  $q_{tax}$ , which is less than  $q_1$  or the optimal supply quantity. A shortage occurs when you include the additional constraint that the price of the goods has to be identical for both supply lines,  $S_{tax}$  and  $S_1$ . When prices are capped but the cost of doing business goes up, the result is that the supplier can only provide  $q_{tax}$  amount of goods, whereas the customers want to buy  $q_1$  quantity of product. Hence, the difference between  $q_{tax}$  and  $q_1$  is the amount by which demand exceeds supply.

The combination of price ceilings and cost floors determines what profits are available to the manufacturer after selling the product. Profits equal revenue minus costs<sup>119</sup>. For drugs that are in short supply, the maximum profit-per-unit is equivalent to the price ceiling minus the cost floor for that drug. A summary of the contributors to price ceilings and cost floors is shown below.



**Figure 6: Causes of Drug Shortages and the Price Ceiling/Cost Floor Model**

At the top is the “price ceiling” line, which is the maximum price manufacturers can charge for their products. Price caps implemented by Medicare Part B and 340B drug rebate programs contribute to the price ceiling. GPO contracts also impose price ceilings because they generally pay a fixed price for a package of drugs. In addition, stiff market competition (or at least, the threat of it) limits the amount manufacturers can charge. At the bottom is the “cost floor” line, representing the minimum costs of production for manufacturers. Besides expenses

<sup>119</sup> Revenue is calculated by multiplying the quantity of goods sold by the price; for the purposes of this paper, it is assumed that the goods are sold at a fixed price (i.e. that there is no price discrimination). Costs are calculated by multiplying the cost floor (also known as “average cost” in economics lingo) by the quantity of goods sold.



associated with operating the plants and purchasing the raw materials, there are also regulatory compliance costs and litigation expenses. Between the price ceiling and cost floor lines are the profits available to the manufacturer for the particular drug. The entirety of this amount may not be available to the manufacturer. The manufacturer may have to split its profits with a physician to ensure the product is prescribed to patients. Total profits are a function of the total sales volume, though as previously discussed, demand is fairly inelastic for sterile injectables.

***3. Price floor/cost ceiling model for multiple competitors***

The price floor/cost ceiling model applies well in the context of an individual firm. The model gives a simple presentation of the factors that determine how much profit there is to make in a particular endeavor. However, the model doesn't take into account the interactions among firms. It looks at the simplified case of a single manufacturer supplying a particular drug. Obviously, this is not the market reality. The drug industry is competitive and natural monopolies are rare. As a result, it makes sense to consider how the price ceiling/cost floor model works when there are multiple competitors. Each drug manufacturer is going to have its own price ceiling and cost floor. Even for the same drugs, firms differ on how much profit they can generate. And even with the same profits, firms differ on how much profit they need to stay in a market. As a result, it makes sense to consider how firms interact with each other .

To begin, consider a case where four competitors decide to enter a promising market for the same generic sterile injectable drug. Assume the competitors – Firms A, B, C and D – have identical fixed costs but different marginal costs of production. Assume Firm A is the most competitive – that is, it has the lowest costs – all the way down to Firm D which is the least competitive.

	<b>Firm A</b>	<b>Firm B</b>	<b>Firm C</b>	<b>Firm D</b>
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<b>Fixed costs (per plant)</b>	\$1 million	\$1 million	\$1 million	\$1 million
<b>Marginal costs (per unit produced)</b>	\$1	\$2	\$3	\$4
<b>Breakeven point if one million units are produced</b>	\$2 million	\$3 million	\$4 million	\$5 million

Since the drugs these firms produce are substitutable (one firm's product is bioequivalent to another firm's product), they will compete for the same group of customers. Because the market initially has four firms, competition will be fierce. To recoup the large fixed costs associated with drug manufacture, the firms will compete on volume. Assume that initially, there is a market demand for four million units. At first, all firms will be producing at capacity, though at different costs. Assuming that a price of at least \$10 per unit can be charged, every firm will have an incentive to manufacture at full capacity.

Though the demand may initially be satisfied by all four competitors, eventually the lower-cost firms will want to increase their market share. They can attract customers away from their rivals by charging a lower price than their competitors. For example, Firm A will be willing to charge less than \$10 per unit since its costs are only \$1 per unit. To satisfy the additional demand, Firm A will be willing to construct additional plants or invest in new production lines. Rival firms will respond by cutting their costs. Assuming a market for 4 million units, Firm A will expand its operations and be willing to supply two, then three and finally four million units

at a lower price than its competitors. That is, Firm A will try to gain market share by achieving economies of scale<sup>120</sup>.

In the end, vigorous competition will drive price down to cost. With each successive round of price-cutting, firms with higher costs will be forced out. Since Firm A has the lowest cost, it will be willing to sell to consumers at a price less than \$10 per unit. Perhaps it will sell at \$5 per unit, in which case, Firm E will be on the verge of exit because \$5 is its breakeven point with respect to profits. Such price-cutting will continue for successive rounds until Firm A will price close to cost. For example, Firm A may be capable of supplying four million units – the entire demand – at only \$1.5 per unit. At this price point, Firms B, C and D will all exit because they will not be able to cover their costs. The result of such price-cutting may be that Firm A will monopolize the market. Even in more optimistic scenarios – for example, one where the price is high enough to cover the costs for all manufacturers – higher-cost firms may exit because they can get higher profits elsewhere<sup>121</sup>. Whatever the exact figures are, the general trend will be toward driving out higher-cost competitors, leaving only a few firms supplying the entire demand. The influence of price ceilings and cost floors on this process of market concentration should be obvious: The lower the price ceiling and the higher the cost floor, the less profitable manufacture is, and the more likely higher-cost firms will have to exit.

As this discussion has suggested, high fixed cost industries can result in price-cutting that drives out many firms. The remaining firms may have little incentive to increase production to

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<sup>120</sup> “Economies of scale” refers to the cost advantages that firms obtain through expansion. The result of functional economies of scale is that average costs (“cost floors” in this paper) decrease. Such economies are most common in industries characterized by large fixed costs. Drug manufacture is one such industry for which huge quantities of production are needed in order to bring average cost down.

<sup>121</sup> The minimum level of profits that a firm needs in order to continue production is a function of its opportunity costs. An “opportunity cost” is the difference between the total profit of the enterprise that was chosen and the total profit of alternative enterprises that were not chosen. All things being equal, an economically rational firm will chose to exit a market if higher profits are available elsewhere.

meet ethereal increases in demand. Consider the following stylized example for a drug that is currently supplied by a single firm.

	<b>Scenario A</b>	<b>Scenario B</b>
<b>Demand</b>	1 million units	1.5 million units
<b>Fixed costs</b>	\$1 million for one plant (total capacity of 1 million units)	\$2 million for two plants (total capacity of 2 million units)
<b>Marginal revenue (calculated by subtracting marginal cost from price)</b>	\$1.20 for each unit sold	\$1.20 for each unit sold
<b>Total profit (assuming the entire demand is satisfied)</b>	\$1.2 million - \$1 million = \$200,000 (subtract fixed costs from the total profits)	\$1.8 million - \$2 million = loss of \$200,000

In this example, Scenario A represents a demand of one million units. Using the figures shown in the table, the end result is that a firm will have \$200,000 of profit by producing at full capacity and selling at a marginal revenue of \$1.20 per unit. This total profit is calculated by subtracting the fixed costs from the marginal revenue (since marginal revenue only includes marginal but not fixed costs).

In Scenario B, the demand for the drug has gone up to 1.5 million units. Assuming the cost floor and price ceiling remain unchanged, the supplier in this market will be unwilling to incur the fixed costs of constructing another plant in order to satisfy the increased demand. The reasons are as follows: Assume the firm decides to produce 1.5 million units. To do so, it will have to construct an additional plant to run at half-capacity. The total fixed costs for constructing

both plants will be \$2 million. However, the marginal revenue remains unchanged because of, for example, government-imposed price caps and *de facto* cost floors. The result is that the firm can only earn \$1.8 million in revenue by satisfying the total demand. However, its fixed costs are \$2 million, which means that in Scenario B, the firm incurs a loss of \$200,000. Obviously, the economically-rational option in Scenario B is to avoid constructing another plant and to simply produce one million units – the capacity of a single plant. This results in a supply shortage.

Going back to the price ceiling/cost floor model, we can readily see the effect of dampened prices and heightened costs on this phenomenon. De facto price ceilings reduce revenues, which affects the incentives of existing and new entrants. Likewise, cost floors also cut into the potential profits. In the example above, price ceilings and cost floors will reduce the marginal profits of production. If marginal revenue decreases, total profits decrease as well. The reduction in profits makes it even less likely that an existing firm will expand its production in Scenario B (or that a new firm will enter the market to satisfy the additional demand).

## **VI. PREVENTING AND MITIGATING DRUG SHORTAGES**

If the price-ceiling/cost-floor model of drug shortages is accepted, the next question becomes, *what, if anything, can be done to resolve the problem?* As discussed, all of the commonly-cited contributors to drug shortages can be understood as dampening profits in one way or another. Some factors impose price ceilings which prevent the manufacturer from increasing its profits by raising the cost of its products. Other contributors create cost floors which stymie any attempt by a manufacturer to further cut costs to keep profits at an attractive level.

What the model shows is that an effective solution has to do one of three things: (1) It can increase the price ceiling, thereby allowing the manufacturer to charge more for its products; (2) it can reduce the cost floor, which makes it cheaper for the manufacture to produce its products; (3) it can allocate a greater proportion of the end profits to the manufacturer, thereby reducing the opportunity cost of continuing drug production. Whatever route is taken, it is imperative that the solutions be long-term fixes. The highly capital-intensive nature of drug production means that manufacturers need confidence that they can sustain any price hikes or cost savings over the long-term. Short-term solutions deter all but the most risk-preferring firms. It is also important that any strategy help private parties help themselves. Solutions that help private parties tailor their own fixes are more likely to stick.

### ***1. Tax subsidies via credits and deductions***

Tax subsidies are one potential fix. Whether in the form of credits or deductions, tax subsidies reduce the cost floor, thus lowering business expenses. Tax subsidies are common in the pharmaceutical industry. Of particular relevance to the drug shortages problem are the tax subsidies established by the Orphan Drug Act of 1983. The purpose of the Orphan Drug Act was to promote the development of drugs used to treat rare diseases or conditions<sup>122</sup>. The Act established a fifty percent tax credit on clinical trial expenses for orphan drugs<sup>123</sup>. The effects of this tax subsidy are difficult to separate from other potential causes, but there has been a marked

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<sup>122</sup> An orphan drug is a drug for a rare disease or condition which affects such few people that there are insufficient financial incentives for firms to develop such drugs. A rare disease or condition means “any disease or condition which... affects less than 200,000 persons in the United States”. 21 U.S.C. § 360aa-ee (2011).

<sup>123</sup> See Sheila R. Shulman et al., *Implementation of the Orphan Drug Act: 1983-1991*, 47 Food & Drug L.J. 363, 365 (among the production incentives created by the Orphan Drug Act were “development grants, protocol 'assistance from the FDA for nonclinical and clinical investigations, tax credits for 50% of qualified clinical testing expenses, and a seven-year period of marketing exclusivity.”).

increase in the number of orphan drugs released since its passage<sup>124</sup>. The success of the tax credit established by the Orphan Drug Act makes this approach particularly attractive for sterile injectables. The expected returns from drugs that treat rare diseases are too low to cover the high fixed costs of research and development<sup>125</sup>. Market incentives such as tax subsidies make up the profit shortfall and boost the attractiveness of orphan drug manufacture. More specifically, tax credits are a type of “push program” which work to reduce the costs of development for orphan drugs<sup>126</sup>.

Similar “push programs” could be used to incentivize sterile injectables production. If the purpose is to encourage improvements to the production process, tax subsidies could be offered to firms that introduce streamlined manufacturing procedures or upgrade existing facilities (e.g. by installing new technologies that reduce quality control expenses). If the purpose is to encourage production of specific types of drugs, tax subsidies could be limited to new entrants or new manufacturing lines for drugs that are likely to be in short supply (e.g. tying credits or deductions to manufacturing sterile injectables). The precise details are a matter for tax authorities to work out, though the advantages of a tax subsidy approach are significant if the administrative costs are kept down.

In terms of supply-demand curves, tax subsidies shift the supply curve to the right. This rightward shift means that the manufacturer will be willing to supply a larger quantity of goods at a particular price. Because the demand curve will remain unchanged, the manufacturer will be willing to accept a lower price for the goods than before. A portion of the surplus from the

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<sup>124</sup> See Henry Grabowski, *Increasing R&D Incentives for Neglected Diseases: Lessons from the Orphan Drug Act* 12 (2003) (noting that although causation is difficult to isolate, “...the more than tenfold increase in the rate of orphan drug approvals since 1983 is indicative that the Act has indeed been a powerful stimulus to increased R&D investment on rare illnesses”).

<sup>125</sup> See *id.* at 2.

<sup>126</sup> See *id.* at 9. (“In the push category, one has R&D cost sharing or subsidy programs. These can be done through tax credits, research grants, and related economic incentives.”).

subsidy will be kept by the manufacturer (in the form of increased profits), and a portion will be transferred to consumer wallets. One potential problem with tax subsidies is that they tend to distort economic behavior. When one activity is subsidized, you are likely to see more of it, for better or for worse. The distortion is not necessarily bad if it can be tailored to achieve desirable outcomes such as the increased production of drugs in short supply.

## ***2. Less stringent CGMPs and cross-border harmonization***

Another valuable fix would be to cut back on FDA regulations in the drug production industry. FDA regulatory prowess contributes to overall consumer safety by ensuring drug integrity. Rigorous FDA regulation of drug production also comes with a cost: Efficiency losses in terms of time and money. The challenge in any regulatory debate is at what point the costs exceed the benefits: Where does one draw the line between excessive red tape and necessary government involvement? Line-drawing is always a difficult exercise, but as discussed previously, there are indications that the current FDA regulations are stricter than they should be.

The goal for the FDA should be to make its regulations as efficient as possible without compromising public safety. It can do so through several changes. First, the Current Good Manufacturing Processes should be relaxed. The FDA should remove any unnecessary barriers to safe and reliable production. Some suggested changes are to streamlining the process for remediating facilities recently taken off line as a result of regulatory action<sup>127</sup>; expediting review of supplements (i.e. requests to expand or modernize manufacturing facilities) to generic drug manufacturing<sup>128</sup>; and fast-tracking Abbreviated New Drug Applications for drugs vulnerable to

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<sup>127</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research).

<sup>128</sup> For the rest of the almost 3,000 supplements that are on backlog, these applications can sit for months and sometimes years owing to a lack of resources to enable their timely review. Though the FDA has an expedited review procedure, it only kicks in when the drugs approach shortage status.



shortages<sup>129</sup>. In terms of supply-demand curves, reduced regulation translates to lower costs for manufacturers. When production costs decline, the supply curve shifts right, meaning that a greater quantity of goods will be supplied at a particular price.

Another regulatory improvement would be to harmonize CGMP requirements across borders. Harmonization means a reduction in cross-border regulatory barriers: A company that has multiple production facilities worldwide can comply with a single set of regulations. Cross-border harmonization would increase the size of markets for manufacturers and make large-scale investments in production more attractive<sup>130</sup>. On the supply-demand curve, the supply curve would again shift right to account for the reduced regulatory costs. Another possible effect is that the demand curve will shift right as the volume demanded increases. When the market grows, the manufacturer will have a greater audience for its products and hence, a greater incentive to increase the quantity supplied.

The most salient criticism of rolling back regulations is that it could compromise safety. as the argument goes, each additional layer of FDA regulations leads to significant gains in terms of health and welfare. One problem with this criticism is that it assumes that regulatory efficiency is a zero-sum game. However, there is no reason to believe that consumer safety is necessarily sacrificed if regulatory burdens are softened. The FDA itself has relaxed regulations to deal with drug shortages, with little or no effect on consumer safety<sup>131</sup>.

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<sup>129</sup> See *Examining the Increase in Drug Shortages: Hearing Before the H. Comm. on Energy & Commerce*, 112th Cong. (Sept. 23, 2011) (statement of Dr. W. Charles Penley, American Society of Clinical Oncology).

<sup>130</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research).

<sup>131</sup> One of the most common responses to drug shortages by the FDA has been to exercise “regulatory flexibility and discretion” and “expedite regulatory reviews”. Though what is meant by “regulatory discretion” is never clearly defined, a report by the FDA suggests that this finding meant that “the benefit

Another problem with this criticism is that it privileges salient gains over invisible losses. If the FDA had more lenient manufacturing standards, for example, it is quite possible that some people would be harmed by defective products. Any system of regulation is imperfect, but the more lenient the standards, the more probable it is that a defective drug will slip through unnoticed. To dodge public criticism, the FDA may have an incentive to avoid these highly visible costs<sup>132</sup>. The resulting invisible losses never enter the accounting. For every patient whose life is saved by rigorous production standards, there may be a patient who never had a chance because the regulations were too onerous.

### ***3. Flexible Medicare Part B reimbursement schedules***

Perhaps the best candidate for reform is the prime suspect in the drug shortages debate: Medicare Part B. The reimbursement policies of Medicare Part B effectively act as price controls by imposing a 6% ceiling on manufacturer profits and a race-to-the-bottom pricing formula. A modest proposal for reform is to move away from the ASP pricing methodology and adopt flexible reimbursement schedules that are better tailored to market conditions. In terms of supply-demand curves, when the price goes up, the quantity supplied increases correspondingly. Demand decreases to the extent it is inelastic, which is usually not the case for life-saving drugs.

One possibility is to base reimbursement on the Wholesale Acquisition Cost (WAC), the price paid by wholesalers on the open market<sup>133</sup>. The WAC is a market-based price that allows

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of the drug was judged to outweigh the risk of the quality or manufacturing issue". See *A Review of FDA's Approach to Medical Product Shortages*, supra note 74, at 20-21.

<sup>132</sup> Daniel P. Carpenter, *The Political Economy of FDA Drug Review: Processing, Politics, And Lessons for Policy*, 23 *Health Affairs* 52,53 ("deciding not just if but when to terminate drug review and approve an application... is driven by the FDA's desire to safeguard its reputation for protecting the public's health").

<sup>133</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research).

firms to incorporate rising production costs and demand<sup>134</sup>. Another option is to increase the reimbursement for drugs deemed in short supply (or drugs susceptible to shortages), with the precise reimbursement amount determined by an individualized review by CMS or some other body<sup>135</sup>. Of course, any reform of Medicare reimbursement policies should account for the risks of price-gouging that motivated the switch to ASP in the first place<sup>136</sup>. There are ways to mitigate price-gouging behavior. For example, reimbursement rates can be tied to prices charged by manufacturers for similar products in other countries or by other payors<sup>137</sup>. Comparison-pricing would force manufacturers to raise prices for several markets at once or else discount Medicare charges. Medicare Part B could also replace its group billing codes with individualized billing codes<sup>138</sup>. This would allow CWS to base its reimbursement on prices for *individual* drugs, rather than the prices for all drugs within a certain *category*.

A more extreme proposal is to transfer drugs from Medicare Part B into Medicare Part D or to adopt the Medicare Part D competitive bidding process for Medicare Part B drugs<sup>139</sup>. Unlike Medicare Part B, Medicare Part D does not impose price controls on prescription drugs. Drugs covered by Medicare Part D are priced via a competitive bidding process<sup>140</sup>. By contrast,

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<sup>134</sup> *Id.*

<sup>135</sup> This would entail “resetting” the ASP of the affected drugs to either the WAC or some other price that better reflects market conditions. *Id.*

<sup>136</sup> See *Medicare Payments for Covered Outpatient Drugs Exceed Providers' Cost*, United States General Accounting Office, Sept. 2001 (“the average wholesale prices – the “list prices” or “sticker prices” set by drug manufacturers and used by Medicare to calculate payment rates – were not representative of the actual costs of these drugs to providers”).

<sup>137</sup> Joseph P. Newhouse, *How Much Should Medicare Pay For Drugs?*, 23 *Health Affairs* 89, 95-96 (2004).

<sup>138</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Scott Gottlieb, Resident Fellow, American Enterprise Institute for Public Policy Research).

<sup>139</sup> See *Strengthening Health and Retirement Security: Hearing Before the H. Budget Comm.*, 112th Cong. (Feb. 28, 2012) (statement of Rep. Paul Ryan, Chairman, H. Budget Comm.).

<sup>140</sup> More specifically, what happens with Medicare Part D is that insurers submit bids to Medicare for the cost of standard coverage in their plans. From these bids, a national average bid is computed, and

drugs covered by Medicare Part B are priced through an administrative mechanism that does not harness market forces to set an appropriate price.

#### ***4. Guaranteed purchase programs and stockpiling***

Besides tinkering with reimbursement rates, some commentators have pushed for guaranteed-purchase programs as well as stockpiling for affected drugs<sup>141</sup>. Under a guaranteed-purchase program, the government would provide a fixed demand for affected drugs by agreeing to purchase a minimum quantity in a certain time period. The guaranteed purchase would remove some of the uncertainty inherent to generics injectables manufacture and encourage production of these products. Under a stockpiling system, the government would purchase and store an emergency supply of drugs that are experiencing (or prone to experience) shortages. Stockpiling would increase demand for drugs, as well as supplement any emergency need for life-saving medication. For reasons discussed at length in the next section, neither guaranteed-purchase programs nor stockpiling are likely to be successful fixes to drug shortages.

#### ***5. Limiting the scope of the 340B drug discount program***

Closely related to Medicare Part B is the 340B drug discount program which also creates a price ceiling for covered prescriptions<sup>142</sup>. Nearly a third of all U.S. hospitals qualify as “covered entities” that are entitled to force drug discounts from manufacturers<sup>143</sup>. The purpose of

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participating insurance plans are subsidized this average amount. By involving market forces in setting the subsidy rate, competitive bidding more accurately reflects the actual costs of the plans.

<sup>141</sup> See Gardiner Harris, *U.S. Scrambling to Ease Shortage of Vital Medicine*, N.Y. Times, Aug. 19, 2011; ASHP, Drug Shortages Summit Summary Report at 7 (Nov. 5 2010).

<sup>142</sup> The 340B program contributes to the price ceiling in two ways. First, it directly limits the price for all drugs sold to covered entities under the program. Second, the program also indirectly contributes to Medicare Part B price caps because 340B prices are incorporated into the reported ASP for each covered drug. See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Rena Conti, Assistant Professor, University of Chicago).

<sup>143</sup> See *Manufacturer Discounts in the Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement*, supra note 41, at 20.

the 340B program is to enable covered entities to stretch scarce federal funding. There is no reason why more rigorous requirements to qualify as a covered entity would not further this goal. The great scope of the program suggests it has become less the exception than the rule for many U.S. hospitals. Alternatively, the Health Resources and Services Administration should perform more rigorous oversight of covered entities to ensure they are not reselling discounted drugs and pocketing the price difference<sup>144</sup>. The HRSA should also be held to task for confirming the eligibility of covered entities<sup>145</sup>. If 340B participation is policed more thoroughly, manufacturer profit margins will not be as severely squeezed by deep discounting. Lastly, a more total solution would be to completely eliminate the program to remove the harmful influence of deep discounts on market pricing<sup>146</sup>. This option may not be politically viable due to the entrenched interests that are unlikely to give up the discounts easily. Regardless, any cuts to the scale of the 340B program will have beneficial effects on the drug shortages problem. The 340B program imposes price ceilings for drug sales to covered entities; limiting the scope of the program removes some of these price ceilings, which will increase the quantity supplied.

## VII. LEARNING FROM VACCINE SHORTAGES

The experience of vaccine shortages, whether for flu vaccines or those involving childhood illnesses, is analogous to the current shortages problem. Between 2000 and 2005, the

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<sup>144</sup> See Gov't Accountability Office, *Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement* 1 (2011).

<sup>145</sup> See *id.* (“Other than relying on self-policing, HRSA engages in few activities to oversee the 340B program. For example, the agency does not periodically confirm eligibility for all covered entity types, and has never conducted an audit to determine whether program violations have occurred.”).

<sup>146</sup> See *Drug Shortages: Why They Happen and What They Mean: Hearing Before the S. Comm. on Fin.*, 112th Cong. (Dec. 7, 2011) (statement of Dr. Rena Conti, Assistant Professor, University of Chicago) (“The elimination of the program would eliminate the deep discounts for drugs that this program offers to some providers in the marketplace. This would in turn raise the reported ASP level for a variety of drugs over a short period of time across the entirety of the domestic market as 340B prices are incorporated into manufacturers’ reported ASPs for each drug.”).

United States experienced severe shortages of vaccines used against influenza and childhood diseases<sup>147</sup>. Although most of the supply disruptions are now resolved, vaccine shortages remain a threat for the foreseeable future<sup>148</sup>. Although there are significant differences between the vaccine and sterile injectables markets, the market similarities warrant a closer look at the vaccine shortage experience.

In terms of similarities, vaccine manufacture is a complicated process because it involves biologics (i.e. biological products) rather than simply chemicals<sup>149</sup>. Sterile injectables involved a similarly complex production process which leads to high production costs that must be recouped. Just as generic manufacture is less attractive than branded manufacture in the ordinary drug market, in the vaccine field it is more lucrative for firms to enter new markets (e.g. by developing the first vaccine for a condition) than to compete in crowded existing markets<sup>150</sup>. The vaccine market also mirrors the sterile injectable market in that vaccine manufacture involves high fixed costs with relatively inelastic demand that attracts only a few producers per vaccine<sup>151</sup>.

### ***1. Causes of vaccine shortages***

The usual suspects are at play when it comes to possible contributors to vaccine shortages. For several years, vaccines sold to the federal government have been subject to statutory price caps, though these have since been repealed<sup>152</sup>. *De facto* price controls can still

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<sup>147</sup> See Alan R. Hinman et al., *Vaccine Shortages: History, Impact and Prospects for the Future*, 27 Annual Review Pub. Health 235, 255 (2006).

<sup>148</sup> See Lance E. Rodewald et al., *Vaccine Supply Problems: A Perspective of the Centers for Disease Control and Prevention*, 42 Clinical Infectious Diseases, 104, 104 (2006).

<sup>149</sup> See Hinman et al., *supra* note 150, at 238.

<sup>150</sup> *Id.* at 239 (“There seems to be more interest among companies in reaching new markets than in competing for existing markets of other companies.”).

<sup>151</sup> See Patricia M. Danzon & Nuno S. Pereira, *Vaccine Supply: Effects of Regulation and Competition*, National Bureau of Economic Research 10 (2011).

<sup>152</sup> See *id.* at 12.

exist if the government plays hardball in price negotiations. To a far greater extent than for ordinary medications, vaccines are primarily purchased by public authorities (whether state, local or federal governments). As the dominant buyer, the government can force deep discounts but with the consequence of making vaccine production unattractive<sup>153</sup>.

Vaccine production is also plagued by excessively rigorous CGMP standards. At about the same time that vaccine shortages became more common, the FDA had begun to adopt more demanding regulatory requirements. Stricter rules for quality control systems, in-process testing and process validation imposed significant costs on facilities<sup>154</sup>. Some plants that had previously passed inspections were now failing, contributing to the exits of a number of vaccine manufacturers<sup>155</sup>.

Large capital costs for vaccine manufacture added fuel to the fire. The high fixed sunk costs of vaccine development and manufacture reflect the complexity of the research and development underlying vaccine production<sup>156</sup>. Marginal costs may also be high for each batch of vaccines, though the marginal cost for each vaccine within that batch may be low<sup>157</sup>. High costs combined with low prices<sup>158</sup> shrink profit margins.

One factor that distinguishes vaccine manufacture from ordinary drug production is litigation expenses. Product liability is a more significant risk for vaccines than for ordinary drugs because vaccines are often administered to otherwise healthy individuals<sup>159</sup>. Without the

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<sup>153</sup> See Tracy A. Lieu et al., *Overcoming Economic Barriers to the Optimal Use of Vaccines*, 24 Health Affairs 666, 670 (2005).

<sup>154</sup> See Hinman et al., *supra* note 150, at 249.

<sup>155</sup> See *id.*

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

<sup>157</sup> See Danzon & Pereira, *supra* note 154, at 9.

<sup>158</sup> Besides *de facto* price ceilings imposed by government purchasers, there are also effective price caps due to vaccines being undervalued in consumer markets as compared to therapeutic measures. See Hinman et al., *supra* note 150, at 249.

<sup>159</sup> See Danzon & Pereira, *supra* note 154, at 10.

shield of tort reform, legal expenses would have been prohibitive for vaccine firms hit with product liability suits. The threat of an avalanche of suits following a Fifth Circuit decision on vaccine-related injuries<sup>160</sup> led Congress to establish the National Vaccine Injury Compensation Program (VICP) in 1988 as a no-fault alternative to state tort claims<sup>161</sup>.

These contributors fit nicely into the price ceiling/cost floor model. As a study by the National Bureau of Economic Research found, “high fixed costs of regulation and production are not barriers to entry if these costs can, with reasonable certainty, be recouped over large volume or high margins, or both”<sup>162</sup>. That is, vaccine manufacturers have three ways to try to increase profits: Increasing sales volume, raising prices or reducing costs. While attractive in theory, each of these three methods is likely to fail in practice. Increasing sales volume is difficult because demand can be difficult to forecast and the shelf life for vaccines is often very short.<sup>163</sup> Raising prices is often not an option for vaccine manufacturers because prices are usually set by contracts with dominant purchasers who have significant bargaining power. Reducing costs is also difficult for highly-regulated, highly-expensive forms of manufacture like that for biologics-type vaccines. Litigation expenses also contribute to cost floors, though its influence may have waned since the VICP was established.

For vaccines, price ceilings are attributable to federal government lowballing of vaccine sales prices. Though price ceilings are not as crippling for vaccines because many of the statutory price caps have been repealed, the failure to make up the large fixed sunk costs with

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<sup>160</sup> See *Reyes v. Wyeth Lab.*, 498 F.2d 1264 (5th Cir. 1974) (establishing that manufacturers could be liable for adverse events following an immunization unless the patient received the vaccine in an individualized setting that delegated the duty to warn to the physician or other official administering the vaccine).

<sup>161</sup> W. K. Mariner, *The National Vaccine Injury Compensation Program*, 11 Health Affairs, 255, 256 (1992).

<sup>162</sup> See Danzon & Pereira, *supra* note 154, at 710.

<sup>163</sup> See Hinman et al., *supra* note 150, at 253.



market share led to shortages. Cost floors result from significant vaccine development and manufacturing costs and significant CGMP compliance expenses. These costs can be hard to forecast or control, which further dampens profit expectations for already financially-squeezed vaccine manufacturers.

## ***2. Responses to vaccine shortages***

To alleviate vaccine shortages, measures taken include stockpiling and guaranteed purchase agreements. Six-month stockpiles were established by Congress for certain childhood vaccines<sup>164</sup>. Assuming price is adequate, stockpiles increase demand for vaccines, making production more attractive. One difficulty with stockpiling is that the government has to predict in advance which vaccines it needs. While the demand for childhood vaccines is generally stable, demand may be more difficult to forecast for regular drugs. There are less than a dozen childhood diseases for which vaccination is routine, but many more conditions are treated by regular drugs. Deciding which medications to stockpile and which to leave in short supply would be an administrative nightmare.. Manufacturers may also be dissuaded from maintaining stockpiles because of revenue recognition rules of the Securities and Exchange Commission<sup>165</sup>. Another difficulty with non-vaccine drugs is the limited shelf-life of the products (especially for sterile injectables) as well as deciding which drugs to prioritize. In addition, stockpiles are not cheap: They require advance financial commitments and invite risks that the government may be unable to handle<sup>166</sup>. In sum, stockpiles are not effective long-term solutions to drug shortages. A few months of additional supply would not be enough to cover the demand until new entrants

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<sup>164</sup> See Hinman et al., *supra* note 150, at 248.

<sup>165</sup> See Margaret S. Coleman, et al., *Factors Affecting U.S. Manufacturers' Decisions to Produce Vaccines*, 24 *Health Affairs*, 635, 641 (2005) (“manufacturers believe that they will be prevented from creating and holding vaccines in stockpiles in their own facilities because of Securities and Exchange Commission revenue recognition rules. These rules require that a sale not be credited on the company accounts until the product is delivered.”).

<sup>166</sup> See Rodewald et al, *supra* note 151, at 109.

enter the field, if they do so at all. The attendant difficulties of forecasting demand and storing supply make stockpiling even less viable as a long-term fix. It's one thing to consider which of a dozen childhood vaccines to stockpile; it's quite another to select from over one hundred sterile injectables treating a myriad of different conditions for different populations.

Besides stockpiling, other options are guaranteed purchase agreements where the government commits in advance to buying a fixed quantity of drugs or vaccines. By establishing a fixed demand (and possibly price) for a product, manufacturers have an easier time forecasting expected profits and making a rational economic decision to enter a market<sup>167</sup>. Guaranteed purchase agreements are particularly valuable for vaccines with a short market life, such as influenza vaccines. Such agreements reduce the financial risk for manufacturers who may be stuck with unsold batches at the end of the flu season<sup>168</sup>. In theory, guaranteed purchase agreements are an attractive option; in practice, they are riddled with the same weaknesses as stockpiling. One difficulty with guaranteed purchase agreements is deciding *what* drugs to buy: There is no easy way to decide which life-saving drugs to prioritize. In addition, contracting via a “winner-take-all” strategy (where the lowest bidder gets the deal) can have perverse consequences by leading to low prices and great uncertainty for suppliers<sup>169</sup>. Doling out contracts based on the market share of suppliers (e.g. awarding 25% of the purchase quantity to a supplier with 25% of market share) invites problems if the market shares change (for example, if some manufacturers are unable to meet their obligations due to supply disruptions)<sup>170</sup>. Guaranteed purchase agreements also run the risk of enshrining the current market participants. Potential

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<sup>167</sup> See Hinman et al., *supra* note 150, at 248.

<sup>168</sup> See *id.*

<sup>169</sup> The CDC used a winner-takes all strategy prior to 1993. The result was low prices and great uncertainty for suppliers, which affected the quality and quantity of vaccines available. As a result, since 1998, the CDC abandoned this approach. See Danzon & Pereira, *supra* note 154, at 707.

<sup>170</sup> See Rodewald et al, *supra* note 151, at 109.

competitors may be reluctant to enter a market where existing firms have a guaranteed demand for their products.

## **VIII. CONCLUDING REMARKS**

Drug shortages are a recent occurrence in the United States. The scope and severity of drug shortages caught the attention of many prominent government officials and organizations. The White House responded with an executive order signed by President Barack Obama that directed the FDA to do whatever it could to mitigate shortages. Both houses of Congress have held committee hearings to investigate drug shortages. Both the House and Senate have also proposed legislation that would require drug manufacturers to provide the FDA with advance notice of any impending shortage. Lastly, the FDA has been extremely active in detecting shortages and trying to find short-term fixes such as allowing streamlined importation of alternative drugs.

Several suspects have been implicated for either causing or exacerbating drug shortages. Among the contributors are the Medicare Part B reimbursement policies, the 340B federal drug rebate program, market consolidation and competition, regulatory overreach by the FDA, product liability litigation, oncologist prescribing patterns and production-related problems. Though many of these causes appear plausible, the shortages discourse has ignored the possibility that these potential contributors have a common-denominator: Insufficient profits. Instead, correlation is confused with causation. As a result, though the responses to shortages are laudable for raising public awareness, they are also likely to fall short of what is needed to combat the problem.

This paper has made a modest proposal to “zoom-out” and focus on the ultimate issue underlying many of the potential causes: Inadequate profits for drug manufacturers. Viewing drug shortages as a problem of low price ceilings and high cost floors has the benefit of providing an easy-to-understand framework for looking at the complex interplay of causes. Price ceilings limit the price that manufacturers can charge for their products. Potential contributors to price ceilings include Medicare Part B reimbursement policies, as well as private insurance reimbursement policies that closely track Medicare payout schedules. Cost floors represent the minimum production and capital expenses incurred to manufacture products. Potential contributors to cost floors include FDA regulatory overreach.

Having outlined the potential contributors to drug shortages, as well as the likely primary culprit, this paper has looked at ways to mitigate the problem. At one end are solutions that would raise the price ceiling and allow manufacturers to charge more for their products. At another end are fixes that would reduce the cost flow and bring down the costs associated with manufacture. These proposed solutions aim to make drug production more profitable by increasing revenues and reducing costs. Another potential fix would be to increase the size of the market for these products. However, this fix would likely have only a minor, if any, impact on shortages problems. The drugs affected by shortages are predominantly those with a fairly sticky demand.

Rising healthcare costs are an important domestic issue. In the healthcare reform debate, spiraling prescription drug costs are a popular concern<sup>171</sup>. The salience of rising drug costs

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<sup>171</sup> See, e.g., Jonathan D. Rockoff, *Drug Prices Rise Despite Calls for Cuts*, Wall St. J., Mar. 17, 2011 (“Even as government and private health plans push to restrain spending on medicines, the prices of brand name prescriptions are climbing rapidly, reaching the steepest rate of the decade last year.”); Ann Carrns, *AARP Study Says Price of Popular Drugs Rose 26%*, N.Y. Times, Mar. 6 2012 (“The prices of drugs used most widely by older Americans rose by nearly 26 percent from 2005 to 2009 — nearly twice the rate of inflation”); Christopher Lee, *Medicare Helps Push Drug Spending Up*, Wash. Post, Jan. 8, 2008

makes it politically difficult to argue in favor of more profitable drug manufacturers. Drug shortages notwithstanding, it will be hard to suggest that “corporate villains” like Big Pharma should actually be making more money. Inevitably, some difficult balance will have to be struck. There is no way around elementary economics: Manufacturers will supply a drug if there is a profit to be made, and if something intervenes to dampen profits, manufacturers will decide not to play the game. The lesson from the drug shortages experience is that without profits, incentives to produce evaporate.

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(“Spending on prescription drugs rose briskly in 2006 as the Medicare drug benefit kicked in and the government's share of expenditures for medicines surged”).