

# Bloomberg GOVERNMENT

Bloomberg Government Study »

## Medicare Price Controls Worsen Drug Shortages, Boost Gray Market

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## EXECUTIVE SUMMARY

### KEY FINDING »

The number of drugs that the FDA considers to be in short supply has risen dramatically in the past five years. Many of the affected pharmaceuticals are older generic drugs that must be administered in a hospital or in a provider's office. The increase in shortages has coincided with a change in Medicare's reimbursement policy and increased FDA inspection activity.

### IMPACT »

Hospitals and other providers looking to respond to shortages are forced to purchase the sought-after drugs on the gray market at prices well above their reimbursement levels, acquire more expensive alternatives through normal channels, or delay patient treatments.

### WHAT'S NEXT »

Neither the President's Executive Order in October 2011 or the 2012 FDA user-fee reauthorization address the most likely cause of the surge in drug shortages: excessively restrictive reimbursement policy. Efforts at deficit reduction, which seek to tighten reimbursements further, may worsen the drug-shortage problem.

The number of drug shortages in the U.S. nearly quintupled during the past five years, costing health-care providers billions of dollars, this Bloomberg Government Study finds. The shortages probably are driven by Medicare price controls and increased regulatory scrutiny of the pharmaceutical industry, among other factors.

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 user level."<sup>1</sup>

Most of the drugs in short supply are older, generic injectable cancer drugs, anesthetics and other drugs that must be administered by a health-care professional. These complex drugs are often manufactured by only a few companies, and any disruption in their supply can have significant consequences.

The study finds that:

- The 2003 Medicare Modernization Act, which altered Medicare's Part B drug reimbursement formula for providers and prevented drug prices from rising more than 6 percent every six months, reduced the incentive for suppliers to expand capacity in response to drug shortages. Low margins also increase the pressure on suppliers to hold down costs at the expense of quality control.
- The number of drug shortages in the U.S. nearly quintupled during the past five years to 251 in 2011 from just 56 in 2006.
- A secondary "gray market" for drugs in short supply has emerged. The markups that providers pay to obtain drugs through these unauthorized channels can exceed 1,000 percent.
- Anecdotal evidence suggests that hospitals spend about one percent of their drug budgets addressing the drug-shortage problem, or roughly \$3 billion annually. Only some of this additional cost is likely to be recovered through higher reimbursements to hospitals from non-government payers.

## INTRODUCTION

Generic drugs have grown in importance in recent years. About 78 percent of all prescriptions written in the U.S. during 2010 were for generic drugs,<sup>2</sup> and the FDA has estimated that the use of generics instead of more expensive brand-name drugs has saved the nation's health-care system \$931 billion during the past decade.<sup>3</sup>

The vast majority of the drugs affected by the recent surge in shortages aren't the new brand-name therapies but are instead the decades-old cancer drugs, anesthetic agents, and other generic injectable drugs that cost as little as \$1 per vial.<sup>4</sup>

Why has the number of drug shortages surged higher in recent years, and why do they mainly involve generic injectable drugs? The answer appears to be a confluence of factors including government price controls emanating from changes in Medicare's reimbursement formula, company business decisions, and increased FDA vigilance. This Bloomberg Government study analyzes these causes, explores the shortages' impact on providers, and discusses steps to address the problem.

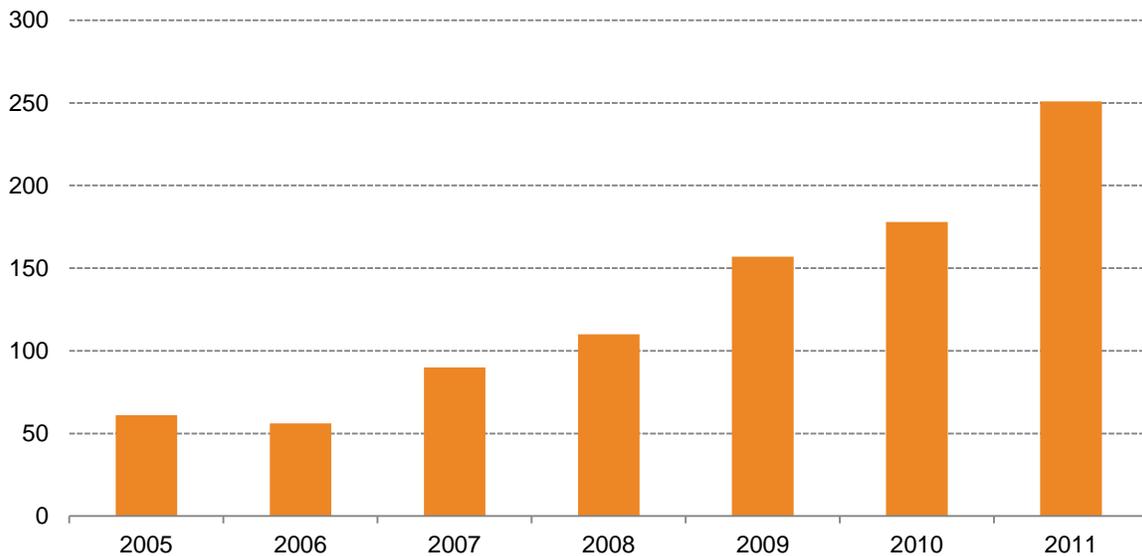
## SECTION 1: DRUG SHORTAGE OVERVIEW

### Shortages Have Surged in Recent Years

As illustrated by Chart 1, the number of drugs that the FDA considers to be in critically short supply rose dramatically from 2006 through 2011.

**Chart 1: Drug Shortages Quintupled in Five Years**

**Number of Drugs**



Source: U.S. Congress<sup>5</sup>

More than 70 percent of the drug shortages in 2011 occurred in so-called sterile injectable drugs.<sup>6</sup> These drugs include various forms of chemotherapy and anesthetics that are typically administered intravenously or through a subcutaneous injection.

An FDA analysis of the causes for the growing shortages of sterile injectable drugs found that the top three reasons were product quality issues such as contamination (54 percent), capacity constraints (25 percent), and business decisions to discontinue making certain drugs (11 percent).<sup>7</sup>

While the FDA's analysis helped explain why some companies slowed or ceased production of certain drugs, it shed little light on why competitors often declined to step into the void and exploit an imbalance between supply and demand. To answer the question of why industry participants have been unable or unwilling to increase production of a drug in response to a problem with another company, it may be helpful to explore the effects of legislation that went into effect just prior to this surge in shortages.

## Rise in Shortages Followed Medicare Law

The Medicare Modernization Act, signed into law by President George W. Bush in December 2003, went into effect in 2005 and is most famous for introducing the Part D prescription drug benefit. However, the bill also made changes to Medicare's Part B reimbursement method for sterile injectables and other drugs administered in a provider setting. Previously, reimbursement to providers was based on the "average wholesale price" of the drugs, which often didn't reflect the actual price of a given drug and was derisively referred to as "ain't what's paid." The 2003 law changed this reimbursement to a formula based on the actual average sales price (ASP) recorded in the marketplace: ASP plus a markup of 6 percent. This change resulted in lower reimbursement levels for many drugs.

This lower reimbursement to providers worked its way back up the supply chain through drug wholesalers, group purchasing organizations (GPOs) representing individual provider groups, and to the manufacturers. As noted in a congressional report, "GPO contracts, which are structured to take advantage of large economies of scale in drug production, result in only a few large manufacturers producing each generic injectable medication...In 2010, 90% of generic injectable oncology drugs were produced by three or fewer manufacturers."<sup>8</sup>

The 2003 law effectively capped manufacturer price increases for these drugs at no more than 6 percent every six months.<sup>9</sup> These price caps are particularly important given that generic drug prices can plummet quickly. As explained by Dr. Ezekiel Emanuel, former health-care advisor to the Obama administration, during "the first two or three months after a cancer drug goes generic, its price can drop by as much as 90 percent as manufacturers compete for market share. But if a shortage develops, the drug's price should be able to increase again to attract more manufacturers. Because the 2003 act effectively limits drug price increases, it prevents this from happening."<sup>10</sup>

This theory suggests that drug shortages are likely to occur when a drug's price has been falling, and this appears to be the case. An October 2011 report by the Department of Health and Human Services' Assistant Secretary for Planning and Evaluation noted that within "the group of drugs that eventually experience a shortage, average prices decreased in every year leading up to a shortage. In contrast, the average prices of drugs that never experienced a shortage over this period did not change substantially either in the earlier or later period."<sup>11</sup>

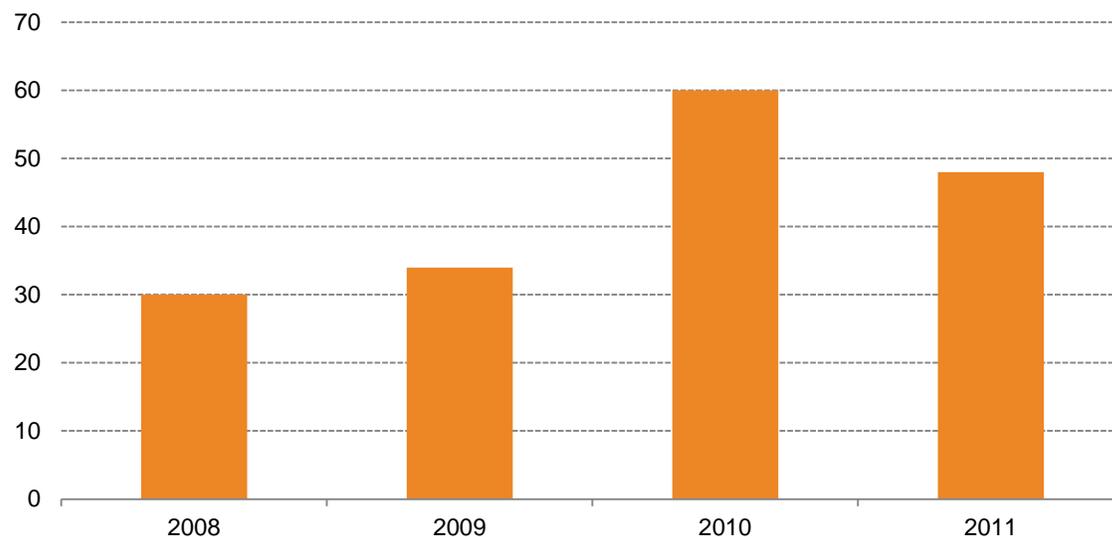
Drug shortages existed prior to the new Medicare law's passage, as competitive pressures and the negotiating leverage of wholesalers and group purchasing organizations were already affecting the drug companies' decisions. However, it appears likely that the cuts in provider reimbursement exacerbated the existing pressures on manufacturers and made the shortages worse.

## Heightened FDA Scrutiny Also May Be a Factor

Dr. Margaret Hamburg was confirmed as commissioner of the Food and Drug Administration in May 2009. Hamburg's appointment by President Obama came soon after contaminated batches of heparin, a sterile injectable drug used primarily as a blood thinner, were linked to more than 80 deaths in the U.S. during 2007 and 2008.<sup>12</sup>

In the wake of the deaths, the FDA was pressured to take greater action to prevent contaminated drugs from reaching the market, and the agency responded. In August 2009, Hamburg told the Food and Drug Law Institute: "The FDA is fortunate to have received significant funding increases for the current and next fiscal year that will be devoted to additional inspection and compliance activities that will support the elements of an effective enforcement strategy that I have outlined."<sup>13</sup> As Chart 2 illustrates, the number of warning letters related to pharmaceutical manufacturing issues from the FDA's drug division doubled to 60 in 2010 (the year after Hamburg's arrival) from 30 in 2008 (the year prior to her appointment). The number of warnings declined from 2010 to 2011 but was still well above the number of letters issued by the FDA prior to Hamburg's arrival.

**Chart 2: CDER Warnings Surged Following a Change in FDA Leadership**



Source: U.S. Food and Drug Administration<sup>14</sup>

The growth in these warning letters could be considered a contributing factor to the acceleration in shortages seen from 2009 to 2011. In some cases, these warning letters can result in the company halting production of drugs due to issues raised by the FDA, as the agency tells companies that failure to comply with its directives can result in legal action and the seizure of products.<sup>15</sup> Thus, while the agency has told Congress that companies are halting production voluntarily,<sup>16</sup> it's no surprise that company executives respond in such a serious manner when faced with the explicit threat of legal action from the FDA.

Nearly 60 percent of the drugs in short supply as of February 2012 were reportedly being made by one or more facilities working to resolve issues raised by the FDA.<sup>17</sup> For example, the FDA conducted three separate inspections of a Sandoz manufacturing plant in Quebec during the summer of 2011 and issued a warning letter in November about possible contamination of some of its sterile injectable drugs. The Canadian drug authority conducted a separate inspection soon thereafter and identified no problems, but faced with possible FDA sanctions, Sandoz scaled back its production of several drugs to address the manufacturing concerns.<sup>18</sup>

Many of the drugs that are the subject of shortages are older generic sterile injectable drugs, which have higher fixed costs and require a more complex manufacturing process than standard pills. Manufacturers' low margins — under pressure from both Medicare's revised reimbursement formulas and the negotiating leverage enjoyed by intermediaries in the drug supply chain — reduce their incentives to make investments in equipment maintenance and upgrades that can help prevent manufacturing problems from surfacing or to even make these drugs in the first place.

A working paper published by the National Bureau of Economic Research supports this theory, noting "that the reactions of manufacturers to reducing health care expenditures likely reduced capacity and maintenance investments."<sup>19</sup>

## **New Generic Drug User Fees Could Boost Inspections Further**

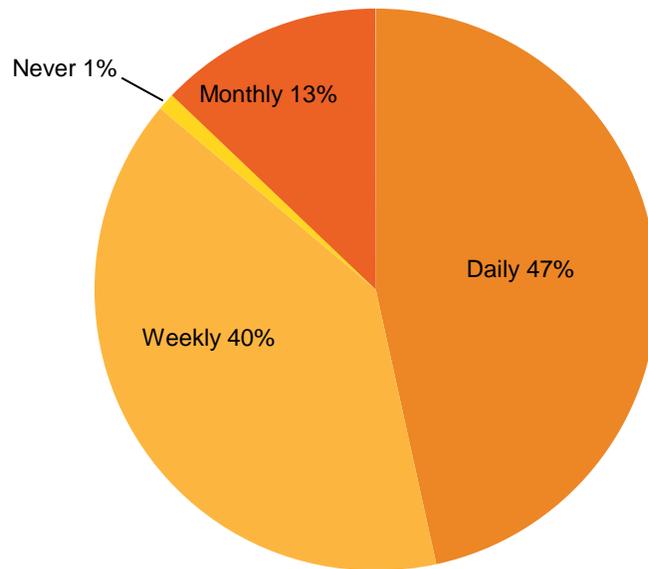
A generic drug user fee program signed into law in July is slated to generate \$1.5 billion in funding for the FDA over the next five years. The new program is designed to provide the FDA with additional resources to speed up reviews of generic drug applications, addressing an existing backlog of more than 2,500 applications and reducing the 31-month review time now confronting new applicants.<sup>20</sup>

However, the FDA also intends to use the funds to expand its global inspection program for manufacturers of active pharmaceutical ingredients (API) as well as the final drugs. Questions have arisen about the quality of overseas facilities, where more than 80 percent of the APIs for U.S. drugs are made.<sup>21</sup> The increase in global FDA inspections may uncover quality control problems at multiple facilities around the world that could worsen the drug shortage problem, at least in the short run. Even if the finished-form manufacturers in North America are in compliance and able to make the final drugs, they won't have the key ingredients if a foreign supplier of those ingredients is shut down.

## SECTION 2: IMPACT ON HEALTH-CARE COMPANIES

In addition to drug manufacturers, the shortage problem is also affecting hospitals, emergency medical personnel, and other providers. An internal survey conducted by the American Hospital Association in June 2011 revealed that 99.5 percent of the 820 responding hospitals had experienced one or more drug shortages during the preceding six months, with nearly half of the hospitals dealing with it on a daily basis.<sup>22</sup>

**Chart 3: Frequency of Hospital Drug Shortages**



Source: American Hospital Association<sup>23</sup>  
Total doesn't add to 100% due to rounding.

About 20 percent of the participating hospitals reported that they "always" or "frequently" delayed patient treatment as a result of a drug shortage.<sup>24</sup> These delays in treatment may prolong hospital stays or result in additional health problems, increasing the nation's health expenditures, though the AHA has not shared data on this front.

### "Gray Market" Driving Providers' Costs Higher

According to the same AHA survey, 92 percent of the responding hospitals indicated that their drug costs increased as a direct result of these shortages. This can result from having to purchase more expensive generic or even brand-name alternatives, and from a more shadowy effort to procure drugs from unauthorized distributors via a so-called gray market.

In a normal distribution chain, the manufacturer sells its drug to a wholesaler, which then sells it at a markup to a secondary distributor or directly to a pharmacy for final distribution. The pharmaceutical wholesaling business is dominated by the "Big Three" — McKesson, Cardinal Health, and AmerisourceBergen — which collectively control 85 percent of this \$320 billion business.<sup>25</sup>

The gray market occurs when drugs exit this normal distribution chain and are reintroduced into a prolonged cycle of sales among distributors, with huge markups along the way. As previously mentioned, the 2003 Medicare law effectively caps prices that manufacturers of generic drugs can charge. However, when a shortage exists, the life-saving nature of these drugs means that they are relatively price inelastic, and many providers are willing to pay significantly more than their reimbursement levels to obtain these critical products. Gray-market distributors take advantage of this gap.

A congressional investigation revealed that, in 69 percent of the cases studied, drugs entered the gray market through pharmacy entities.<sup>26</sup> That is, instead of distributing the drugs to patients, certain pharmacies would resell them to gray market distributors at a significant markup. That gray-market distributor would then sell the drug to another distributor for an additional markup. This process can repeat itself several times until the drug ends up at its final destination. It can be especially lucrative when providers feel pressure to obtain the drug at any cost, as with cancer drugs or anesthetics.

Table 1 details an actual example of a gray market transaction. It started when a pharmacy re-introduced the generic cancer drug fluorouracil, which it purchased from an authorized distributor for \$7 per dose, back into the supply chain. This entire selling process took place during a single week in September 2011 before a hospital pharmacy paid \$600 per dose for the same drug.

**Table 1: An Expensive One-Week Trip Through the Gray Market**

	Price Paid	Percentage Markup
Initial Pharmacy	\$7	—
Distributor #1	\$50	614%
Distributor #2	\$69	38%
Distributor #3	\$95	38%
Distributor #4	\$275	189%
Distributor #5	\$375	36%
Destination Hospital	\$600	60%
<b>Cumulative Markup Paid by Hospital</b>	—	<b>8471%</b>

Source: U.S. Congress<sup>27</sup>

The hospital wound up paying far above its reimbursement level for this decades-old chemotherapy agent. Is this legal? The answer is complicated. There are no federal laws prohibiting what one might term price-gouging activity, so unless the gray-market distributors are colluding with one another, they are in the clear. In fact, given the size of the Big Three wholesalers and the leverage of the larger GPOs, some smaller distributors are effectively blocked from the normal supply chain and rely on gray-market transactions to stay in business. Assessing whether the larger organizations exercise too much power in the pharmaceutical supply chain is outside the scope of this study.

Some of the pharmacies that sell drugs back into the supply chain instead of distributing them to providers or patients may be violating their states' regulations, which limit sales back into the supply chain.<sup>28</sup> A congressional report noted that Maryland pharmacies must "obtain separate wholesaler licenses if they re-sell more than 5% of their products," yet some pharmacies in the state reportedly generated far greater levels of revenue from such transactions.<sup>29</sup>

Because the gray market operates outside the authorized supply chains, there are no reliable records on the aggregate cost of the gray-market premium to providers. Hartford Hospital in Connecticut estimates that "the cost of shortage is roughly 1 percent of our [drug] budget."<sup>30</sup> According to data from the American Society of Health-System Pharmacists, total drug expenditures within U.S. hospitals approximate \$28 billion.<sup>31</sup> Thus, if gray-market premiums and other effects of the drug shortages account for 1 percent of U.S. hospitals' total drug expenditures, the industry is spending about \$3 billion each year to address the problem.

Some hospitals possess a sufficiently large market presence that they can make up for losses by negotiating for higher reimbursement rates for both brand-name and generic drugs with non-government payers. For example, the University of North Carolina Health Care system reportedly collected 14 times the average sales price for the generic chemotherapy drug cisplatin from non-government payers.<sup>32</sup>

## Problems Also Affect Makers of Brand-Name Drugs

Although the drug shortages most acutely affect providers and their patients, makers of brand-name drugs can be adversely affected. Many drug companies file patent applications for their drugs in development, so there is a keen interest in avoiding delays during clinical trials to obtain FDA approval quickly and maximize the drugs' revenue-generating period before patents expire and the generic floodgates open.

However, many of breakthrough cancer drugs in development are tested either in conjunction with, or in comparison to, older sterile injectable cancer drugs. Drug companies need access to these older drugs to complete their FDA-mandated studies prior to seeking approval, so any shortages of these generic drugs can delay a new drug's development. In one example, a shortage of the older chemotherapy drug doxorubicin delayed a trial for a new cancer drug by five months.<sup>33</sup> A Bloomberg Government study estimates that a five-month delay in obtaining approval costs a drug company \$11 million on average.<sup>34</sup>

## SECTION 3: EFFORTS TO ADDRESS THE ISSUE

### President Obama's Executive Order

In October 2011, President Obama issued an executive order aimed at reducing these drug shortages. However, the order carries little practical significance. It directs the FDA to take steps, many already in place or in the process of being implemented, that address the company-specific drug-shortage issues, but not the root causes of the industry-wide problem. For example, the order says "To the extent practicable, and consistent with its statutory responsibility to ensure the safety and effectiveness of the drug supply, the FDA shall take steps to expand its current efforts to expedite its regulatory reviews...whenever it determines that expedited review would help to avoid or mitigate existing or potential drug shortages."<sup>35</sup>

### User Fee Reauthorization Law Provisions

Legislation reauthorizing FDA user fees paid by drug and device companies for five years was signed into law by Obama in July 2012. It included a section on drug shortages,<sup>36</sup> and the following are some key provisions.

#### Six Months' Notice

Drug companies must notify the FDA six months in advance of an anticipated issue that "is likely to lead to a meaningful disruption in the supply of that drug in the United States," with the FDA then responsible for relaying this information to health-care providers. However, there is no penalty for non-compliance. Previously, only sole-source manufacturers were required to give the FDA such a heads-up. This advance notice may help the FDA and the drug companies take corrective action earlier, but it may also result in hoarding by worried provider groups or opportunistic gray-market participants, exacerbating the shortage problem.

#### Expedited Facility Inspections and New Application Reviews

If the FDA believes that an inspection of a particular manufacturing facility could help address a likely shortage, the FDA can alter its inspection schedule to address the most pressing needs first.

#### Reporting and Task Force Requirements

The FDA must submit a report to Congress by the end of each year that summarizes the number and nature of shortages, along with the steps taken by the agency to address them. Additionally, the law orders the formation of a task force to develop a long-term strategic plan to address drug shortages, with that plan due to Congress by the summer of 2013.

#### GAO Study Requirement

The law orders the Government Accountability Office to deliver a study to Congress no later than January 2014 analyzing the drug shortage situation, with recommendations to address it.

## FDA Incorporating Drug-Shortage Language in New Warnings

Recent warning letters from the FDA include drug-shortage language that was absent in earlier years. For example, an FDA warning letter to generic drug maker APP Pharmaceuticals in February 2012 included the following statement: "If, as a result of receiving this Warning Letter or in general, you are considering making a decision that will result in a decreased number of finished drug products or active pharmaceutical ingredients produced by your manufacturing facility, FDA requests that you contact CDER's Drug Shortages Program immediately."<sup>37</sup>

The agency also appears to have employed greater levels of regulatory discretion to address the problem, allowing the importation of similar drugs (sometimes lacking approval from the FDA for a particular use) from foreign countries, for example.<sup>38</sup>

## Supercommittee Considered Reducing Reimbursement Levels

Neither the executive order nor the provisions contained within the user-fee legislation attempt to address the price controls built into Medicare's reimbursement formula for sterile injectable drugs, which appear to influence drug companies' decision-making processes regarding the types and amounts of drugs to produce.

While raising the allowable limit on price increases may have appeal as a means of alleviating some of the shortage problems, political realities make this unlikely, at least in the near-term.

In fact, recently considered proposals aimed at reducing the deficit recommended the opposite. The so-called supercommittee of six Republicans and six Democrats reportedly considered cutting the Part B drug reimbursement formula from ASP plus 6 percent to ASP plus 3 percent.<sup>39</sup> Such a change could worsen the drug-shortage problem by further reducing the incentives for companies to make generic injectable drugs.

## CONCLUSION

Multiple factors are contributing to the surge in drug shortages during the past five years, though the primary causes appear to be economic. Thin margins associated with many older sterile injectable drugs, resulting from generic competitive pressures and the negotiating leverage enjoyed by major drug intermediaries and exacerbated by a change in Medicare reimbursement policy, have caused many drug companies to scale back their production of these drugs in favor of higher-margin products. Few shortages take place with brand-name drugs, where patent protections give manufacturers pricing power that makers of older generic drugs lack.

At the same time, a rise in the number of warning letters from the FDA has led to an increase in production interruptions among the manufacturers. While some accuse the FDA of being overly vigilant, the complexity of the sterile injectable drugs and the fact that they are often manufactured in older facilities suggests that the recent jump in warning letters may be warranted.

The FDA should strive to consider whether the timing and content of its warning letters are encouraging overly severe reactions from drug manufacturers and needlessly affecting the public health. Language in more recent warning letters suggests that the agency is aware of the need to do this.

Most importantly, the price controls in the Medicare reimbursement formula implemented in 2005 should be revisited. Any effort to increase Medicare reimbursements for drugs is likely to meet with stiff opposition given the current political focus on deficit reduction and entitlement reform. The supercommittee's consideration of a proposal to reduce reimbursements indicated that policy makers are leaning in the opposite direction. However, lawmakers must be aware that such efforts may exacerbate an already dangerous situation in which hospitals and patients in need find it ever more difficult to obtain life-saving drugs.

## » ABOUT THE ANALYST



Brian Rye is a health-care financial analyst with Bloomberg Government. He spent 12 years as an equity research analyst at SunTrust, Raymond James and Janney Montgomery Scott. In those capacities, he followed biotech, pharmaceutical and other health-care companies. Rye also served as a senior business management analyst for Booz Allen Hamilton's civil health group. He received a bachelor's degree in economics from Vanderbilt University and holds the Chartered Financial Analyst designation.

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