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## DRUG SHORTAGES

# FDA's Ability to Respond Should Be Strengthened

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Mr. Chairman and Members of the Committee:

I am pleased to be here today to discuss the Food and Drug Administration's (FDA) response to prescription drug shortages. According to FDA, a record number of drugs were in short supply in 2010, and the number of drug shortages has continued to grow throughout 2011. A variety of factors can trigger drug shortages, such as disruptions in the supply of the active pharmaceutical ingredients required to manufacture the drug, manufacturing problems, manufacturers' business decisions, and increased demand for products. Drug shortages directly threaten public health by preventing patients from accessing medications that are essential to their care. During shortages, physicians may have to ration their supplies, delay treatments, or use alternative medications that may be less effective for the condition, carry unwanted side effects, or cost more. Consistent with its mission of protecting the public health, FDA, an agency within the Department of Health and Human Services (HHS), established a Drug Shortage Program to help prevent, alleviate, and resolve shortages.

Drug shortages may be reported to FDA by manufacturers, health professionals, or the public. FDA also obtains information from the American Society of Health-System Pharmacists (ASHP), which tracks and makes information publicly available about nationwide drug shortages through a partnership with the University of Utah Drug Information Service (UUDIS).<sup>1</sup>

My statement will highlight key findings from our November 2011 report, which is being released today, that reviews trends in prescription drug shortages and FDA's response.<sup>2</sup> In that report, we (1) reviewed trends in prescription drug shortages that occurred from January 2001 through June 2011, (2) identified the reported causes of selected drug shortages that occurred from January 2009 through June 2011, (3) described FDA's response to drug shortages, and (4) evaluated the extent to which FDA is able to protect the public health through its response to drug shortages.

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<sup>1</sup>ASHP posts information about drug shortages on its website. See <http://www.ashp.org/menu/PracticePolicy/ResourceCenters/DrugShortages.aspx>.

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

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To identify trends in drug shortages, we analyzed UUDIS data on the number and duration of prescription drug shortages reported to ASHP from January 2001 through June 20, 2011. We examined these data because FDA did not have a database containing information on drug shortages for the time period we reviewed, and UUDIS is generally regarded as the most comprehensive and reliable source of such information. Using these data, we identified the number of drugs that had been in short supply on multiple occasions and the collective duration of these shortages. Using Red Book data, we examined the characteristics of 269 critical drug shortages that were identified during a shorter time period, January 1, 2009, through June 20, 2011.<sup>3</sup>

To identify the reported causes of selected drug shortages that occurred from January 2009 through June 2011, we focused our analysis on a nongeneralizable sample of 15 drug shortages that have had a significant impact on public health. The drugs involved in these shortages—all sterile injectables—are from three therapeutic classes: anesthesia, oncology, and anti-infective drugs.<sup>4</sup> We asked FDA officials to provide information on the causes of these 15 drug shortages, as reported to the agency by manufacturers. For additional information on the causes of shortages, we obtained information from four manufacturers of sterile injectable drugs—APP Pharmaceuticals, Bedford Laboratories, Hospira, and Teva Pharmaceuticals. All of these manufacturers produce drugs that recently were in short supply, and all of the 15 drug shortages we selected for review involved drugs that were manufactured by one or more of these manufacturers.

To describe FDA's response to drug shortages, we interviewed FDA officials and reviewed agency documents, including policies and procedures. To describe how FDA responded to the 15 selected drug shortages we reviewed in detail, we examined information the agency

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<sup>3</sup>Red Book is a compendium published by Thomson Reuters that includes information about the characteristics of drug products. UUDIS recognized these shortages as critical because alternative medications were unavailable, the shortages affected multiple manufacturers, or the shortages were widely reported; because the shortages were determined to be critical, they were posted to ASHP's website.

<sup>4</sup>Specifically, we reviewed information about shortages for five anesthesia drugs (epinephrine, neostigmine, propofol, thiopental, and succinylcholine), five oncology drugs (cisplatin, cytarabine, doxorubicin, etoposide, and vincristine) and five anti-infective drugs (acyclovir, amikacin, cefotetan, clindamycin, and sulfamethoxazole-trimethoprim). Most of these drugs have been available in generic form for over 15 years.

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provided about its response to these shortages. We also analyzed FDA information on potential drug shortages the agency prevented from January 2010 through June 2011.

To evaluate the extent to which FDA is able to protect public health through its response to drug shortages, we analyzed FDA's authority under the Federal Food, Drug, and Cosmetic Act, and reviewed relevant FDA regulations, policies, procedures, and documents. In addition, we evaluated FDA's approach to managing its response to drug shortages using standards for internal control—including those for information and communications, monitoring, and risk assessment.<sup>5</sup> We also interviewed a variety of stakeholders—including drug manufacturers, health professional associations, and others involved in drug production and the drug supply chain—to obtain information about FDA's response to drug shortages. Our work was performed in accordance with generally accepted government auditing standards.

In brief, we found that the number of drug shortages has grown substantially in recent years, and FDA is constrained in its ability to protect the public health from the impact of these shortages.

- *The number of drug shortages has grown substantially since 2006, and many shortages involved generic injectable drugs.* In total, 1,190 shortages were reported from January 1, 2001, through June 20, 2011, according to UUDIS data. From 2006 through 2010, the number of drug shortages increased each year and grew by more than 200 percent over this period. A record number of shortages (196) were reported in 2010, and 2011 is on pace to surpass 2010's record, with 146 shortages reported through June 20, 2011. Over half (64 percent) of the 1,190 shortages represent 283 drugs that were in short supply more than once. On average, these 283 drugs were each in short supply between two and eight times during this period, with an average of 2.7 times per drug. While the duration of all reported shortages varied considerably, most shortages lasted 1 year or less. On average, shortages lasted 286 days (over 9 months). Over half of shortages reported from January 1, 2009, through June 20, 2011, that UUDIS identified as critical—because, for example, alternative drugs were not available—involved generic injectable drugs. Certain

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<sup>5</sup>See GAO, *Standards for Internal Control in the Federal Government*, [GAO/AIMD-00-21.3.1](#) (Washington, D.C.: November 1999).

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therapeutic classes (such as anesthetic, oncology, and anti-infective drugs) were among those most often in short supply.

- *The drug shortages we reviewed in detail were generally caused by manufacturing problems and exacerbated by multiple difficulties.* Twelve of the 15 drug shortages we reviewed in detail were primarily caused by manufacturing problems, including those that resulted in manufacturing shutdowns, according to information provided by FDA and by manufacturers. For example, one manufacturer shut down a facility that produces sterile injectable drugs in order to improve the facility's manufacturing capabilities. While the manufacturer expected that the upgrade would take 3 months, it instead it took one year to complete, and as a result, multiple drugs that were produced at this facility went into short supply. The remaining 3 shortages we reviewed were reportedly caused by disruptions in the supply of active pharmaceutical ingredients. Officials from FDA and manufacturers explained that sterile injectable drugs are complex to make, and as such, can be prone to manufacturing and quality problems. In addition, certain types of sterile injectable drugs, such as anti-infective and oncology drugs, can be particularly challenging to manufacture. FDA also pointed out that sterile injectable drugs are being made by a decreasing number of aging facilities, which may contribute to the recent increase in manufacturing problems. In addition to the initial problems that caused the shortages, over half of the shortages we reviewed (8 of 15) were subsequently exacerbated by multiple other difficulties that arose after the shortages began. These 8 shortages were each affected by an average of four distinct difficulties that occurred in addition to the primary cause of the shortage and generally affected multiple manufacturers. During these shortages, multiple manufacturers sometimes experienced the same exacerbating issues once a shortage was already ongoing. For example, 9 of the 15 shortages we reviewed were extended as a result of manufacturing problems that occurred in addition to the shortages' primary causes. It is also important to recognize that some drugs may only be produced by a few manufacturers. The drugs involved in the 15 shortages we reviewed were produced by an average of three manufacturers at the time the drug went into short supply. According to officials from FDA and industry officials, when only a few manufacturers make a drug and one cannot maintain production, it can be difficult for the other manufacturers to substantially increase production to ensure that demand for a drug is met—even in the absence of any other problems. Officials from one manufacturer described recent shortage situations as a perfect storm

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of several manufacturers coincidentally experiencing manufacturing problems all at the same time.

- *FDA responds to known drug shortages by taking actions to address their underlying causes and to enhance product availability.* FDA officials explained that they respond to all of the shortages of which the agency becomes aware, and they determine how to address each shortage based on its cause and the public health risk associated with the shortage. For example, the agency may provide assistance to manufacturers to resolve manufacturing or quality problems that can result in a shortage. Our review of FDA's response to 15 shortages of sterile injectable drugs showed that FDA typically used two or more types of actions to respond to each shortage, and for 8 shortages, the agency responded with four or more types of actions. FDA most frequently offered assistance to manufacturers to prevent, alleviate, or resolve the shortage, or notified other manufacturers to expect increased demand or encouraged them to increase production. FDA has demonstrated that it can prevent the majority of shortages from occurring when it learns of potential supply disruptions in advance. FDA prevented 50 potential shortages during the first half of 2011—about 1.5 times the number of potential drug shortages (35) prevented during all of 2010. To prevent these potential shortages, FDA took some of the same types of actions it uses to alleviate and resolve shortages. As part of its response to drug shortages, FDA communicates information about shortages to the public via its website, which lists both current and resolved shortages.<sup>6</sup>
- *FDA is constrained in its ability to protect public health from drug shortages.* Specifically, FDA is constrained by its lack of authority to require manufacturers to provide the agency and the public with information about shortages, or require that manufacturers take certain actions to prevent, alleviate, or resolve shortages. FDA's sole authority related to manufacturers' reporting of drug shortages pertains to the discontinuation of approved drugs that are life-supporting, life-sustaining, or for use in the prevention of a debilitating disease or condition, when such drugs are produced by only one

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<sup>6</sup>See <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>.

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manufacturer.<sup>7</sup> In such instances, companies are required to provide FDA with at least 6 months notice of discontinuations. However, such discontinuations have not been the primary cause of most recent drug shortages. As a result of these constraints, the agency's approach to managing drug shortages is predominately reactive. While FDA has encouraged manufacturers to report supply disruptions to the agency, according to agency officials, less than half of all shortages are reported to the agency by manufacturers. Instead, FDA is most often notified by ASHP, health care providers, or consumers when they are unable to purchase a drug—a point at which the shortage is already affecting public health. FDA's ability to protect public health is also constrained by management challenges that weaken its ability to respond to drug shortages. Specifically, FDA does not maintain data on drug shortages, such as their causes and the agency's response. Without such data, FDA is unable to systematically monitor trends and enhance its ability to address the causes of drug shortages. In addition, despite the increase in the number of drug shortages reported in recent years, FDA has not identified drug shortages as an area of strategic importance for the agency. It has consistently staffed its Drug Shortage Program with a small number of employees. While FDA has recognized the significant public health consequences that can result from drug shortages, the agency has not developed a set of results-oriented performance metrics related to drug shortages, and has not identified drug shortages as an area of strategic importance for the agency. Without such management tools, FDA may be unable to effectively evaluate its work and improve its ability to protect the public health.

In conclusion, the number of drug shortages has substantially increased in recent years—including those for life-saving medications such as oncology drugs—a situation that has jeopardized the public health. While FDA may not always be able to prevent shortages from occurring, the agency's response to drug shortages is constrained by its lack of authority to require manufacturers to report potential or current shortages to the agency. FDA has demonstrated that when it learns of shortages in advance, it can prevent the majority of such shortages from occurring.

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<sup>7</sup>See 21 U.S.C § 356c; 21 C.F.R. § 314.81(b)(3)(iii) (2011). FDA does not have the authority to enforce this requirement, for example, by seeking civil monetary penalties. To the maximum extent possible, FDA is to distribute information on the discontinuance of these products to appropriate physician and patient organizations.

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However, it does not currently have the authority to require manufacturers to provide it with information about potential or current shortages, and therefore it can only prevent the shortages that it becomes aware of through voluntary reporting. FDA's ability to protect the public health is also constrained by its own management challenges. The agency has not elevated the priority it places on its response to drug shortages, despite the rapid escalation of these shortages. Not only have its resources not kept pace with this escalation, the agency has not developed the metrics to manage this growing public health problem. Without data and results-oriented performance measures, FDA cannot systematically monitor drug shortages and their causes, nor can it adequately track or assess its own success in preventing or mitigating shortages. Although FDA recognizes the serious threat these shortages pose, we believe the agency can and must do more to protect the public health.

Our report includes a matter for Congressional consideration that would establish a requirement for manufacturers to report to FDA any changes that could affect the supply of their drugs. In addition, our report recommends that FDA take steps to strengthen its ability to respond to drug shortages by (1) assessing the resources allocated to the Drug Shortage Program; (2) developing an information system to enable the Drug Shortage Program to manage its daily workload in a systematic manner, track data about drug shortages—including their causes and FDA's response—and share information across FDA offices regarding drugs that are in short supply; (3) ensuring that FDA's strategic plan articulates goals and priorities for maintaining the availability of all medically necessary drugs; and (4) developing results-oriented performance metrics to assess and quantify the implementation of the agency's goals and FDA's response to drug shortages.

In commenting on a draft of the report upon which this testimony is based, HHS stated that it supports legislation that would require manufacturers to report potential or actual supply disruptions to FDA. In addition, HHS outlined actions it plans to take that are consistent with our recommendations.

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Mr. Chairman, this concludes my statement. I would be pleased to respond to any questions you or other Members of the Committee may have.



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For questions about this testimony, please contact Marcia Crosse at (202) 512-7114 or [crossem@gao.gov](mailto:crossem@gao.gov). Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this testimony. Individuals who made key contributions to this testimony include Geraldine Redican-Bigott, Assistant Director; Nick Bartine; Emily Goodman; Cathleen Hamann; Yesook Merrill; Lisa Motley; and Patricia Roy.

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