



Testimony

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Committee on Energy and Commerce,
House of Representatives

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DRUG SHORTAGES

Threat to Public Health Persists, Despite Actions to Help Maintain Product Availability

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GAO Highlights

Highlights of [GAO-14-339T](#), a testimony before the Subcommittee on Health, Committee on Energy and Commerce, House of Representatives

Why GAO Did This Study

From prolonged duration of a disease, to permanent injury, to death, drug shortages have led to harmful patient outcomes. FDA—an agency within the Department of Health and Human Services (HHS)—works to prevent, alleviate, and resolve shortages. In 2011, GAO recommended that FDA should enhance its ability to respond to shortages. In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) gave FDA new authorities to address drug shortages. FDASIA also mandated GAO to study drug shortages.

In this statement, and in the report on which it is based, GAO focuses on (1) trends in recent drug shortages and describes what is known about their effect on patients and providers; (2) the causes of drug shortages; and (3) the progress FDA has made in addressing drug shortages. GAO analyzed data from FDA and the University of Utah Drug Information Service, which is generally regarded as the most comprehensive source of drug shortage information for the time period we reviewed. GAO interviewed officials from FDA, organizations representing providers, and drug manufacturers. GAO also reviewed the literature, relevant statutes, regulations, and documents.

What GAO Recommends

GAO recommended that FDA strengthen internal controls over its drug shortage data and conduct periodic analyses to routinely and systematically assess drug shortage information, using this information to proactively identify drug shortage risk factors. HHS agreed with GAO's recommendations.

View [GAO-14-339T](#). For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

February 10, 2014

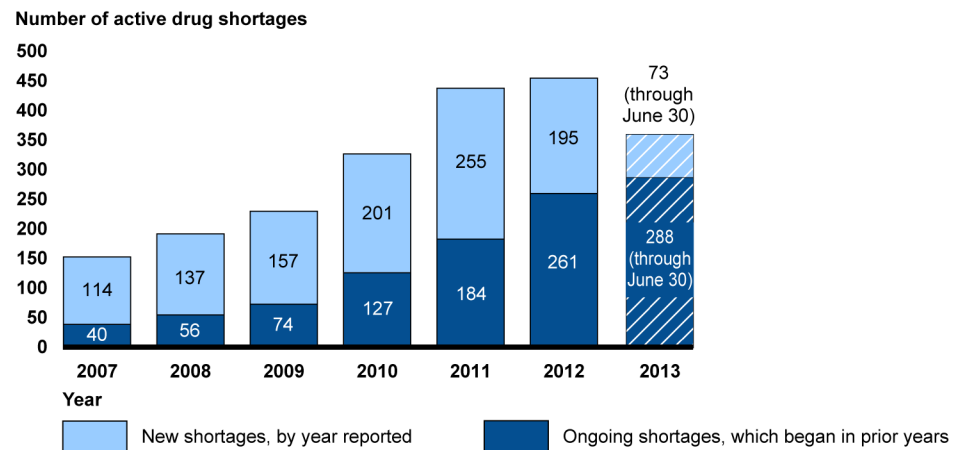
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Threat to Public Health Persists, Despite Actions to Help Maintain Product Availability

What GAO Found

The number of drug shortages remains high. Although reports of new drug shortages declined in 2012, the total number of shortages active during a given year—including both new shortages reported and ongoing shortages that began in a prior year—has increased since 2007. Many shortages are of generic sterile injectable drugs. Provider association representatives reported that drug shortages may force providers to ration care or face difficulties finding alternative drugs.

Number of Active Drug Shortages from January 2007 through June 2013



Source: GAO analysis of University of Utah Drug Information Service data.

The immediate cause of drug shortages can generally be traced to a manufacturer halting or slowing production to address quality problems, triggering a supply disruption. Other manufacturers have a limited ability to respond to supply disruptions due to constrained manufacturing capacity. GAO also identified potential underlying causes specific to the economics of the generic sterile injectable drug market, including that low profit margins have limited infrastructure investments or led some manufacturers to exit the market.

While shortages have persisted, the Food and Drug Administration (FDA) has prevented more potential shortages in the last 2 years by improving its responsiveness. FDA has initiated steps to improve its response to shortages, such as modifying the information on its drug shortages website. However, there are shortcomings in its management of drug shortage data that are inconsistent with federal internal control standards. For example, FDA has not created policies or procedures governing the management of the data and has not conducted routine analyses using these data. Such shortcomings could ultimately hinder FDA's efforts to understand the causes of specific shortages as well as undermine its efforts to prevent them from occurring.

Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee:

We are pleased to be here today to discuss our work on drug shortages. Drug shortages have led to harmful outcomes for patients of all ages: from prolonged duration of a disease, to permanent injury, to death. Over the last decade, an increasing number of prescription drugs have been in short supply. The Food and Drug Administration (FDA)—an agency within the Department of Health and Human Services (HHS)—is responsible for overseeing the safety and effectiveness of drugs marketed in the United States, including by addressing drug shortages.¹ A unit within FDA, referred to as the Drug Shortage Staff (DSS), coordinates the agency’s activities to prevent, alleviate, and resolve shortages. In November 2011, we found that the agency lacked sufficient authority to respond to shortages. We recommended that FDA strengthen its response and suggested that Congress consider establishing a requirement for manufacturers to report potential or actual supply disruptions to FDA.² The Food and Drug Administration Safety and Innovation Act (FDASIA), enacted in July 2012, provided FDA new authorities to address drug shortages and assigned the agency new responsibilities.³ It also mandated us to update our work on drug shortages. This statement summarizes the findings in our report, being released today, entitled *Drug Shortages: Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability*.⁴

As part of its oversight of drugs, FDA’s approval is required before new drugs and generic drugs can be marketed for sale and its responsibilities continue once a drug is approved for marketing.⁵ If FDA identifies a violation of law or regulations, it may issue a warning letter or take an enforcement action. In some cases, FDA may exercise its regulatory

¹FDA 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.

²GAO, *Drug Shortages: FDA’s Ability to Respond Should be Strengthened*, [GAO-12-116](#) (Washington, D.C.: Nov. 21, 2011).

³Pub. L. No. 112-144, 126 Stat. 993 (2012).

⁴[GAO-14-194](#) (Washington, D.C.: Feb. 10, 2014).

⁵21 U.S.C. § 355.

discretion and assess whether the risks of taking a certain enforcement or other action will outweigh the benefits; for example, when an action may cause or exacerbate a drug shortage, FDA may exercise its regulatory discretion and refrain from taking action.⁶

When FDA is informed of a potential shortage in advance, it may take steps to prevent the shortage, such as providing assistance to the manufacturer to address manufacturing problems.⁷ For example, it may offer feedback on a manufacturer's proposed approach to responding to quality concerns. In addition, FDA can expedite the review of a drug application or can expedite inspections once remediation to address quality problems has been completed.⁸ While there are a number of steps FDA can take to address a shortage, FDA cannot require manufacturers to start producing or continue producing a drug. It also cannot require manufacturers to maintain or introduce manufacturing redundancies in their establishments to provide them with increased flexibility to respond to shortages.

FDASIA required us to examine several different aspects of shortages. Our report, and my remarks today, focus on 1) the trends in recent drug shortages and describes what is known about their effect on patients and providers, 2) the causes of drug shortages, and 3) the progress FDA has made in addressing drug shortages.⁹ To address these issues, we analyzed data from the University of Utah Drug Information Service (UUDIS) on drugs that were in short supply from January 1, 2007,

⁶In determining how to respond to a shortage, FDA takes steps to assess whether a drug is medically necessary, defined as any drug that is used to treat or prevent a serious disease or medical condition for which there is no other adequately available drug that is judged by medical staff to be an appropriate substitute.

⁷FDA officials said that they take steps to address shortages of both medically necessary drugs and non-medically necessary drugs, though they give priority to shortages of medically necessary drugs.

⁸FDA periodically inspects drug manufacturing establishments to assess their ongoing compliance with Current Good Manufacturing Practice regulations. These regulations provide a framework for a manufacturer to follow to produce safe, pure, and high-quality drugs. See 21 C.F.R. pts. 210-211.

⁹Our report also describes steps federal agencies have taken to respond to gray market activities and describes incentives that have been proposed to prevent shortages. [GAO-14-194](#).

through June 30, 2013.¹⁰ We interviewed representatives from 10 national associations representing health care providers—including physicians, hospitals, and pharmacists—and from eight drug manufacturers and associations representing them, and reviewed relevant documents from these groups.¹¹ We performed a search of research databases to identify literature on the causes of drug shortages, and analyzed FDA data on the reported causes of shortages that occurred from January 1, 2011, through June 30, 2013.¹² We reviewed documentation and interviewed FDA officials regarding the agency’s current approach to managing drug shortages and implementing FDASIA requirements, and compared this approach to the relevant standards described in the *Standards for Internal Control in the Federal Government* and to the agency’s requirements under FDASIA.¹³ Our work was performed in accordance with generally accepted government auditing standards.

We found that the number of drug shortages remains high and that providers experience challenges responding to drug shortages without adversely affecting patient care. From 2007 through 2011, the number of drug shortages reported increased each year, with a record 255 shortages reported in 2011.¹⁴ However, in 2012, 195 shortages were reported; this was the first decrease from one year to the next since 2006.

¹⁰These data are generally regarded as the most comprehensive and reliable source of drug shortage information for the time period we reviewed. We reviewed all UUDIS data used for reasonableness, outliers, and consistency; based on our review, we determined that the data were sufficiently reliable for our purposes.

¹¹We interviewed three leading national associations representing drug manufacturers, both brand-name and generic, and five generic sterile injectable manufacturers. Specifically, we selected the top three manufacturers of generic sterile injectables between 2010 and 2012. We also selected two additional manufacturers, which were among the manufacturers associated with the highest number of shortages, according to the following report: IMS Institute for Healthcare Informatics, *Drug Shortages: A Closer Look at Products, Suppliers, and Volume Volatility*. (Parsippany, N.J.: November 2011).

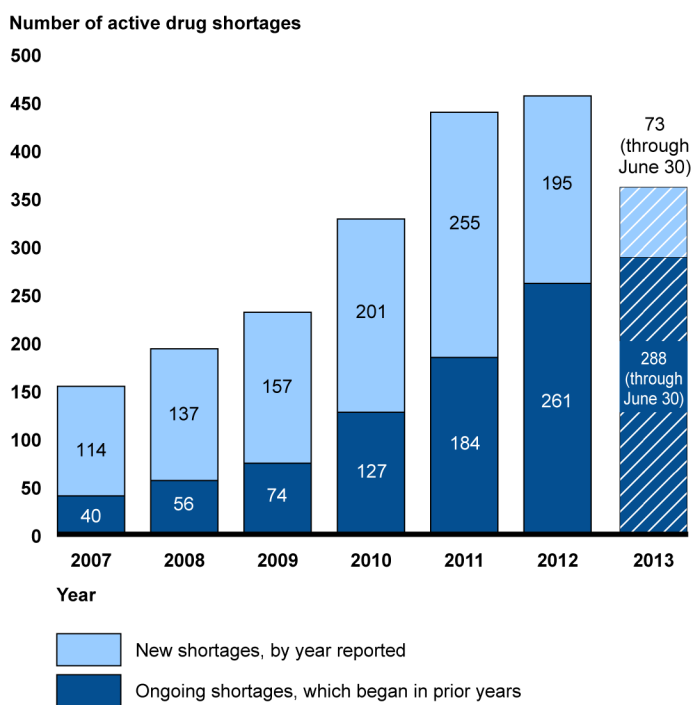
¹²We reviewed all FDA data used for reasonableness, outliers, and consistency; based on our review, we determined that the data were sufficiently reliable for our purposes.

¹³See GAO, *Standards for Internal Control in the Federal Government*, [GAO/AIMD-00-21.3.1](#) (Washington, D.C.: November 1999).

¹⁴A shortage is only counted in the total for “reported” shortages in the year that UUDIS is first notified of the shortage. For example, a shortage reported in July 2010 and resolved in March 2012 would only be counted as a reported shortage in 2010. It would not be counted as a reported shortage in either 2011 or 2012, although it would be counted in the total number of active shortages in each of those years.

Though the number of newly reported shortages has recently declined, due to ongoing shortages that began in prior years, the number of active shortages has increased steadily since 2007 and remains high.¹⁵ The number of active shortages each year almost tripled between 2007 and 2012 from 154 in 2007 to 456 in 2012 (see fig. 1).

Figure 1: Number of Active Drug Shortages from January 2007 through June 2013



Source: GAO analysis of University of Utah Drug Information Service data.

Note: The active shortage total for each year includes 1) new shortages reported that year and 2) shortages that started in a prior year that were still ongoing.

We found that many shortages involved generic sterile injectable drugs. Specifically, based on our review of the characteristics of a subset of critical drug shortages, we found that 44 percent of the 219 critical

¹⁵The active shortage total for each year includes both (1) new shortages reported that year and (2) shortages that started in a prior year that were still ongoing. For example, a shortage reported in July 2010 and resolved in March 2012 would be counted as an active shortage in three different years (2010, 2011, and 2012).

shortages involved generic sterile injectable drugs.¹⁶ Further, four therapeutic classes—anti-infective, anesthetic and central nervous system, cardiovascular, and nutritive—comprised 53 percent of critical drug shortages.¹⁷

Faced with this continuing problem, provider association representatives identified challenges in responding to drug shortages without adversely affecting patient care. Provider association representatives told us that a number of the challenges that we reported in 2011 were still relevant for their members. Providers may be challenged by delays in or rationing of care, difficulties finding alternative drugs, risk associated with medication errors, higher costs, and reduced time for patient care.

We also found that quality problems resulting in supply disruptions and constrained manufacturing capacity were frequently cited as the immediate causes of recent drug shortages. We determined that the most frequently cited immediate cause of a drug shortage was when a manufacturer halted or slowed production after a quality problem was identified, resulting in a supply disruption.¹⁸ These supply disruptions were linked to, among other things, such problems as bacterial contamination or the presence of glass or metal particles in drug vials. Although quality problems were a frequently cited issue, there was not complete agreement as to whether quality problems were always the primary trigger for the supply disruptions that cause shortages, with two studies and three manufacturers suggesting that changes in FDA inspections of manufacturing establishments also played a role. In

¹⁶UUDIS identified 219 of the 382 shortages reported from June 1, 2011, through June 30, 2013, as critical shortages. We reviewed the characteristics of those 219 critical shortages, which represented 57 percent of all shortages reported during this time. These shortages were identified by UUDIS as critical because alternative medicines were not available, the shortages affected multiple manufacturers, or it received multiple reports from different institutions.

¹⁷Examples of shortages in these therapeutic classes during this time period included acyclovir and doxycycline (anti-infective); propofol and diazepam (anesthesia and central nervous system); nitroglycerin and verapamil (cardiovascular); and potassium chloride and sodium phosphate (nutritive).

¹⁸As shortages have been concentrated in the generic sterile injectable market in recent years, the literature on the subject of shortages and comments from manufacturer representatives largely focused on the causes of shortages specific to that market. As a result, our discussion about the causes of shortages may not be applicable to all shortages.

reviewing the literature, we identified a number of additional factors that can cause supply disruptions and ultimately result in shortages—such as permanent product discontinuations or the unavailability of raw materials—but our analysis of FDA data and interviews with representatives of drug manufacturers suggested that these factors play a relatively small role overall.

Constrained manufacturing capacity limits other manufacturers' ability to respond to supply disruptions. There are few generic sterile injectable manufacturers overall, and the existing manufacturers are producing a large number of drugs. For a variety of reasons, these manufacturers have little flexibility to increase production in existing facilities or move production to alternative facilities.

In addition, half of the studies we reviewed suggested that the immediate causes of drug shortages, such as quality problems, are driven by an underlying cause that stems from the economics of the generic sterile injectable drug market. However, the studies that cited underlying causes did not all focus on the same underlying cause. The potential underlying causes cited in the literature were that competition in the generic drug market focuses primarily on price; the possible role of group purchasing organizations; and a change in Medicare Part B reimbursement policy. The studies that cited these underlying causes generally suggested that such causes led to low profit margins, which limited infrastructure investments or led some manufacturers to exit the market. Manufacturer representatives had mixed views on the potential underlying causes we identified in the literature.

Finally, we determined that FDA has prevented more potential shortages and improved its ability to respond to shortages since we issued our prior report on this topic in 2011. Based on our analysis of FDA data from January 2011 through June 2013, FDA was able to prevent 89 potential shortages in 2011, 154 potential shortages in 2012, and 50 potential shortages through June 2013.¹⁹ This is more than the 35 potential

¹⁹As we did in analyzing data for our 2011 report, we grouped together shortages of multiple versions of the same drug to identify the total number of potential shortages prevented. While FDA had reported preventing 195 potential shortages in 2011, 282 potential shortages in 2012, and 80 potential shortages through June 2013, we found that these data represented the number of individual drug products for which a shortage had been averted.

shortages we found that FDA prevented in 2010 and the 50 prevented through June 2011.

FDA officials told us that FDASIA's requirement that manufacturers notify FDA in advance of a potential shortage allowed FDA to employ various steps to prevent or resolve shortages sooner.²⁰ Such steps include expediting a number of agency actions to prevent or resolve shortages, contacting manufacturers regarding their ability to increase production, and facilitating the availability of drugs from alternate sources to help prevent or resolve a shortage. FDA has taken steps to further enhance its ability to respond to shortages, such as modifying the information the agency displays on its drug shortages website, developing a drug shortage database, and increasing the number of DSS personnel from 4 in 2011 to 11 in 2013.

While FDA is planning on establishing a new information system to track drug shortage data, we found that it still lacks policies, procedures, and specific training materials related to management and use of its existing drug shortage database. This lack of documentation may limit the agency's ability to communicate proper use of the existing and new databases to staff and could also ultimately lead to inconsistencies in the use of the database. The lack of policies and procedures is also inconsistent with internal control standards for the federal government, which state that agencies should have controls over information processes, including procedures and standards to ensure the completeness and accuracy of processed data.²¹ In addition, we found that FDA has not conducted routine analyses of its existing drug shortage database to identify, evaluate, and respond to the risks of drug shortages proactively. Again, according to the internal control standards for the federal government, agencies should comprehensively identify risk through qualitative and quantitative methods, including data collected in

²⁰Consistent with the matter for Congressional consideration contained in our 2011 report, FDASIA required manufacturers to notify FDA at least 6 months prior to the date of a discontinuance or interruption (or as soon as possible if 6 months notice is not feasible) in the manufacture of a drug that is life supporting, life sustaining, or used to treat debilitating health issues. FDASIA required FDA to issue a final rule implementing this requirement by January 9, 2014. § 1001(a), 126 Stat. at 1099 (to be codified at 21 U.S.C. § 356c). FDA issued a proposed rule on November 4, 2013, with a 60-day comment period. 78 Fed. Reg. 65904 (Nov. 4, 2013) (to be codified at 21 C.F.R. pts. 20, 310, 314, and 600).

²¹[GAO/AIMD-00-21.3.1](#).

the course of their work.²² We determined that FDA currently uses data on an ad hoc basis to respond to specific shortages as opposed to using the data to identify trends or patterns that may help it predict and possibly prevent shortages. By only using the database to respond to individual shortages as they occur, FDA is missing opportunities to use the data proactively to enhance the agency's ability to prevent and mitigate drug shortages.

Based on our work, we have identified two actions that we recommend the Commissioner of FDA take to enhance its oversight of drug shortages:

- develop policies and procedures for the use of the existing drug shortages database (and, ultimately, the new drug shortages information system) to ensure staff enter information into the database in a consistent manner and to ensure the accuracy of the information in the database; and
- conduct periodic analyses using the existing drug shortages database (and, eventually, the new drug shortages information system) to routinely and systematically assess drug shortage information, and use this information proactively to identify risk factors for potential drug shortages early, thereby potentially helping FDA to recognize trends, clarify causes, and resolve problems before drugs go into short supply.

In commenting on a draft of our report HHS agreed with our recommendations and stated that it will continue improving the collection of drug shortage data as part of a larger system that would help identify problems with quality drug manufacturing as they evolve. HHS also stated that it agrees that policies and procedures for drug shortage data entry are important and noted that FDA has ongoing work to ensure such policies and procedures are established.

Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee, this concludes my prepared remarks. I would be pleased to respond to any questions you may have.

²²[GAO/AIMD-00-21.3.1](#).

For future contacts regarding this statement, please contact Marcia Crosse ((202) 512-7114 or crossem@gao.gov). Individuals making key contributions to this testimony and the report on which it is based include Geri Redican-Bigott, Assistant Director; Katherine L. Amoroso; Alison Goetsch; and Eagan Kemp.

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