

November 2011

# DRUG SHORTAGES

## FDA's Ability to Respond Should Be Strengthened

U.S. Government Accountability Office

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## Why GAO Did This Study

In recent years, nationwide shortages of prescription drugs have increased, preventing patients from accessing medications essential to their care. The Food and Drug Administration (FDA), an agency within the Department of Health and Human Services (HHS), established a Drug Shortage Program with a mission of helping to prevent, alleviate, and resolve shortages. FDA receives information about shortages from manufacturers, though this reporting is generally voluntary, as well as from the American Society of Health-System Pharmacists (ASHP). ASHP tracks nationwide shortages for its members through a partnership with the University of Utah Drug Information Service (UUDIS).

GAO was asked to review trends in shortages and examine FDA's response. In this report, GAO (1) reviews trends in drug shortages, (2) describes FDA's response, and (3) evaluates FDA's ability to protect public health through its response to drug shortages. GAO analyzed UUDIS data, interviewed officials from FDA, health care professional associations, and industry, and also examined relevant statutes, regulations, information, and documents.

## What GAO Recommends

Congress should consider establishing a requirement for manufacturers to report to FDA any changes that could affect the supply of their drugs. In addition, FDA should enhance its ability to respond to drug shortages, for example, by developing an information system to manage data about shortages. HHS outlined actions it plans to take that are consistent with GAO's recommendations.

View [GAO-12-116](#) or key components. For more information, contact Marcia Crosse at (202) 512-7114 or [crossem@gao.gov](mailto:crossem@gao.gov).

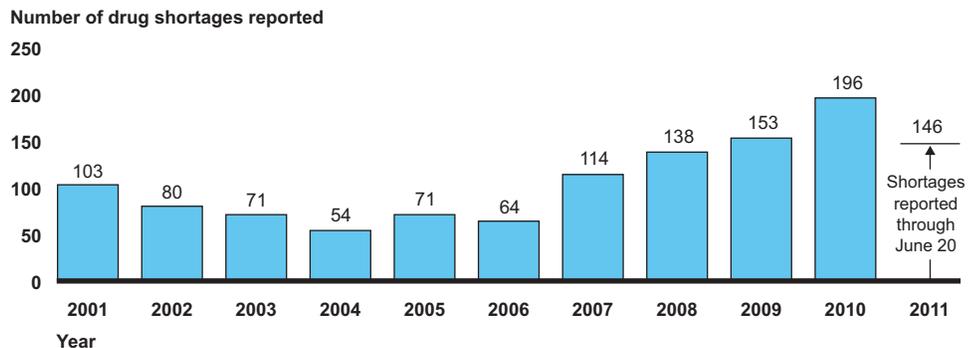
# DRUG SHORTAGES

## FDA's Ability to Respond Should Be Strengthened

### What GAO Found

The number of drug shortages has grown substantially since 2006. 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. A record number of shortages were reported in 2010, and 2011 is on pace to surpass 2010's record. Sixty-four percent of shortages involved drugs that were in short supply more than once. 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 therapeutic classes (such as anesthetic, oncology, and anti-infective drugs) were among those most often in short supply.

**Drug Shortages Reported January 1, 2001 through June 20, 2011, by Year**



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

FDA responds to drug shortages by taking actions to address the underlying causes and to enhance product availability, for example by providing assistance to manufacturers to resolve manufacturing or quality problems that can result in a shortage. When informed of the possibility of a shortage in advance, FDA has increasingly been able to prevent potential drug shortages from occurring. FDA prevented 50 potential shortages during the first half of 2011. As part of its response, FDA provides general information about drug shortages to the public via its website.

FDA is constrained in its ability to protect public health from drug shortages due to its lack of authority to require manufacturers to report actual or potential shortages to the agency or the public, or to require manufacturers to take certain actions to prevent, alleviate, or resolve shortages. As a result, the agency's approach to managing drug shortages is predominately reactive. FDA's ability to protect public health is also constrained by management challenges that weaken its ability to respond to drug shortages. For example, FDA does not systematically maintain data on drug shortages, without which it is unable to monitor trends and enhance its ability to address the causes of drug shortages. In addition, FDA has provided limited resources to manage its response to drug shortages and lacks related performance measures and priorities.

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## Abbreviations

ANDA	abbreviated new drug application
API	active pharmaceutical ingredient
ASA	American Society of Anesthesiologists
ASCO	American Society of Clinical Oncology
ASHP	American Society of Health-System Pharmacists
CDER	Center for Drug Evaluation and Research
CNS	central nervous system
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
IDSA	Infectious Diseases Society of America
NDA	new drug application
NDC	national drug code
OGD	Office of Generic Drugs
OND	Office of New Drugs
UUDIS	University of Utah Drug Information Service

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**G A O**

Accountability \* Integrity \* Reliability

**United States Government Accountability Office**  
Washington, DC 20548

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November 21, 2011

The Honorable Tom Harkin  
Chairman  
Committee on Health, Education, Labor, and Pensions  
United States Senate

The Honorable Richard Blumenthal  
United States Senate

The Honorable Robert P. Casey, Jr.  
United States Senate

In recent years, hospitals and health care professionals have increasingly reported nationwide shortages of prescription drugs, including those that are life-saving and life-sustaining. Drug shortages directly threaten public health by preventing patients from accessing medications that are essential to their care. For example, recent shortages of oncology drugs have sparked concerns from health care professionals about how to care for cancer patients that need such medications in order to survive. 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 are more costly.

The Food and Drug Administration (FDA)—an agency within the Department of Health and Human Services (HHS) that is responsible for overseeing the safety and effectiveness of drugs marketed in the United States—has recognized the significant public health consequences that can result from drug shortages. According to FDA, a record number of drugs were in short supply in 2010, and the number of drug shortages continued to grow during 2011. Consistent with its mission of protecting the public health, FDA established its Drug Shortage Program in 1999 out of growing concern over the increasing number of drug shortages. The purpose of this program is to help prevent, alleviate, and resolve shortage situations. To do this, FDA must identify and monitor potential and actual drug shortages, which may be reported to the agency by manufacturers, health professionals, and the public. To develop more comprehensive information on drug shortages, FDA also obtains information from the American Society of Health-System Pharmacists (ASHP). ASHP began tracking data on drug shortages—in partnership with the University of Utah Drug Information Service (UUDIS)—in 2001 to inform its members,

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such as hospital pharmacists, and the public about the status of new, ongoing, and resolved shortages.<sup>1</sup>

You asked us to examine issues related to the causes of prescription drug shortages and FDA's response to these shortages. This report (1) reviews trends in prescription drug shortages that occurred from January 2001 through June 2011, (2) identifies the reported causes of selected drug shortages that occurred from January 2009 through June 2011, (3) describes FDA's response to drug shortages, and (4) evaluates the extent to which FDA is able to protect the public health through its response to drug shortages.

To review trends in prescription drug shortages that occurred from January 2001 through June 2011, we analyzed UUDIS data on the number of shortages reported to ASHP during that time period, 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. We reviewed UUDIS data to determine the number of shortages of prescription drugs that were identified each year and the duration of these shortages.<sup>2</sup> To identify the number of drugs that had been in short supply on multiple occasions and the collective duration of these shortages, we grouped together shortages that involved clinically interchangeable versions of a drug that is administered through the same route—for example, by injection. We confirmed our identification of clinically interchangeable versions of a drug with a knowledgeable UUDIS pharmacist. We also 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> UUDIS recognized these shortages as critical because alternative medications were unavailable, the shortages affected multiple manufacturers, or the

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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>Because our analysis focused on shortages of prescription drugs, we excluded from our analysis shortages of over-the-counter drugs, biologics (including vaccines), medical devices, and orally-administered vitamins, which UUDIS also tracks and includes in its data.

<sup>3</sup>These 269 shortages represent 54 percent of the 495 shortages reported during that time period.

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shortages were widely reported, and because the shortages were determined to be critical, they were posted to ASHP's website. We obtained from UUDIS the national drug codes (NDC) that were associated with each of these critical shortages; UUDIS does not consistently track the NDCs associated with shortages that it determines are not critical.<sup>4</sup> Using these NDCs, we analyzed Red Book data to determine the routes of administration, therapeutic classes, and number of manufacturers associated with each shortage.<sup>5</sup> To obtain context for the trends we identified, we interviewed officials at FDA, UUDIS, and ASHP. We also discussed the data with knowledgeable officials at UUDIS, and we reviewed all data for reasonableness, outliers, and consistency; we determined that the data were sufficiently reliable for our purposes.

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. To assist in the selection of shortages for our detailed review, we asked representatives from the American Society of Anesthesiologists (ASA), the American Society of Clinical Oncology (ASCO), and the Infectious Diseases Society of America (IDSA) to each identify 5 shortages of sterile injectable drugs that were specific to their members' practice areas, that occurred from January 2009 through June 2011, and that had a significant impact on patient care or public health. Our analysis reflects the 15 drug shortages suggested by these associations.<sup>6</sup> We asked FDA officials to provide information on the causes of these 15 drug shortages, as reported by manufacturers. Using

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<sup>4</sup>NDCs identify a drug's manufacturer, product name, route of administration, dosage form, and package size, among other information. One drug can have multiple NDCs associated with it. For example, a drug made by one manufacturer in one strength but in three package sizes would have three NDCs.

<sup>5</sup>Red Book is a compendium published by Thomson Reuters that includes information about the characteristics of drug products.

<sup>6</sup>Specifically, the associations suggested, and 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).

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the information FDA provided, we determined the first event that resulted in the shortage. We also captured information on other events that affected the availability of the drug before the shortage was resolved. 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. The results of our review of the 15 drug shortages are not generalizable to other drug shortages.

To describe FDA's response to drug shortages, we interviewed FDA officials and reviewed agency documents, including policies and procedures.<sup>7</sup> To describe how FDA responded to the 15 selected drug shortages we reviewed in detail, we examined information the agency 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 determine the number of shortages prevented, we grouped together shortages that involved multiple versions of a drug that had the same route of administration.

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. We also examined relevant FDA regulations, policies, and procedures, and reviewed FDA's strategic priorities regarding drug availability. 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>8</sup> In addition, we considered information in our previous reports on strategic planning, workforce planning, and the establishment of results-oriented performance measures. We also obtained the health care community's perspective on FDA's response to, and communication about, drug shortages by interviewing officials from ASA, ASCO, ASHP, IDSA, and the Institute for Safe Medication

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<sup>7</sup>Our work did not include a review of FDA's response to shortages of biological products, such as vaccines.

<sup>8</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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Practices. To obtain drug manufacturers' perspective on FDA's response to shortages, we interviewed officials from the four manufacturers of generic drugs noted above, as well as officials from the Generic Pharmaceutical Association, the Pharmaceutical Research and Manufacturers of America, and the Biotechnology Industry Organization. We also interviewed officials from Premier Healthcare Alliance, a group purchasing organization, the Healthcare Distribution Management Association, and the United States Pharmacopoeia to obtain the perspective of other stakeholders involved in drug production and the drug supply chain.

We conducted this performance audit from June 2011 to October 2011 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

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## Background

The unavailability of drugs can result in problems that directly affect the public health and increase costs for providers and patients. FDA's role in overseeing the safety and effectiveness of drugs provides the agency an opportunity to take actions to prevent, alleviate, and resolve drug shortages.

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## Factors Affecting Drug Availability

A variety of factors can trigger drug availability problems. These factors can involve any segment of the supply chain, from problems related to the growth or harvest of ingredients required to manufacture a drug, to increased demand for products by consumers or providers.<sup>9</sup> They include the following:

- Disruption in the supply of raw materials. Manufacturers are sometimes unable to obtain the raw materials used in producing a drug, including the active pharmaceutical ingredients (API) and

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<sup>9</sup>The causes of drug shortages have been widely reported. See for example, American Society of Health-System Pharmacists, *ASHP Guidelines on Managing Drug Product Shortages*, American Journal of Health-System Pharmacists, vol. 58, no. 1445-50 (2001): 26-30.

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inactive ingredients.<sup>10</sup> APIs may become in short supply as a result of climactic or environmental changes that depress the growth of plants from which the materials are extracted, or the APIs could be contaminated or degraded during harvesting, storage, or transport. API manufacturers may encounter problems synthesizing the chemical components of an API or face shortages of their ingredients. Finally, firms involved in the harvest, manufacture, storage, or transport of these materials could decide to exit the market, which could affect the availability of these materials for the manufacture of finished drug products. According to FDA, the majority of APIs used in FDA-approved drugs are imported from foreign countries, which may add to challenges related to their availability. For example, regulations issued by foreign countries regarding the use or export of these materials could affect their availability. In addition, APIs may be held for examination during the importation process, delaying their availability.

- Manufacturing problems. Manufacturers may have problems producing a finished drug that is safe, pure, and of high quality. Manufacturers may identify these problems themselves, or FDA may identify them during an inspection. Regardless of how the problems are identified, a manufacturer may voluntarily decide to stop producing a drug until the problem can be resolved. In addition, the manufacturer may decide to recall a drug in order to remove it from the market.<sup>11</sup>
- Manufacturers' business decisions. Manufacturers' business decisions may affect the production and supply of a drug. For example, a manufacturer may decide to discontinue its production of a drug as a result of decreased profitability. Or, a manufacturer may decide to renovate a facility, requiring a temporary shutdown of production.

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<sup>10</sup>An API is any component that is intended to provide pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease. FDA defines inactive ingredients as any component of a drug product other than the API, such as materials that improve the appearance, stability, and palatability of the product. See 21 C.F.R. § 210.3(b)(7), (8) (2011).

<sup>11</sup>See 21 C.F.R. § 7.40 (2011). Manufacturers may also decide to recall a product for other reasons, such as errors in the product's labeling.

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- Industry consolidations. Recent mergers and acquisitions within the drug industry have reduced the number of manufacturers making drugs. Many drugs that have recently been in short supply are only produced by a few manufacturers. As the number of manufacturers of a product decreases, there is an increased likelihood that a problem with one manufacturer will lead to a shortage of all versions of that drug. For example, if only three manufacturers make a drug and one manufacturer halts production, it is often difficult—if not impossible—for the remaining two manufacturers to increase their production enough to meet consumer demand.
  - Unexpected increase in demand. A shortage may occur due to unexpected shifts in demand caused, for example, by a change in the clinical use of a product or due to a shortage of a similar drug. Shortages may also occur when hospitals or other health care providers stockpile particular drugs to take advantage of low prices, by placing orders that exceed normal demand.<sup>12</sup>
  - Natural disasters. Natural disasters can create drug shortages when they affect the supply of raw materials or manufacturing facilities.
  - Unstable supply chain. An increasingly unstable supply chain for drugs also contributes to drug shortages. Recent changes in supply chain management have increased the cost-effectiveness of individual participants in the supply chain, but have also resulted in a reduction in individual participants' capacity to respond to supply disruptions. Factors that impact the availability of drugs in the supply chain include the complex nature of the global supply chain, reduced manufacturing capacity, and lean inventory systems.
    - *Complex, global supply chain*. The supply chain for drugs is highly complex, increasingly global, and involves a large number of organizations that are highly dependent on each other.

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<sup>12</sup>For example, we recently found evidence of drug shortages related to stockpiling within the 340B Drug Pricing Program—a program through which participating drug manufacturers give certain entities, such as federally funded health centers and other federal grantees, access to discounted prices on outpatient drugs. In some cases when the price of a 340B drug dropped, providers with access to 340B's discounted prices stockpiled a drug, resulting in shortages in the supply of that drug for other providers. See GAO, *Drug Pricing: Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement*, [GAO-11-836](#) (Washington, D.C.: Sept. 23, 2011).

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Manufacturers of finished drug products rely on an increasingly global supply chain in which each manufacturing step may be outsourced to foreign establishments.<sup>13</sup> For example, manufacturers of finished drug products are dependent on manufacturers of active and inactive ingredients as well as the distribution of those products to the manufacturing site where the finished drug is produced. As a result of the large numbers of entities involved in the supply chain, every individual member of the chain has less control, and is less able to respond to problems experienced by those on which it is dependent.

- *Manufacturing capacity constraints.* Some companies may have reduced manufacturing redundancies to save on costs—for example, by cutting back on the number of their manufacturing facilities, or the number of manufacturing lines available to produce certain drugs. These changes reduce the manufacturer’s capacity to respond to its own manufacturing problems. In addition, some companies produce multiple drugs using the same manufacturing line. If a problem occurs with the manufacturing line, it can affect the production of all drugs made on that line.
- *Lean inventory systems.* Manufacturers, distributors, hospitals, and other health care providers have been increasingly using leaner “just-in-time” inventory systems that allow them to maintain smaller inventories of drugs at any given time. Many providers have reduced on-hand inventories to the extent that they are dependent on daily replenishments from suppliers. As a result, all parts of the supply chain are more likely to feel the effects of a shortage more quickly.

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## Potential Effects of Drug Shortages

Shortages of drugs can result in a variety of problems, ranging from those that directly affect patient care to those that increase costs for providers and patients. These include the following:

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<sup>13</sup>We have previously reported on the challenges FDA faces in overseeing an increasingly complex foreign drug manufacturing supply chain. For example, see GAO, *Drug Safety: FDA Faces Challenges Overseeing the Foreign Drug Manufacturing Supply Chain*, [GAO-11-936T](#) (Washington, D.C.: Sept. 14, 2011).

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- Delays in patient care. Some shortages result in situations where a viable alternative drug is not available, and a patient may be unable to receive treatment. Some hospitals and ambulatory surgery centers have been forced to postpone surgeries due to a shortage of anesthetic drugs.<sup>14</sup> A lack of treatment can have serious consequences. For example, a recent shortage of anti-infective drugs contributed to patient deaths from infections that were only treatable by drugs that were in short supply.
  - Ethical dilemmas. When drugs are in short supply, providers may be unable to obtain needed drugs to treat all of their patients. They may therefore have to make difficult choices, such as deciding which cancer patients should start or complete a round of chemotherapy.
  - Treatment with less effective alternative drugs. Alternative drugs may be able to treat some patients. However, some alternative treatments may provide a lower rate of effectiveness and a higher likelihood of adverse events.
  - Medication errors. Drug shortages can result in the need to treat patients with unfamiliar drugs, for example, different drugs, or the same drug that is available in a different strength. Administering such products can result in medication errors.<sup>15</sup>
  - Increased costs for providers and patients. Shortages require time and resources to manage. Health care providers need to determine how to obtain the drug in short supply, or staff must spend time searching for available treatment options. In addition, the use of alternative medications can result in the need for additional training. In order to learn how to avoid medication errors, health care providers need to learn how to accurately prescribe and administer the alternative products, with which they may lack familiarity. Finally, the

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<sup>14</sup>According to a 2011 American Hospital Association survey, over 80 percent of the 820 responding hospitals reported that patient treatment had been delayed as a result of drug shortages. American Hospital Association, *AHA Survey on Drug Shortages* (Washington, D.C.: July 12, 2011).

<sup>15</sup>According to a report issued by the Institute for Safe Medication Practices, about 25 percent of the 1,800 health care practitioners that responded to its 2010 survey reported medication errors which occurred as a result of a drug shortage. Institute for Safe Medication Practices, *Drug Shortages: National Survey Reveals High Level of Frustration, Low Level of Safety* (Horsham, Pa.: Sept. 23, 2010).

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cost of the drug in short supply—or available alternative—may be higher than usual.<sup>16</sup>

- Use of the gray market. Providers who are unable to obtain drugs from their regular distributors may resort to purchasing drugs from distribution channels that were not authorized by the manufacturer, referred to as the gray market.<sup>17</sup> Gray market suppliers typically obtain small quantities of a drug that is in short supply and offer it for purchase to others at an inflated price.<sup>18</sup> Because the origin of gray market drugs may be unknown, there is no guarantee of the drug's pedigree or assurance that it was stored and transported appropriately. As a result, patients who receive treatment with such drugs may experience adverse events or receive inadequate or inappropriate treatment.<sup>19</sup>
- Unauthorized use of compounding pharmacies. In some cases, those unable to purchase drugs from their regular distribution channels have turned to compounding pharmacies.<sup>20</sup> While compounding pharmacies play a vital role in health care by tailoring drugs to better meet patients' needs (such as removing a dye from a drug to prevent an allergic reaction) they are not authorized to prepare drugs that are copies of commercially available products.

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<sup>16</sup>According to *AHA Survey on Drug Shortages*, over 90 percent of 820 responding hospitals reported an increase in drug costs as a result of drug shortages.

<sup>17</sup>A report issued by the Institute for Safe Medication Practices noted that over half of the 549 hospitals that participated in its 2011 survey reported receiving daily solicitations from gray market vendors for drugs that were in short supply. Institute for Safe Medication Practices, *Gray Market, Black Heart: Pharmaceutical Gray Market Finds a Disturbing Niche During the Drug Shortage Crisis* (Horsham, Pa.: Aug. 25, 2011).

<sup>18</sup>Premier healthcare alliance, a group purchasing organization, recently reported that 42 of its member hospitals recorded 1,745 offers to purchase drugs that were in short supply from the gray market during a 2-week period at the beginning of 2011. Prices for these products were, on average, 650 percent greater than Premier's contract price, and ranged up to 4,533 percent greater than their contract price. Premier healthcare alliance, *Buyer Beware: Drug Shortages and the Gray Market* (Charlotte, N.C.: Aug. 16, 2011).

<sup>19</sup>The Institute for Safe Medication Practices reported in *Gray Market, Black Heart*, that over 10 percent of the 549 hospitals that participated in its 2011 survey were aware of product authenticity issues, medication errors, or adverse drug reactions that were associated with the use of products purchased from the gray market during the last 2 years.

<sup>20</sup>Compounding pharmacies, like other pharmacies, are primarily regulated by the states.

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- Disruption of the development of new drugs. Ongoing shortages of drugs have affected clinical trials (studies in humans) that are used to gauge the safety and effectiveness of a newly developed drug to that of a drug known to be effective. The inability to obtain adequate supplies of drugs, such as oncology drugs, has resulted in clinical trials being suspended indefinitely. Without such trials, new drugs cannot move forward through the development process.

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## FDA Oversight of Drugs

FDA is responsible for overseeing the safety and effectiveness of drugs. Within FDA, the Center for Drug Evaluation and Research (CDER) manages these responsibilities. FDA's approval is required before new drugs and generic drugs—drugs that are copies of approved drugs—can be marketed for sale in the United States.<sup>21</sup> To obtain FDA's approval for a new drug, sponsors must submit a new drug application (NDA) containing data on the safety and effectiveness of the drug as determined through clinical trials and other research for review by CDER's Office of New Drugs (OND). Sponsors of generic drugs may obtain FDA approval by submitting an abbreviated new drug application (ANDA) to the agency for review by CDER's Office of Generic Drugs (OGD). The ANDA contains data showing, among other things, that the generic drug is bioequivalent to, or performs in the same manner as, a drug approved through the NDA process.<sup>22</sup>

Once the agency receives an NDA, it is reviewed by one of OND's medical review divisions, depending on the indication the drug has been proposed to treat. ANDA applications are reviewed by OGD to determine bioequivalence to approved drugs. In reviewing each application, FDA considers whether the proposed product labeling clearly states the condition and population the product is intended to treat. If the agency determines that a new drug is safe and effective for its intended use (that its clinical benefits outweigh its potential health risks) or that a generic drug is bioequivalent to a previously approved drug, and that other requirements are met, it will approve the application. After obtaining FDA's approval, drug companies that want to change any part of their original application—such as changes to product manufacturing location

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<sup>21</sup>21 U.S.C. § 355.

<sup>22</sup>21 U.S.C. § 355(j). The application for generic drugs is abbreviated because FDA does not require sponsors to conduct, or provide evidence from, clinical trials that are required of sponsors of new drugs.

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or process, type or source of active ingredients, or the product's labeling—must generally submit an application supplement to obtain FDA's review and, if the change has a substantial potential to have an adverse effect on the product, approval.<sup>23</sup>

After approving new and generic drugs for marketing, FDA's responsibilities continue as it is charged with monitoring the safety, effectiveness, quality, and promotion of approved drugs, and the agency may take enforcement actions in response to violations of laws and regulations. However, FDA may exercise regulatory discretion in deciding what actions to take or when to take them. For example, as part of its efforts to ensure the safety of approved drugs, FDA periodically inspects drug manufacturing establishments to assess their ongoing compliance with quality standards.<sup>24</sup> If FDA finds manufacturing deficiencies, it may request that the manufacturer take corrective actions, or it may take enforcement action to require the manufacturer to take corrective actions. FDA may also take steps to ensure that manufacturers do not disseminate false or misleading information about a drug. Drugs whose labeling includes information not consistent with the labeling approved by FDA are considered misbranded and may be subject to regulatory action. FDA could seek civil monetary penalties from manufacturers that have misbranded their drugs.

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## FDA Oversight of Drug Shortages

FDA's response to drug shortages is managed by CDER's Drug Shortage Program. The agency maintains a website that includes information about how drug shortages can be reported to the Drug Shortage Program, and encourages manufacturers and the public to report shortages. Once the Drug Shortage Program becomes aware of a potential or actual shortage, agency officials attempt to determine whether the total supply of the drug and any pharmaceutical equivalents is inadequate to meet demand—FDA's definition of a shortage.<sup>25</sup> To make this determination, Drug

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<sup>23</sup>21 C.F.R. §§ 314.70, 314.97 (2011).

<sup>24</sup>These standards, referred to as current good manufacturing practice regulations, provide a framework for a manufacturer to follow to produce safe, pure, and high-quality drugs. See 21 C.F.R. parts 210-211.

<sup>25</sup>A pharmaceutical equivalent is a drug product that is identical in dosage form, API, and strength, and delivers an identical amount of API over an identical dosing period. See 21 C.F.R. § 320.1(c) (2011).

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Shortage Program officials contact manufacturers of the drug to confirm how much inventory remains and how much of the drug they are currently producing. Drug Shortage Program officials compile this information and compare it to pharmaceutical industry sales data, including that which is available from IMS Health, in order to determine historical demand for the product. If the amount of the drug—or pharmaceutical equivalents—is insufficient to meet market demand, the agency considers the drug to be in shortage, and the Drug Shortage Program takes actions intended to alleviate and resolve the shortage.

FDA's Drug Shortage Program also collaborates with ASHP to identify new drug shortages; however, ASHP also tracks shortages that do not meet FDA's definition of a shortage. Once the Drug Shortage Program determines that a shortage is in effect, it may coordinate its response with several CDER offices, including OGD, OND, and the Office of Compliance. If a drug in shortage is manufactured by a company involved in a regulatory action, the Office of Compliance may also work with FDA's Office of Regulatory Affairs and the company to mitigate and remediate the underlying problem.

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## Federal Strategic and Workforce Planning

The use of strategic planning can help federal agencies manage their programs more effectively by developing strategies to address current and future management challenges. To be successful, strategic plans should include clearly established goals and objectives and a description of how program activities can serve those goals. We have previously reported on a variety of leading practices for successful strategic planning.<sup>26</sup> One such practice is the development of a set of results-oriented performance measures, which provide an important way of helping to evaluate program performance, demonstrate progress in achieving results, balance competing priorities, and inform decision making. When possible, such measures should demonstrate a program's contributions toward the long-term outcomes, or the results the agency expects a program to achieve. Given FDA's mission of ensuring the public health, we have previously noted that the agency's long-term outcomes should be focused on this mission.<sup>27</sup> When long-term outcomes

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<sup>26</sup>See, for example, GAO, *Managing for Results: Critical Issues for Improving Federal Agencies' Strategic Plans*, [GAO/GGD-97-180](#) (Washington, D.C.: Sept. 16, 1997).

<sup>27</sup>GAO, *Food and Drug Administration: Opportunities Exist to Better Address Management Challenges*, [GAO-10-279](#) (Washington, D.C.: Feb. 19, 2010).

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may be influenced by multiple agency programs and external factors, short-term and intermediate measures can also demonstrate a program's specific contribution to a long-term outcome.<sup>28</sup>

Another important management tool is workforce planning, which helps agencies to align their workforce with current and future program needs and develop long-term strategies for recruiting, training, and retaining staff.<sup>29</sup> Workforce planning assists agencies in thinking strategically about how to put the right people in the right jobs at the right time. Although approaches to such planning can vary by agency, depending on an agency's unique needs and mission, workforce plans should share certain principles, such as the identification of skills and competencies to fill critical workforce gaps and the strategies needed to recruit them.

We have previously reported on the need for FDA to improve its strategic planning and performance metrics. In 2010, we reported that FDA was not fully utilizing practices for effective strategic and workforce planning.<sup>30</sup> We found that most of FDA's established performance measures were not results-oriented as they did not focus on actual public health outcomes. In addition, we reported that FDA lacked clear linkages between its resources and goals, generally did not track workload by strategic goals, and that only about one-third to one-half of FDA managers used performance information to a great extent in making management decisions, such as setting program priorities. We also noted that FDA's internal coordination was one of the major management challenges facing the agency. We recommended, and FDA agreed, that the agency issue an up-to-date strategic workforce plan, make its performance measures more results-oriented, and more clearly align center and office program activities to FDA's strategic goals. In January 2009 we added FDA's oversight of medical products to our High-Risk List because FDA continued to face multiple challenges that threatened to compromise its ability to protect the public health. In 2011, in an update to our High-Risk Series, we noted that although FDA had begun taking steps to improve its oversight, the agency needs to do more to resolve

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<sup>28</sup>GAO, *Agency Performance Plans: Examples of Practices That Can Improve Usefulness to Decisionmakers*, [GAO/GGD/AIMD-99-69](#) (Washington, D.C.: Feb. 26, 1999).

<sup>29</sup>GAO, *Human Capital: Key Principles for Effective Strategic Workforce Planning*, [GAO-04-39](#) (Washington, D.C.: Dec. 11, 2003).

<sup>30</sup>[GAO-10-279](#).

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concerns, such as by improving resource management and strategic planning, responding to globalization, and overseeing postmarket safety.<sup>31</sup>

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## The Number of Drug Shortages Has Grown Substantially Since 2006, and Many Involved Generic Injectable Drugs

Our analysis of the trends in drug shortages that were reported from January 2001 through June 2011 showed that the number of drug shortages reported has grown substantially since 2006, and many shortages since 2009 have involved generic injectable drugs.

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## The Number of Drug Shortages Has Grown Substantially Since 2006

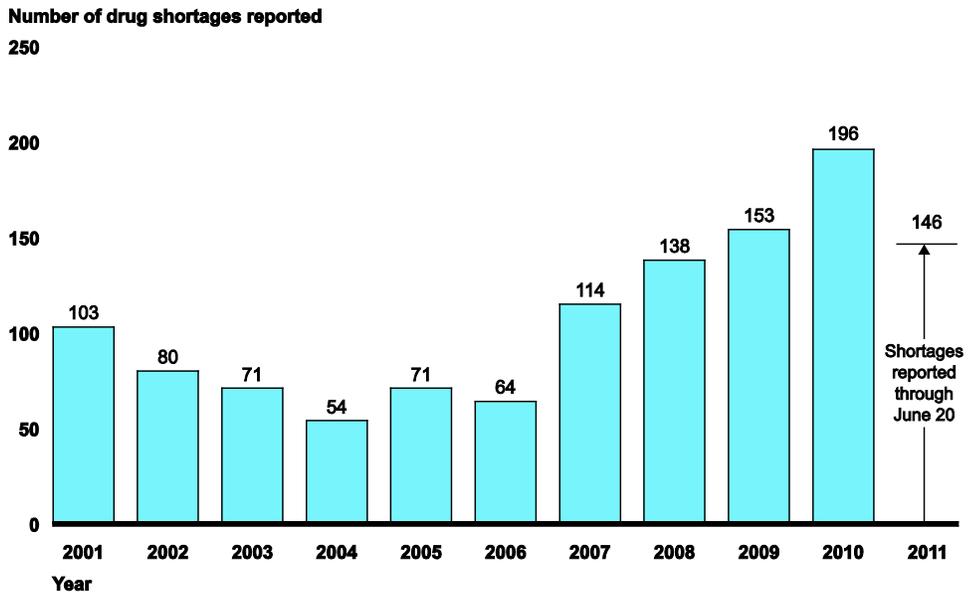
Since 2006, the number of drug shortages reported each year has grown substantially. In total, 1,190 drug shortages were reported to ASHP from January 2001 through June 20, 2011, according to our analysis of UUDIS data.<sup>32</sup> The number of drug shortages reported varied from year to year, and from 2001 through 2006, generally declined. However, 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. (See fig. 1.)

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<sup>31</sup>GAO, *High-Risk Series: An Update*, [GAO-11-278](#) (Washington, D.C.: February 2011).

<sup>32</sup>When tracking shortages, UUDIS groups together shortages of multiple versions—for example, multiple concentrations—of the same drug; the count of shortages reported therefore reflects this grouping. The total number of shortages includes those that have been resolved as well as active shortages. As of June 20, 2011, there were 230 active shortages, including some that were reported in prior years.

**Figure 1: Number of Drug Shortages Reported January 1, 2001, through June 20, 2011, by Year**



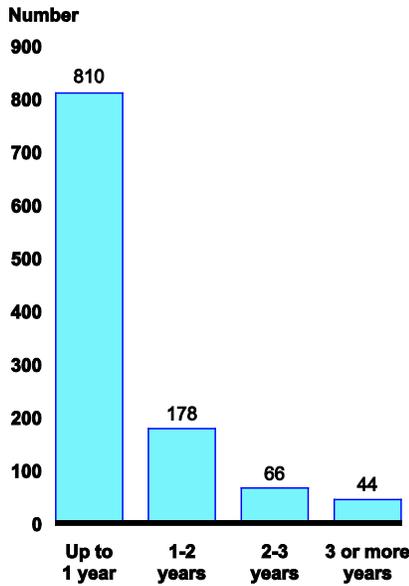
Source: GAO analysis of University of Utah Drug Information Service data.

Over half (64 percent, or 766) of the 1,190 shortages represent drugs that were in shortage more than once. Specifically, 283 drugs were in shortage on multiple occasions during this time frame, representing 766 individual shortages. 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. Over the entire time period, the 283 drugs were in short supply for an average of nearly 2 years.

While the duration of the reported shortages varied considerably, most—74 percent—of the shortages lasted 1 year or less.<sup>33</sup> However, an additional 16 percent, or 178, lasted between 1 and 2 years, and 10 percent (110) lasted more than 2 years. (See fig. 2.) The duration of these shortages varied greatly, ranging from 1 day to over 7 years.

<sup>33</sup>We excluded 92 shortages from this analysis because UUDIS listed these shortages as lasting zero days; the majority of these represented manufacturers' decisions to discontinue their production of a drug.

**Figure 2: Distribution of the Duration of Reported Drug Shortages, January 1, 2001, through June 20, 2011**



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

Note: Our analysis on the duration of the shortages includes 1,098 of the 1,190 total shortages reported from January 1, 2001, through June 20, 2011; we excluded 92 shortages from this analysis because the University of Utah Drug Information Service listed these shortages as lasting zero days; the majority of these represented manufacturers' decisions to discontinue their production of a drug.

Overall, the average duration of the drug shortages over this period was 286 days—or over 9 months. The average duration of shortages was longer for shortages that were active as of June 20, 2011 (360 days, or nearly 12 months) in comparison to those that were resolved by that time (266 days, or nearly 9 months). (See table 1.)

**Table 1: Summary of the Duration of Drug Shortages, January 1, 2001, through June 20, 2011, by Shortage Status**

Summary of shortage duration	Total number of shortages	Average duration (in days)	Median duration (in days)
Resolved shortages	868	266	148
Active shortages (as of June 20, 2011)	230	360	256
All active and resolved shortages	1098	286	159

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

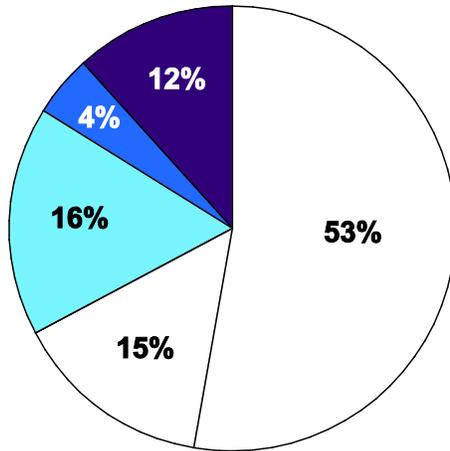
Note: Our analysis on the duration of the shortages includes 1,098 of the 1,190 total shortages reported from January 1, 2001, through June 20, 2011; we excluded 92 shortages from this analysis because the University of Utah Drug Information Service listed these shortages as lasting zero days; the majority of these represented manufacturers' decisions to discontinue their production of a drug.

## Generic Injectable Drugs Comprised Over Half of Critical Shortages Since 2009

Based on our review of the characteristics of a smaller group of critical drug shortages reported between January 1, 2009, and June 20, 2011, we found that over half involved generic injectable drugs. Specifically, 53 percent of the 269 drug shortages reported during this time period involved generic injectable drugs.<sup>34</sup> About 39 percent of shortages involved injectable drugs that were available only in generic form, and about 14 percent involved injectable drugs available in both brand-name and generic form. An additional 15 percent of shortages involved injectable drugs that were available in brand-name form only. The remaining portion of shortages—about 32 percent—involved either brand-name or generic drugs that were administered through other routes. (See fig. 3.)

<sup>34</sup>We reviewed 269, or 54 percent, of the 495 total shortages reported January 1, 2009, through June 20, 2011. These drug shortages were those that UUDIS determined were critical.

**Figure 3: Distribution of 269 Critical Drug Shortages Reported January 1, 2009, through June 20, 2011, by Product Type and Route of Administration**



- Injectable drugs available in generic form
- Injectable drugs available only in brand-name form
- Orally-administered drugs available in generic form
- Orally-administered drugs available only in brand-name form
- Other drugs<sup>a</sup>

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

Note: This figure reflects 269, or 54 percent, of the 495 total shortages reported January 1, 2009, through June 20, 2011. Our analysis was limited to the shortages the University of Utah Drug Information Service identified as critical.

<sup>a</sup>Other drugs include those administered via nasal, inhalation, rectal, topical, ophthalmic, and transdermal methods, as well as those that are available for administration through multiple routes and one drug whose route of administration was unavailable from Red Book.

The share of critical drug shortages involving generic injectable drugs has increased. Specifically, from 2009 through 2010, the share of reported shortages involving generic injectable drugs grew from 37 percent to 64 percent. Forty-six critical shortages reported in 2011 through June 20 involved generic injectable drugs; this represents 56 percent of all such shortages.

Generic drugs were more often in shortage than brand-name drugs. Overall, about three-fourths (76 percent) of the 269 drug shortages involved drugs that were available in generic form, with nearly half of all shortages involving drugs that were available only in generic form. Twenty-four percent of these drug shortages involved only brand-name

drugs. (See table 2.) The share of reported drug shortages involving generic drugs—including those with a brand-name counterpart—remained relatively stable from January 1, 2009, through June 20, 2011.

**Table 2: Summary of 269 Critical Drug Shortages Reported January 1, 2009, through June 20, 2011, by Product Type**

Product type	Number of shortages	Percent
Brand-name only	64	24
Generic only	133	49
Brand-name and generic drugs	72	27
<b>Total</b>	<b>269</b>	<b>100</b>

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

Note: This table reflects 269, or 54 percent, of the 495 total shortages reported January 1, 2009, through June 20, 2011. Our analysis was limited to the shortages the University of Utah Drug Information Service identified as critical.

Among the 269 critical drug shortages, those administered by injection were the most commonly in shortage. In total, 68 percent of drug shortages involved drugs administered by injection. (See table 3.) Additionally, the share of shortages involving injectable drugs grew from 51 percent to 77 percent between 2009 and 2010. Fifty-nine critical shortages reported in 2011 (through June 20) involved injectable drugs; this represents 72 percent of the shortages.

**Table 3: Summary of 269 Critical Drug Shortages Reported January 1, 2009, through June 20, 2011, by Route of Administration**

Route of administration	Number of shortages	Percent
Injection	182	68
Oral	56	21
Other <sup>a</sup>	28	10
Multiple routes	3	1
<b>Total</b>	<b>269</b>	<b>100</b>

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

Note: This table reflects 269, or 54 percent, of the 495 total shortages reported January 1, 2009, through June 20, 2011. Our analysis was limited to the shortages the University of Utah Drug Information Service identified as critical.

<sup>a</sup>Other routes of administration included nasal, inhalation, rectal, topical, ophthalmic, and transdermal, as well as one drug whose route of administration was unavailable from Red Book.

Certain therapeutic classes were more likely than others to be affected by a shortage. Specifically, five therapeutic classes—anesthetic and central nervous system (CNS), anti-infective, cardiovascular, nutritive, and oncology drugs—represented 68 percent of critical drug shortages. Anesthetic and CNS drugs were the most represented therapeutic class, with 23 percent of shortages reported. (See table 4.)

**Table 4: Summary of 269 Critical Drug Shortages Reported January 1, 2009, through June 20, 2011, by Therapeutic Class**

Therapeutic class	Number of shortages	Percent
Anesthetic and central nervous system drugs	61	23
Anti-infective drugs	37	14
Nutritive agents	30	11
Oncology drugs	28	10
Cardiovascular drugs	26	10
Endocrine and metabolic drugs	14	5
Toxicology antidote drugs	10	4
Dermatological drugs	9	3
Musculoskeletal drugs	9	3
Other <sup>a</sup>	41	15
Multiple therapeutic classes	4	1
<b>Total<sup>b</sup></b>	<b>269</b>	<b>99</b>

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

Note: This table reflects 269, or 54 percent, of the 495 total shortages reported January 1, 2009, through June 20, 2011. Our analysis was limited to the shortages the University of Utah Drug Information Service identified as critical.

<sup>a</sup>Includes other therapeutic classes such as gastrointestinal drugs and ophthalmologic drugs, as well as one drug whose therapeutic class was unavailable from Red Book.

<sup>b</sup>Percentages do not sum to 100 due to rounding.

Although the numbers are small, shortages of oncology drugs rose significantly between 2009 and 2010. Specifically, the number of reported shortages for oncology drugs increased by 600 percent, from 2 shortages in 2009 to 14 shortages in 2010. Additionally, the number of reported oncology drug shortages in 2011 (12 shortages as of June 20, 2011) is on pace to surpass the total number of such shortages in 2010. Other therapeutic classes saw increases in the number of shortages reported from 2009 to 2010: endocrine and metabolic drugs (3 to 7, or 133 percent); nutritive agents (5 to 13, or 160 percent); and toxicology antidote drugs (1 to 4, or 300 percent).

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Anesthetic and CNS drugs and anti-infective drugs saw decreases in the number of shortages reported between 2009 and 2010, at 16 and 25 percent, respectively. However, shortages for these therapeutic classes reported through June 20, 2011, are on pace to surpass the total number of such shortages reported in 2010, and remain among the most commonly reported shortages.

We noted several other characteristics among these drug shortages. Specifically, 59 percent of drug shortages involved more than one manufacturer—meaning that most shortages reflected disruptions in the supply of more than one manufacturer’s drugs. Additionally, 35 percent of these drug shortages involved at least one discontinued product—such as one strength or package size of a drug that was in short supply. In such cases, a manufacturer’s decision to discontinue a product may have caused the shortage, or may have occurred during an ongoing shortage.

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## Drug Shortages We Reviewed Were Generally Caused by Manufacturing Problems and Exacerbated by Multiple Difficulties

Our analysis of the causes of 15 sterile injectable drug shortages (involving 5 anesthesia drugs, 5 anti-infective drugs, and 5 oncology drugs) showed that manufacturing problems were the primary cause of most shortages, and over half were exacerbated by multiple difficulties after the drug initially went into short supply.

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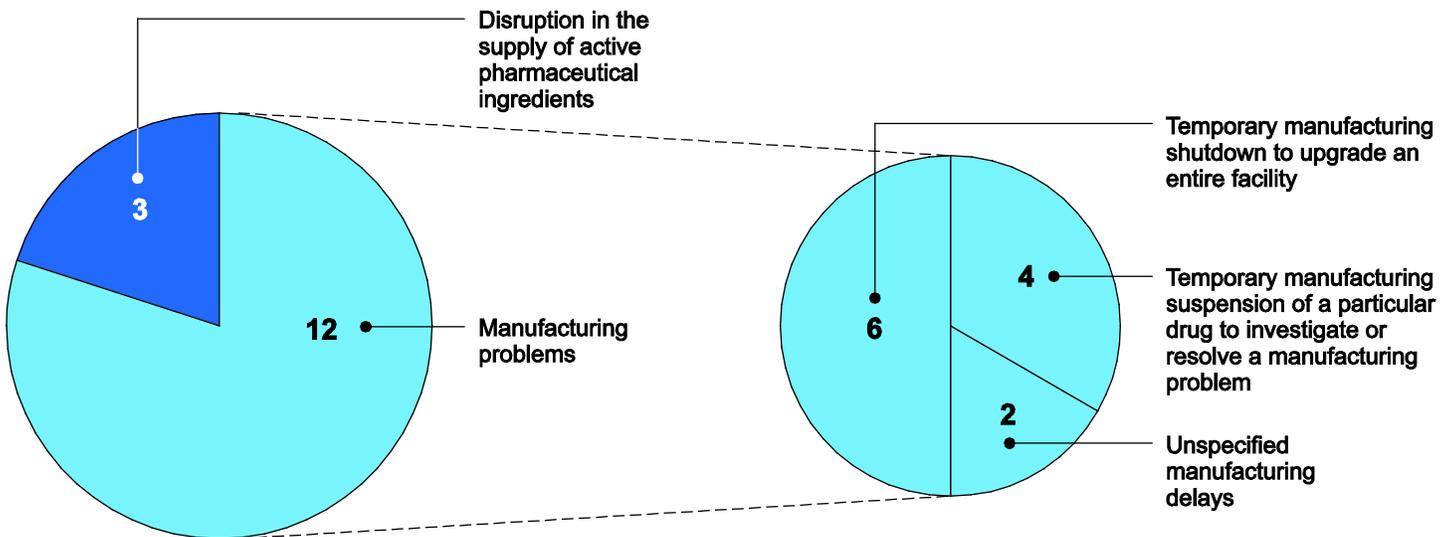
## Manufacturing Problems Reportedly Caused Most of the 15 Shortages of Sterile Injectable Drugs

Most (12 of the 15) drug shortages we reviewed in detail were reportedly caused by manufacturing problems, including those that resulted in manufacturing shutdowns, according to information provided by FDA and manufacturers. The remaining 3 shortages were reportedly caused by disruptions in the supply of APIs. (See fig. 4.) These problems were the primary cause of the shortages reviewed—that is, the first event that triggered the drug shortage.

**Figure 4: Summary of Primary Causes of 15 Sterile Injectable Drug Shortages That Occurred Between January 2009 and June 2011**

**Primary causes of shortages**

**Types of manufacturing problems**



Source: GAO analysis of information provided by FDA and manufacturers.

Of the 12 shortages caused by manufacturing problems, 6 resulted from manufacturers' temporary shutdowns of entire facilities so they could be upgraded. Four of these six shortages were caused by one manufacturer's shutdown of a single facility. Representatives from this manufacturer told us that it shut down the facility in order to improve its manufacturing capabilities. The manufacturer had anticipated that the upgrade would take 3 months, but it took 1 year to complete. Prior to the shortage, the manufacturer built up its inventory to ensure that it could meet the market's demand for its products during the expected 3-month shutdown. However, because the manufacturer had not planned for an extended shutdown, 4 of the 15 drug shortages we reviewed, as well as other sterile injectable drugs produced at that facility, went into short supply.

Another four shortages we reviewed were caused when manufacturers temporarily suspended production of a particular drug in order to investigate or resolve a specific manufacturing problem—for example, a quality problem. The remaining two shortages were caused by unspecified manufacturing delays.

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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. These products require a sterile environment, which is difficult to maintain. FDA officials told us that the most common manufacturing problems experienced for sterile injectable drugs are lack of assurance of sterility and particulate matter included in the drug. According to FDA officials, sterile injectable drugs can take weeks to produce; in comparison, oral tablets may only take up to a few days to produce. The complexity and duration of the manufacturing process for sterile injectable drugs makes these drugs more susceptible to manufacturing problems. In addition, according to FDA, such drugs are being made by a decreasing number of aging facilities, which may contribute to the recent increase in manufacturing problems.

Certain types of sterile injectable drugs, such as anti-infective and oncology drugs, can be particularly challenging to manufacture. Officials from FDA and other organizations we interviewed explained that manufacturers of sterile injectable anti-infective and oncology drugs face unique challenges because of the nature of the drugs' ingredients. Specifically, some anti-infective drugs, such as penicillin, are highly sensitizing and can trigger serious allergic reactions at very low levels. As a result, FDA requires manufacturers to produce penicillin in isolation from other drugs.<sup>35</sup> In addition, some oncology drugs are toxic and can present serious risks to people who come into contact with these compounds, even at low concentrations. As a result, FDA suggests that manufacturers of oncology drugs consider using dedicated production lines in order to ensure that other products are not contaminated. According to FDA officials, the special containment controls necessary for some oncology and anti-infective drugs can limit manufacturers' transfer of production of these drugs to other lines. As a result, manufacturers may have increased difficulty keeping up with demand for such products when they are in short supply.

Most of the drugs involved in the shortages we reviewed have been available in generic form for over 15 years. When asked how the prices and profits for their generic sterile injectable drugs have affected manufacturers' interest in maintaining, upgrading, or increasing redundancy within their manufacturing lines, or in continuing to

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<sup>35</sup>See 21 C.F.R. § 211.42(d) (2011).

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manufacture these drugs, three of the four manufacturers we contacted stated that such factors had no effect on decisions they make for their current product portfolio. These manufacturers indicated that they are committed to the sterile injectable drug market or to appropriately supporting the manufacture of their current portfolio of drugs. However, one of these three manufacturers told us that such factors may affect future decisions it makes about the products it manufactures. In contrast, the fourth manufacturer told us that it carefully weighs factors, including market demand and product price erosion for generic drugs, when making capital investment decisions. This manufacturer added that in its opinion, lower profits available for the manufacture of generic drugs have led to much lower levels of redundancy in manufacturing generic drugs than for brand-name drugs. Despite this, officials from three of the four manufacturers we contacted told us that they continue to produce drugs that garner low or no profits. Rather than assessing the profitability of any single drug product, they instead make business decisions based of their overall portfolio of drugs or concerns for patients.

Three of the 15 shortages of sterile injectable drugs we reviewed in detail were caused by disruptions in the supply of APIs. For 2 of these shortages, manufacturers were not receiving their normal shipments of API because of problems related to the manufacturing of these ingredients. For 1 shortage, the manufacturer's supplier of API discontinued its production of the ingredient, which led to the shortage.

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### Over Half of the 15 Shortages Were Subsequently Exacerbated by Multiple Difficulties

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. Four of these shortages were exacerbated by five or more difficulties—including 1 shortage that was exacerbated by seven distinct difficulties. In addition to the 8 shortages that were exacerbated by multiple issues, 4 were exacerbated by one issue after the drug initially went into short supply. The factors that impacted drug shortages did not vary substantially by the drugs' therapeutic class.

The two most common difficulties that exacerbated shortages after the drugs went into short supply were other manufacturers' inability to keep up with an increased demand for their products once a competitor's drug went into short supply, and manufacturing problems, including those that

involved manufacturing shutdowns. Each of these difficulties affected 9 shortages. 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 manufacturers, when only a few make a drug and one manufacturer's drug is in short supply, it can be difficult for the others to substantially increase production of a drug to ensure that demand for a drug is met—even in the absence of any other problems.

Some of the 15 shortages we reviewed were subsequently exacerbated by other difficulties in addition to their primary causes. For example, 5 shortages were exacerbated by manufacturers' decisions to discontinue a drug. In addition, 3 drug shortages were exacerbated by manufacturers' decisions to recall products for product quality reasons, including 1 shortage that was exacerbated by two drug recalls. Finally, 2 shortages were exacerbated by disruptions in the supply of API, and 1 was exacerbated by a delay related to the importation of a finished drug product. (See table 5.)

**Table 5: Summary of Difficulties That Subsequently Exacerbated 15 Sterile Injectable Drug Shortages That Occurred Between January 2009 and June 2011**

Difficulties affecting drug supply	Number of shortages affected
Manufacturers' inability to keep up with demand	9
Manufacturing problems <sup>a</sup>	9
<i>Temporary manufacturing shutdown in order to upgrade an entire facility</i>	2
<i>Temporary manufacturing suspension of a particular drug in order to investigate or resolve a manufacturing problem</i>	5
<i>Temporary manufacturing shutdown for unspecified reasons</i>	1
<i>Manufacturing delays</i>	3
<i>Other manufacturing problems</i>	1
Product discontinuations	5
Disruption in the supply of active pharmaceutical ingredients	2
Delays associated with the importation of finished drug products	1

Source: GAO analysis of information provided by FDA and manufacturers.

Note: The number of shortages affected by these difficulties is greater than the number of shortages reviewed because most of the shortages we reviewed were affected by multiple difficulties, such as multiple types of manufacturing problems.

<sup>a</sup>As a result of manufacturing problems, three drug shortages were affected by recalls and one of these shortages experienced two product recalls.

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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, as displayed in table 5 above. During 2 of these shortages, three manufacturers of the drugs in shortage each experienced manufacturing problems; during another shortage, two manufacturers each experienced such problems, and during the remaining 6 shortages, one manufacturer experienced manufacturing problems. Officials from one manufacturer described recent shortage situations as a perfect storm of several manufacturers coincidentally experiencing manufacturing problems all at the same time.

Three shortages we reviewed were not affected by issues beyond the primary cause of the shortage. One of these shortages involved a drug that was produced by only one manufacturer at the time of the shortage. The other two shortages were not exacerbated by other issues because, according to FDA, other manufacturers were able to produce enough of the drug to meet the market's demand.

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## **Actions Taken by FDA to Respond to Drug Shortages Are Intended to Resolve Shortages' Underlying Causes and Enhance Product Availability**

FDA responds to drug shortages by taking various actions to address the shortages' underlying causes and enhance product availability. Our analysis of FDA's response to 15 shortages of sterile injectable drugs showed that FDA took a variety of actions to respond to each shortage. In addition, FDA has increasingly prevented drug shortages from occurring. FDA primarily communicates information about drug shortages and product availability to the public through its website.

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## **FDA's Goal Is to Resolve the Underlying Causes of Shortages**

FDA attempts to address the underlying cause of shortages as well as to provide ways to enhance the drug's availability until the underlying cause of the shortage has been addressed and the shortage is resolved, according to FDA officials we interviewed. FDA officials explained that they respond to all of the shortages the agency becomes aware of, and they determine how to address each shortage based on its cause and the public health risk associated with the shortage. Along with this determination, FDA officials told us that the agency places the highest priority on responding to shortages of those drugs that it considers medically necessary—that is, those that have the greatest potential to

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affect public health.<sup>36</sup> FDA defines a medically necessary drug 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.<sup>37</sup> FDA's goal in identifying such drugs is to assist in the prioritization of their response to drug shortages. As such, FDA's determination of whether a drug is medically necessary may differ from a health care provider's assessment that a certain drug is needed to treat a particular patient. FDA officials told us that they sometimes consult with health professional organizations such as ASHP when making a determination regarding the medical necessity of a particular drug. During shortages, FDA officials told us that if a drug is determined to be medically necessary, they will inform the manufacturer of their decision. Appendix I summarizes the criteria FDA uses to determine whether a drug is medically necessary.

FDA may take a variety of actions to respond to the shortages of medically necessary and non-medically necessary drugs by providing assistance directly to the manufacturer. If a manufacturer is experiencing technical problems with its manufacturing processes, FDA may be able to assist in the resolution of those problems—for example, by providing advice on how to address quality issues and ensure compliance with current good manufacturing practice regulations. If the manufacturer is facing difficulties obtaining raw materials, FDA may be able to assist in identifying an alternative supplier. Similarly, if a manufacturer is unable to obtain APIs or a finished drug as a result of importation delays, FDA may be able to coordinate with other entities, such as other federal agencies, to enable these materials to be imported more quickly.

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<sup>36</sup>For example, FDA officials told us that if they were informed of a shortage of a medically necessary and a non-medically necessary drug on the same day, they would first respond to the medically necessary drug shortage.

<sup>37</sup>As part of making this determination, FDA considers whether the drug is being administered to patients for off-label uses—that is, among other things, for conditions or patient populations for which the drug was not approved or in a manner that is inconsistent with the drug's FDA-approved label. Although FDA may not have approved a drug to treat a particular condition or patient population, the agency is aware that physicians may determine that prescribing a drug off label constitutes good care for an individual patient, and therefore factors off-label usage into its determination that a drug is medically necessary for the purpose of prioritizing drug shortages. FDA also considers drugs being studied in clinical trials in making its determination. However, FDA does not consider patient inconvenience, such as needing to take two tablets instead of one, as a reason to classify a drug as medically necessary.

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During a shortage, FDA may encourage manufacturers to increase production of the drug or to seek approval to begin production of a drug in short supply. If more than one manufacturer produces the drug that is in short supply, FDA may contact the other manufacturers to alert them to the potential of increased demand and may encourage them to increase their production of the drug. During shortages involving generic drugs, FDA may also encourage other manufacturers to submit ANDAs for review, so that additional manufacturers can gain FDA approval to produce the drug that is in short supply.

FDA may also expedite its review of ANDAs, ANDA supplements, and NDA supplements during a shortage, but this is largely dependent on the manufacturers' request for an expedited review. Some shortages may be resolved with changes to a manufacturing process or site, or the use of an alternative supplier for an API. FDA reviews manufacturers' requests for such changes, as documented in an application supplement, and any changes that have substantial potential to have an adverse effect on the product must be approved prior to their implementation. To assist in resolving a shortage, FDA may expedite its review of these supplements, or may expedite its review of ANDAs, which can substantially decrease the agency's review time.<sup>38</sup> FDA officials told us that an expedited review involves the same amount of analysis as a review that is not expedited, but can take significantly less time since the agency prioritizes its review of such applications. For example, FDA officials noted that certain expedited ANDA supplements have been approved in as quickly as a few days to a week, in contrast to the year or more it may take for such supplements to be reviewed under the typical process. FDA's review of NDA supplements in 2009 took the agency an average of 5 months, while

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<sup>38</sup>According to FDA, the agency expedited its review of 375 ANDAs, and 289 ANDA supplements from 2008 through July 2011 as a result of potential or current drug shortages; the number of expedited reviews exceeds the number of shortages reported during this period because multiple applications or supplements may be expedited to alleviate a shortage. FDA was unable to provide data regarding the length of time it took for them to expedite their review of these applications, including whether the reviews were completed prior to the resolution of related shortages. The expedited reviews comprise a small portion of the total number of applications pending FDA review as of July 30, 2011, which included 2,485 ANDAs, 6,235 ANDA supplements (which includes 5,040 supplements requesting approval for manufacturing changes and 1,195 supplements requesting approval for labeling changes), and 894 NDA supplements requesting approval for manufacturing changes.

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those that were expedited took an average of 2.5 months.<sup>39</sup> FDA has encouraged manufacturers to note their request for an expedited review due to a shortage in their cover letter to an application supplement or ANDA, or to inform FDA officials working in the Drug Shortage Program, OND, or OGD directly.

FDA may also apply its regulatory discretion to enhance drug availability during shortages of medically necessary drugs.<sup>40</sup> When considering whether to apply its regulatory discretion, the agency weighs the risks and benefits of taking such an approach. For example, FDA may exercise its regulatory discretion for manufacturers to continue marketing a medically necessary drug despite labeling or quality issues that would typically result in regulatory action. While FDA considers a drug with labeling errors to be misbranded, to alleviate or resolve a shortage of a medically necessary drug, agency officials told us that FDA may exercise its regulatory discretion with regard to a manufacturer's continued marketing of a drug with labeling errors. In this scenario, the manufacturer would issue an FDA-reviewed letter to health care professionals informing them of the error, or provide the corrected label text. FDA may also apply its regulatory discretion with regard to manufacturers' continued marketing of medically necessary drugs that have quality problems, if the manufacturer can develop a method to resolve the problem prior to the drug's administration. For example, if a manufacturer finds particulate in a drug and determines that a filter can be used to remove the particulate prior to administration of the drug, at FDA's discretion, the manufacturer may continue to market the drug with the filter. In such cases, FDA would review evidence of the filter's effectiveness provided by the manufacturer, to ensure that it removes the particulate from the drug.

If FDA is unable to resolve or alleviate a shortage of a medically necessary drug within the United States, the agency may use its regulatory discretion with regard to the importation into the United States of "unapproved drugs." These drugs are approved for use in foreign countries, but not the United States. For example, FDA officials told us

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<sup>39</sup>FDA officials were unable to provide data regarding the length of time it took to review ANDAs and ANDA supplements that were expedited as a result of a shortage.

<sup>40</sup>FDA officials told us that they do not typically consider exercising regulatory discretion to respond to shortages of non-medically necessary drugs because these drugs are, by definition, not used to treat serious diseases or medical conditions, or other clinically interchangeable versions of the drug are available.

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that from January 2011 through September 2011, at the agency's discretion, manufacturers imported seven unapproved drugs into the United States to address drug shortages. Four of these importations were ongoing as of October 3, 2011. FDA officials we interviewed explained that they only consider using this option for severe shortages of medically necessary drugs. To explore whether the importation of drugs not approved in the United States is an option for agency discretion during a shortage, agency officials told us that FDA collaborates with foreign regulatory agencies to identify whether a similar drug is manufactured in a country that requires adherence to manufacturing practice standards that are similar to those required by FDA. Once any such manufacturers are identified, FDA asks the firm whether they would be willing to provide the drug for the U.S. market. When possible, FDA selects a firm that has a subsidiary in the United States and an existing distribution network in order to expedite the process and the agency's access to information about the foreign manufacturing facility and drug. To help ensure the quality of the drug, FDA officials told us that they examine information about the manufacturer, its manufacturing facility, the chemical formulation of the drug, and information about the manufacturer's quality control processes. FDA also reviews the firm's compliance history and inspection reports that foreign regulatory agencies make available. Agency officials told us that, depending on the amount and currency of available information about the manufacturing facility, they may conduct an inspection prior to the importation of the unapproved drug into the United States. After a manufacturer has been identified and FDA has completed its quality review, FDA works with the company to reach an agreement on the conditions of the agency's enforcement discretion and monitors the supply and distribution of the drug that comes into the United States. FDA also encourages manufacturers to communicate with health care professionals and the public about potential differences between the imported drug and the drug in shortage through the use of letters to health care professionals. These letters detail any differences in chemical composition, strength, or formulation between the imported drug and the drug in short supply. FDA officials told us that, at their discretion, importation of such drugs may continue until the manufacturers of the FDA-approved drug are able to meet demand.

FDA considers a shortage to be resolved when the supply of the drug meets demand, which FDA calculates using market data that it obtains from IMS Health. FDA officials told us that they continue to monitor recently resolved shortages until any ongoing issues that could affect the supply of the drug are resolved.

## FDA Responded to Selected Shortages with a Variety of Actions

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. At the time of these shortages, FDA determined that all 15 drugs involved with shortages we reviewed in detail were medically necessary. To respond to these shortages, FDA most frequently offered assistance to manufacturers to prevent, alleviate, or resolve the shortage, or notified other manufacturers to expect increased demand or encouraged other manufacturers to increase production, as shown in table 6. (See app. II for information on FDA's response to each of the 15 shortages.)

**Table 6: Summary of Actions Taken by FDA in Response to 15 Shortages of Sterile Injectable Drugs That Occurred Between January 2009 and June 2011**

Types of actions taken by FDA	Number of shortages
FDA offered assistance to manufacturers to prevent, alleviate, or resolve the shortage	15
FDA notified other manufacturers to expect increased demand or encouraged other manufacturers to increase production	13
FDA provided assistance to address manufacturing problems related to drug quality issues	8
FDA searched for a firm willing and able to import a version of the drug in shortage not approved in the United States	7
<i>At FDA's discretion, a manufacturer imported a version of the drug in shortage not approved in the United States</i>	1
FDA expedited its review of an application supplement or abbreviated new drug application	5
At FDA's discretion, a manufacturer continued to market a drug despite labeling or quality issues	5
FDA provided assistance to address importation delays for active pharmaceutical ingredients or finished products	5

Source: GAO analysis of information provided by FDA.

Note: The total number of types of actions taken by FDA is greater than the number of shortages reviewed because FDA used more than one action to respond to most of the shortages we reviewed.

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While FDA responded to all of the 15 shortages of sterile injectable drugs we reviewed, agency officials told us that 3 of these supply disruptions did not meet the agency's criteria for a shortage.<sup>41</sup> Specifically, FDA officials told us that while it was aware of disruptions in the supply of these three drugs, the overall market supply of each drug was able to meet demand, based on the agency's knowledge of manufacturers' production. Even though FDA did not recognize these 3 cases as drug shortages, agency officials nonetheless notified other manufacturers to expect increased demand for their products or encouraged them to increase production, and also offered assistance to the affected manufacturers.

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### FDA Has Increasingly Prevented Potential Drug Shortages from Occurring

FDA has increasingly prevented potential drug shortages from occurring when it has been informed of the potential for a shortage in advance. According to our analysis of information provided by FDA, the agency prevented 50 potential drug shortages during the first 6 months of 2011—about 1.5 times the number of potential drug shortages (35) prevented during all of 2010.<sup>42</sup> FDA officials partially attributed the increase in potential shortages prevented to manufacturers' willingness to report information that could impact the supply of their drugs in advance of a shortage. The recent increase in the number of shortages presented additional opportunities for manufacturers to report potential supply disruptions to the agency. According to our analysis of information provided by FDA, during the first half of 2011, the agency was able to prevent about 90 percent of potential shortages that it learned about in advance.

To prevent these potential shortages, FDA took some of the same types of actions it uses to alleviate and resolve shortages. During 2010 and the first half of 2011, FDA most frequently prevented potential drug shortages by expediting its review of application supplements. FDA also took a

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<sup>41</sup>While these three shortages did not meet FDA's criteria, all of the shortages we reviewed in detail were identified by representatives from ASA, ASCO, and IDSA as recent shortages that had a significant impact on patient care or public health.

<sup>42</sup>We grouped together shortages of multiple versions of the same drug to identify the total number of shortages prevented. FDA officials told us that the agency prevented 38 drug shortages in 2010 and 99 shortages in 2011, through June. However, these data represented the number of individual drug products for which a shortage had been averted, and did not group together multiple versions—for example, multiple concentrations—of the same drug.

variety of other actions to prevent drug shortages during this period. (See table 7.)

**Table 7: Actions Taken by FDA to Prevent Potential Drug Shortages, 2010 and 2011, through June**

Actions taken by FDA	Number of actions taken to prevent potential shortages	
	2010	2011 <sup>a</sup>
FDA expedited review of application supplements	12	37
At FDA's discretion, a manufacturer continued to market a drug despite labeling or quality issues	2	9
FDA helped to ensure timely importation of an active pharmaceutical ingredient or finished products	8	2
FDA either notified firms that they would experience increased demand or encouraged manufacturers to increase production	9	1
FDA provided assistance to address manufacturing problems	6	8
At FDA's discretion, a manufacturer imported a version of the drug in shortage not approved in the United States	0	1
Other <sup>b</sup>	1	2

Source: GAO analysis of information provided by FDA.

Note: The total number of actions taken by FDA exceeds the number of shortages prevented because in some instances, FDA took multiple actions to prevent shortages.

<sup>a</sup>Data presented for 2011 reflect potential shortages prevented through June 2011.

<sup>b</sup>Other actions included FDA applying its regulatory discretion with regard to a manufacturer continuing its production of a drug while using laboratory testing equipment that the agency had not yet reviewed.

## FDA Communicates Information about Shortages to the Public via Its Website

FDA's primary means of communicating information to the public about drug shortages is its website, which lists both current and resolved shortages.<sup>43</sup> FDA officials told us that they post information on their website about shortages of medically necessary drugs, as well as some shortages of non-medically necessary drugs for which it has received multiple requests for information. However, FDA may not post any information about shortages if the agency anticipates that the shortage will be brief in duration. FDA may not immediately post information about current shortages if the agency is concerned that such information could

<sup>43</sup>See <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>.

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make the shortage worse—for example, by inducing hoarding. Once FDA decides to post information about a shortage, it lists the manufacturers of the drug as well as a broad explanation of the cause for the shortage—for example, “manufacturing issues.” FDA may post more detailed information about the cause and expected duration of the shortage, as well as information about other versions of the drug that are available, if manufacturers provide them with text to post on its website, or if the manufacturer makes such information publicly available.

Once the shortage is resolved—that is, once the supply of the drug is sufficient to meet the market’s demand for it—FDA officials told us that they may move information about the shortage from its current shortages web page to its resolved shortages web page. However, FDA officials told us that they may keep listings of resolved shortages on its current shortages web page to inform the public about the availability of the product. In addition, they may keep a shortage listed as current until they are confident that any underlying causes of the shortage are addressed. FDA officials told us that they post information about resolved shortages for 6 months before removing such information from their website.

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## FDA Is Constrained in Its Ability to Protect Public Health from Drug Shortages

FDA is constrained in its ability to protect the public health from drug shortages due to its lack of authority to require manufacturers to take certain actions. In addition, management challenges, such as a lack of systematic data and performance measures, weaken the agency’s response to drug shortages and inhibit its ability to protect public health.

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## FDA Lacks Authority to Require Manufacturers to Report Potential and Actual Shortages

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 one manufacturer.<sup>44</sup> In such instances, companies are required to provide

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<sup>44</sup>See 21 U.S.C § 356c; 21 C.F.R. § 314.81(b)(3)(iii) (2011). To the maximum extent possible, FDA is to distribute information on the discontinuance of these products to appropriate physician and patient organizations. FDA does not have the authority to enforce this requirement, for example, by seeking civil monetary penalties.

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FDA with at least 6 months notice of discontinuations.<sup>45</sup> However, such discontinuations have not been the primary cause of most recent drug shortages. As a result of the constraints on its authority, the agency's approach to managing drug shortages is predominately reactive, which limits its ability to prevent, alleviate, and resolve shortages to protect the public health.

FDA does not have the authority to require manufacturers to report actual or potential shortages—including information about their causes and expected duration—to the agency or the public. FDA has encouraged manufacturers to report potential supply disruptions to the agency. While our draft report was at HHS for comment, the President directed FDA to use all appropriate administrative tools to require drug manufacturers to provide adequate advance notice of situations that could lead to drug shortages, to the extent permitted by law.<sup>46</sup> In addition, on the same day, FDA sent a letter to all drug manufacturers urging them to report potential supply disruptions to the agency. According to FDA officials, while the agency could have been notified in advance of most shortages, less than half of all shortages are reported to the agency by manufacturers. Instead, FDA is most often notified by ASHP, or health care providers or consumers when they are unable to purchase a drug—a point at which the shortage is already impacting public health. As a result, FDA's response to shortages may be delayed.

Without information on current or potential shortages, other manufacturers' ability to increase production of the drug may also be compromised. For example, one manufacturer told us that FDA did not notify it soon enough to enable it to increase production to alleviate or resolve two of the seven shortages that it was involved in and that were included in our review. In both instances, by the time FDA informed the manufacturer of the shortage, demand for its products was already at levels the firm could not support.

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<sup>45</sup>On October 31, 2011, the Commissioner of FDA sent a letter to all drug manufacturers, reminding them of this requirement. See <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm277675.htm>.

<sup>46</sup>Exec. Order No. 13,588, 76 *Fed. Reg.* 68,295 (Nov. 3, 2011).

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Officials from several manufacturers told us that they would like other manufacturers to openly share information with FDA about shortages of their drugs because doing so can speed FDA's response, and can enhance other manufacturers' ability to increase production of the drug in short supply. These officials told us that they support efforts to improve communication between FDA and industry through early notification of potential drug shortages. However, some of these officials also noted that a requirement to report potential drug shortages within a specific time frame would be difficult for manufacturers to observe. They explained that drug shortages can be unpredictable and are often the unexpected result of several factors or causes. As a result, they were concerned that manufacturers may not foresee the impending shortage soon enough to be able to comply with a lengthy advance notification requirement.

FDA officials also told us that manufacturers sometimes do not provide the agency with information about the causes and expected duration of shortages as soon as it is available. As a result, the information posted on FDA's website does not always reflect current information. FDA officials told us that they cannot communicate detailed information about the causes or expected duration of a shortage unless the affected manufacturers provide text for the agency to post on its website. FDA officials explained that such information is generally considered confidential commercial information, which cannot be disclosed by FDA without the manufacturer's consent. Officials at several health care professional associations we interviewed noted that information on the cause and expected duration of a shortage is important for clinicians to understand so that they can determine the best method to treat their patients during a shortage.

FDA does not have the authority to require that manufacturers take certain actions to prevent, alleviate, or resolve shortages, such as by continuing or increasing their production of a drug, or by taking actions to prevent or resolve shortages. FDA does not control the distribution of drugs and also cannot compel manufacturers or distributors to take actions to prevent hoarding or diversion of drugs to the gray market. FDA's ability to respond to a drug shortage may be limited by manufacturers' business decisions, such as a manufacturer choosing to discontinue production of a drug already in shortage. While FDA can encourage a manufacturer not to discontinue its production of a drug, it cannot require the company to continue production. Also, while it may be in manufacturers' interest to increase their production of a drug in short supply, FDA cannot compel a manufacturer to increase its production of a drug. In addition, FDA cannot compel manufacturers to take steps to

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resolve shortages, such as by accepting the agency's offers of assistance. Based on our review of FDA's response to 15 shortages, we found that manufacturers do not always accept FDA's offer of assistance. FDA officials also told us that they encounter challenges finding manufacturers that are willing to import drugs that are not approved in the United States in order to alleviate a shortage. Agency officials told us that some manufacturers had expressed hesitancy in working with FDA to alleviate a shortage in this manner because it would require a substantial financial investment accompanied with a time-limited benefit. In our review of FDA's response to 15 shortages, we found that the agency tried to find firms that were willing to import drugs that were not approved in the United States during 7 shortages, but was only able to find a firm to import a product in order to help alleviate 1 shortage.

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### Management Challenges Further Constrain FDA's Ability to Respond to Drug Shortages

FDA's ability to respond to drug shortages is also constrained by its lack of systematic data, limited resources, and an absence of performance measures and priorities. Although FDA obtains information about drug shortages, the agency does not maintain data related to these shortages, such as their causes and the agency's response. Without such data, FDA is unable to systematically monitor trends and identify actions it could take to address the fundamental or contributing causes of drug shortages. Drug Shortage Program staff currently track drug shortages in individual electronic files, not in a database. To summarize information on drug shortages for other FDA offices, the Drug Shortage Program prepares e-mail status reports, which do not present information in a consistent format and are not conducive to easy retrieval of information or data analysis. In addition, officials from FDA's Drug Shortage Program, OND, OGD, Office of Compliance, and ORA told us that they routinely share information about drug shortages via e-mails, phone calls, or meetings—not in any systematic format or system. FDA's information does not lend itself to analysis—it is not easily retrievable, routinely recorded, or sufficiently reliable. As a result of FDA's lack of systematic data, the agency was unable to provide us with information necessary to analyze trends in drug shortages and we therefore obtained these data from UUDIS.<sup>47</sup>

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<sup>47</sup>FDA officials told us that the best data that they could supply us with would be copies of weekly e-mail messages, containing brief narratives on the status of shortages in effect for the week in question.

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Without a systematic method to store, track, and share data on drug shortages, the agency cannot ensure that it responds to potential and current shortages in a timely and coordinated manner. FDA has faced a growing workload in recent years associated with the increase in the number of drug shortages reported, but Drug Shortage Program staff lack a system to manage information to ensure that they are responding to shortages in a timely manner. The Drug Shortage Program's work requires staff to maintain a large volume of complex information on drug shortages, communicate regularly with other agency officials in other parts of the agency, as well as manufacturers, and monitor significant shortage situations until they are resolved.<sup>48</sup> Other CDER offices that coordinate with the Drug Shortage Program may be unaware of information about current or potential shortages and therefore miss opportunities to respond to shortages—for example, by neglecting to recognize that supplements submitted for review could help to alleviate a shortage. While FDA officials told us they review applications and supplements in the queue to determine whether any should be expedited in order to alleviate a shortage, representatives from organizations we interviewed noted concerns about the agency's ability to review ANDA supplements in a timely manner to prevent, alleviate, or resolve shortages. Specifically, some representatives told us that they were aware of instances where manufacturers had submitted ANDA supplements, which, if approved, could have helped to alleviate or resolve a shortage.<sup>49</sup> According to these representatives, FDA's review of these supplements can take several years. In addition, representatives noted that in at least one case, FDA's review was not expedited until months after the supplement was received.

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<sup>48</sup>For example, many shortages involve multiple manufacturers and each may face multiple problems related to the production of the drug before the shortage is resolved. During shortages, Drug Shortage Program officials may need to communicate with officials from each manufacturer to obtain information, as well as communicate with different offices within FDA to share information related to the agency's response.

<sup>49</sup>In addition, we previously reported that, in response to a potential shortage of heparin in 2008, FDA encouraged a manufacturer to submit an ANDA, for which it had granted an expedited review. However, despite the expedited designation, the approval process for the application took 18 months, so this product was not available until well after the supply of heparin had stabilized. See GAO, *Food and Drug Administration: Response to Heparin Contamination Helped Protect Public Health; Controls That Were Needed for Working With External Entities Were Recently Added*, [GAO-11-95](#) (Washington, D.C.: Oct. 29, 2010), 18.

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FDA officials have acknowledged that a database is needed to store current and historic data on drug shortages, and in response to this need, they recently developed, and are in the process of implementing, an electronic spreadsheet to gather such data. Agency officials told us that they intend to use this spreadsheet to monitor shortages and conduct descriptive analyses of shortages in a more standardized format. In addition, they plan to use this spreadsheet to generate data to use for annual reporting. We reviewed an early draft of FDA's spreadsheet and identified several weaknesses. For example, while the spreadsheet will enhance the agency's ability to more rapidly obtain and analyze data on drug shortages, it was not intended to—nor will it provide—a method for FDA to systematically manage information about drug shortages on a daily basis or provide a means to share information about drug shortages with other FDA offices. FDA's newly developed spreadsheet will not enable the agency to improve the management of its workload, such as its ability to organize the large volume of information about drug shortages that it receives in a systematic manner, safeguard institutional knowledge about past shortages, or help Drug Shortage Program officials share information with other FDA offices. In addition, because the spreadsheet requires additional resources for data entry, it will add to the workload of the Drug Shortage Program—instead of alleviating it. The spreadsheet is also incomplete and does not allow the agency to track a variety of datapoints. For example, the spreadsheet does not have a mechanism for the agency to group together shortages of multiple versions of the same drug; without this capability, it will be difficult for FDA to track the number of similar products affected by a shortage.

The spreadsheet also does not include space for FDA to track the NDCs associated with each drug shortage. Such data are necessary in order to fully analyze the characteristics of drugs that have been in short supply. In addition, because FDA's current spreadsheet only includes space to note one action FDA took to respond to each shortage, it will not be able to provide the agency with systematic data on multiple actions the agency takes in response to a shortage. For example, for shortages involving drugs produced by multiple manufacturers, the spreadsheet will not be able to systematically capture multiple types of actions FDA takes to address each shortage.

FDA has consistently staffed its Drug Shortage Program—which is responsible for the coordination of all of the agency's activities related to the prevention and mitigation of drug shortages—with a small number of employees. Despite a dramatic increase in the number of drug shortages reported in recent years, the number of staff working in the Drug Shortage

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Program remained constant at three full-time employees from 2009 until February 2011, when FDA hired a fourth staff person for the Drug Shortage Program. As of October 2011, FDA had hired a fifth staff person, but was unable to provide a time frame for when that person would start work.<sup>50</sup> Because FDA has lacked detailed data on drug shortages, it may not have been able to develop reliable estimates of the current and future resource needs of the Drug Shortage Program, a topic on which we have previously reported.<sup>51</sup> However, representatives from many of the organizations we interviewed told us that they are concerned that the agency does not have adequate staffing to effectively respond to drug shortages.

FDA also does not have a set of results-oriented performance metrics and strategic priorities related to drug shortages. As a result, FDA may be unable to effectively evaluate its work and improve its ability to protect the public health. FDA has not developed a set of results-oriented performance metrics to measure the success of the agency's response to drug shortages in either the long term or the short term. FDA recently began tracking information on one results-oriented performance metric—the number of drug shortages prevented in a year. However, FDA lacks other measures that could be used to measure the results of its work—such as the effectiveness of the actions the agency takes to respond to shortages. Without such metrics, FDA may be unable to evaluate how it could most effectively improve the program's ability to respond to drug shortages and protect the public health. Furthermore, while FDA has recognized the significant public health consequences that can result from drug shortages, the agency has not identified drug shortages as an

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<sup>50</sup>Agency officials estimated that, in addition to those staff working in the Drug Shortage Program, about 25 full-time equivalent employees provide some level of assistance in preventing, alleviating, and resolving shortages—for example, by conducting determinations of medical necessity and reviewing application supplements. However, these additional staff also have other primary responsibilities.

<sup>51</sup>See GAO, *Food and Drug Administration: FDA Faces Challenges Meeting Its Growing Medical Product Responsibilities and Should Develop Complete Estimates of Its Resource Needs*, [GAO-09-581](#) (Washington, D.C.: June 19, 2009).

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area of strategic importance for the agency.<sup>52</sup> As a result, the agency may be unable to coordinate an agencywide response to drug shortages, and make decisions on the best ways that it can employ its resources to fulfill its mission to protect the public health.

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## Conclusions

The number of drug shortages has substantially increased in recent years—including those for life-saving medications such as oncology drugs, which has jeopardized the public health. Health care providers and patients have struggled with the consequences of these shortages and have raised concerns about what the federal government is doing to prevent and resolve these shortages.

FDA may not always be able to prevent shortages from occurring, in part because it does not have control over private companies' business decisions, for example, regarding whether to continue making a drug. Further, 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. 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. As a result, FDA's response to shortages is most frequently reactive. Also, information communicated to health care providers and the public about shortages may remain incomplete, because FDA cannot disclose detailed information to the public without manufacturers' consent.

We have been critical of FDA in the past for not paying sufficient attention to strategic and workforce planning and reliably estimating needed resources. Our prior reports have also expressed concern that the agency has not established result-oriented performance metrics, that agency managers often do not use existing performance measures to set

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<sup>52</sup>FDA has incorporated the concept of availability of drugs into one of its strategic objectives; however, this objective is focused solely on the processes FDA takes to ensure the availability of safe and effective new drugs for the market. As such, it does not encompass the availability of all drugs, including many medically necessary drugs that are no longer manufactured by the company that marketed the brand-name version of the drug and are thus available in generic form only.

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program priorities, and that coordination between internal FDA offices is a significant management challenge. These concerns are echoed in the agency's current approach to managing its Drug Shortage Program. Despite the recent increase in drug shortages, FDA has not substantially changed the resources or priority it places on its response to drug shortages. Although FDA recognizes the significant public health consequences that can result from drug shortages, it has not taken the important step of developing metrics that would help it manage the Drug Shortage Program. Indeed, the agency does not maintain data in a manner that would enhance its ability to understand trends in the shortages that are, and are not, occurring. The agency has not identified drug shortages as an area of strategic priority, and generally does not track its own performance related to preventing or mitigating the effects of drug shortages. Therefore, FDA cannot fully understand the extent to which its actions are effective. FDA lacks a systematic method to manage its complex workload related to drug shortages—and to share this information among the many offices within the agency whose efforts must be coordinated. Without sufficient data, prioritization, or performance metrics, FDA cannot ensure that it is doing all it can to protect the public health.

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## Matter for Congressional Consideration

To strengthen FDA's ability to respond to drug shortages, Congress should consider establishing a requirement for manufacturers to report potential or actual supply disruptions to FDA. Such notification requirements should call for manufacturers to notify FDA of any changes, interruptions, or adjustments that could affect the supply of their drugs. Congress may also wish to consider providing FDA with the authority to seek civil monetary penalties or use other enforcement mechanisms to ensure compliance with this requirement.

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## Recommendations for Executive Action

To strengthen FDA's ability to protect the public health through its response to drug shortages, we recommend that the Commissioner of FDA take the following four actions:

- assess the resources allocated to the Drug Shortage Program to determine whether reallocation is needed to improve the agency's response to drug shortages;

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- develop an information system that will 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;
  - ensure that FDA’s strategic plan articulates goals and priorities for maintaining the availability of all medically necessary drugs—including generic drugs; and
  - develop results-oriented performance metrics to assess and quantify the implementation of the agency’s goals and FDA’s response to drug shortages.

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## Agency and Third-Party Comments and Our Evaluation

In its comments on a draft of this report, HHS acknowledged that drug shortages pose serious risks to public health and emphasized the agency’s position on addressing this challenge. HHS stated that it supports legislation that would require manufacturers to report potential or actual supply disruptions to FDA. In addition, HHS outlined its intent to take actions that are consistent with our recommendations. For example, it noted that it has plans to increase the number of staff working in the Drug Shortage Program, and that it has identified some potential performance metrics that it may use to gauge the success of FDA’s response to drug shortages. We believe that such plans are an important first step toward enhancing the agency’s response to drug shortages.

HHS’s comments also stated that FDA has developed a database to analyze drug shortages in real time. As noted in our report, we believe that the spreadsheet FDA refers to as a database will not enable the agency to optimally manage drug shortage information on a systematic basis, and we encourage the agency to implement our recommendation to develop a more robust information system to manage these data. In addition, HHS stated that FDA has prevented 137 drug shortages from 2010 through September 2011. Our counts of prevented drug shortages differ from FDA’s because we consider a prevented shortage of multiple versions of the same drug (for example, multiple concentrations of the same drug) as one prevented shortage, whereas FDA counted each separately. Thus for example, we reported 50 potential shortages avoided during the first half of 2011 in contrast to FDA reporting 99.

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HHS's comments also cited a number of actions that the Administration has taken since receiving our draft report for review. Specifically, while our draft report was at HHS for comment, the President issued an Executive Order on October 31, 2011, that directs FDA to take steps that are intended to support, enhance, and amplify the agency's response to drug shortages.<sup>53</sup> The order directed FDA to expand its efforts to expedite reviews of applications that would help to prevent or resolve shortages. FDA also issued a report summarizing its approach to drug shortages, which includes a list of actions the agency should take in order to strengthen its response to drug shortages.<sup>54</sup> HHS's Office of the Assistant Secretary for Planning and Evaluation also issued a report summarizing the economic factors that cause drug shortages.<sup>55</sup> We are encouraged by the Administration's response to this issue, and believe its expeditious implementation of the recommendations included in our report, as well as the executive order and FDA's report, will serve to strengthen the agency's ability to prevent, alleviate, and resolve drug shortages.

HHS's comments are reprinted in appendix III. We also provided UUDIS with excerpts of the draft report related to the number of drug shortages. We received technical comments from both HHS and UUDIS, which we incorporated as appropriate.

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As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to the Commissioner of FDA and appropriate congressional committees. The report also will be available at no charge on the GAO website at <http://www.gao.gov>.

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<sup>53</sup>Exec. Order No. 13,588, 76 *Fed. Reg.* 68,295 (Nov. 3, 2011).

<sup>54</sup>Food and Drug Administration, *A Review of FDA's Approach to Medical Product Shortages* (Silver Spring, Md.: Oct. 31, 2011).

<sup>55</sup>Office of the Assistant Secretary for Planning and Evaluation, *Economic Analysis of the Causes of Drug Shortages* (Washington, D.C.: Oct. 31, 2011).

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If you or your staff have any questions about this report, please contact me 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 report. GAO staff who made key contributions to this report are listed in appendix IV.



Marcia Crosse  
Director, Health Care

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# Appendix I: FDA Criteria for Determining Whether a Drug Is Medically Necessary

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FDA's Drug Shortage Program places the highest priority on responding to shortages of medically necessary drugs, since such shortages have the greatest potential to impact the public health. FDA defines a medically necessary drug 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 to be an appropriate substitute.<sup>1</sup> To determine whether a drug is medically necessary for the purpose of prioritizing its response to drug shortages, FDA's Drug Shortage Program requests the input of medical officers in the Office of New Drugs (OND) who have relevant expertise with the drug.<sup>2</sup> Specifically, the Drug Shortage Program asks OND medical officers to complete a form that requests information about the drug and requests the official's judgment regarding whether the drug meets the agency's criteria for medical necessity. FDA officials told us that they ensure consistency in the process by ensuring that each completed form is reviewed by three FDA officials who have expertise with the drug before it is finalized and provided to the Drug Shortage Program. In addition, FDA officials told us that they sometimes consult with health professional organizations such as the American Society of Health-System Pharmacists when determining whether a drug is medically necessary.

The background questions listed on the form request information about the drug, such as its trade name or generic name and the product's formulation(s). It also includes questions about the manufacturer, including its name, address, and phone number, and whether the drug is available from more than one manufacturer. In addition to requesting this background information about the drug, the form includes several questions, the responses to which are used to determine whether the drug meets the agency's definition of medically necessary. (See fig. 5.)

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<sup>1</sup>FDA does not consider patient inconvenience alone as a sufficient reason to classify a product as medically necessary.

<sup>2</sup>FDA officials told us that if a drug is used to treat multiple therapeutic conditions, they will request the input of multiple medical officers, each of whom would have relevant expertise with the drug.

Figure 5: Questions Included on FDA's Medical Necessity Determination Form

**1. Is the product used to treat a serious disease or medical condition?**  
 No  
 Yes - Explain

**2. What are the labeled indications for this product?**

**3. Are there important off-label uses, such as those for a serious medical condition?**  
(Please note that off-label uses can be considered medically necessary.)

**4. Are there generic forms of this product?**  
 No  
 Yes - Are there any special benefits/risks associated with the generic product(s)?

**5. Are there alternative products available?**  
 No  
 Yes - Please explain the risk(s) and benefit(s) of the alternative product(s).  
Please cite the trade name(s) and generic name(s).

**6. From the above assessment, is this product medically necessary?**  
(Please note that this question refers only to the overall medical necessity of the product(s),  
not whether the specific (manufacturer's) product in question is appropriate for continued  
administration to patients.)  
 No  
 Yes - Please state if this is only for specific indications.

**7. Additional comments:**

Source: Excerpted from FDA Medical Necessity Determination form.

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# Appendix II: Summary of FDA's Response to 15 Selected Drug Shortages

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Based on our review of FDA's response to 15 drug shortages, we found that the agency took multiple actions to address the causes of shortages and to enhance the drugs' availability. Specifically, we reviewed FDA's response to shortages involving 5 anti-infective drugs (acyclovir, amikacin, cefotetan, clindamycin, and sulfamethoxazole-trimethoprim), 5 oncology drugs (cisplatin, cytarabine, doxorubicin, etoposide, and vincristine), and 5 anesthesia drugs (epinephrine, neostigmine, propofol, thiopental, and succinylcholine). At the time of these shortages, FDA determined that all 15 drugs involved with the shortages we reviewed in detail were medically necessary.<sup>1</sup> Our analysis showed that FDA typically used two or more types of actions to respond to each shortage, and for 8 of these shortages, the agency responded with four or more types of actions. For example, during the shortage of doxorubicin, an oncology drug, FDA used seven types of actions to respond to the shortage, including providing assistance to address manufacturing problems related to drug quality issues and providing assistance to address importation delays for active pharmaceutical ingredients or finished products. Our analysis also showed that while FDA searched for a firm willing and able to import a version of the drug in shortage not approved in the United States during 7 of the 15 shortages we reviewed, the agency applied its regulatory discretion regarding the importation of a version of the drug that was not approved in the United States in order to alleviate 1 shortage. Figure 6 displays FDA's response to each of the 15 drug shortages we reviewed.

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<sup>1</sup>Twelve of these drugs are FDA-approved and 3—epinephrine, neostigmine, and thiopental—were not FDA-approved as of October 2011. According to FDA, the 3 unapproved drugs have been marketed in the United States since before 1938, which is when the Federal Food, Drug, and Cosmetic Act was enacted. The Act required FDA to approve new drugs prior to their being marketed for sale. Because manufacturers of these 3 drugs have not obtained FDA's approval, the agency considers the drugs to be illegally marketed. FDA estimates that there are as many as several thousand unapproved drug products that are marketed illegally. While unapproved drugs are subject to enforcement action, FDA gives a higher priority to taking action against unapproved drugs in certain categories, such as drugs with potential safety risks and drugs that lack evidence of effectiveness. However, FDA officials told us that some unapproved drugs may have medically necessary uses.

Figure 6: Actions Taken by FDA in Response to Sterile Injectable Drug Shortages That Were Reported Between January 2009 and June 2011, by Drug Class and Name

FDA action	Drug class and name														
	Anti-infective drugs					Oncology drugs					Anesthesia drugs				
	Acyclovir <sup>a</sup>	Amikacin	Cefotetan	Clindamycin <sup>a</sup>	Sulfamethoxazole trimethoprim	Cisplatin	Cytarabine	Doxorubicin	Etoposide	Vincristine	Epinephrine <sup>a</sup>	Neostigmine	Propofol	Succinylcholine	Thiopental
FDA offered assistance to manufacturers to prevent, alleviate, or resolve the shortage	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
FDA notified other manufacturers to expect increased demand or encouraged other manufacturers to increase production	✓	✓	✓	○	○	✓	✓	✓	✓	✓	✓	✓	✓	○	○
FDA provided assistance to address manufacturing problems related to drug quality issues				✓	✓	✓	✓			✓	✓	✓			
FDA searched for a firm willing and able to import a version of the drug in shortage not approved in the United States		✓				✓	✓	✓	✓			✓	✓		
At FDA's discretion, a manufacturer imported a version of the drug in shortage not approved in the United States												✓			
FDA expedited its review of an application supplement or abbreviated new drug application		✓	✓					✓				✓	✓		
At FDA's discretion, a manufacturer continued to market a drug despite labeling or quality issues				✓		✓	✓			✓		✓			
FDA provided assistance to address importation delays for active pharmaceutical ingredients or finished products						✓	✓				✓	✓	✓		

✓ Denotes FDA action.

○ At the time of the shortage, this drug was produced by a single manufacturer, therefore there were no other manufacturers that FDA could notify of an expected increase in demand or to encourage increased production.

Source: GAO analysis of information provided by FDA.

Note: Not all potential FDA actions are relevant for every shortage. For example, during a shortage caused by a disruption in the supply of an active pharmaceutical ingredient, it would not be necessary for FDA to provide assistance to address manufacturing problems.

<sup>a</sup>Agency officials told us that although all of these shortages involved medically necessary drugs, three did not meet the agency's criteria for a shortage. While these three shortages did not meet FDA's criteria, all shortages we reviewed in detail were identified by representatives from the American Society of Anesthesiologists, American Society of Clinical Oncology, and the Infectious Diseases Society of America as recent shortages that had significant impact on patient care or public health.

# Appendix III: Comments from the Department of Health and Human Services



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation  
Washington, DC 20201

Marcia Crosse, Director  
Health Care  
U.S. Government Accountability Office  
441 G Street NW  
Washington, DC 20548

NOV 03 2011

Dear Ms. Crosse:

Attached are comments on the U.S. Government Accountability Office's (GAO) draft report entitled, "DRUG SHORTAGES: FDA's Ability to Respond Should Be Strengthened" (GAO-12-116).

The Department appreciates the opportunity to review this report prior to publication.

Sincerely,

A handwritten signature in cursive script that reads "Jim R. Esquea".

Jim R. Esquea  
Assistant Secretary for Legislation

Attachment

**GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "DRUG SHORTAGES: FDA'S ABILITY TO RESPOND SHOULD BE STRENGTHENED" (GAO-12-116)**

The Department appreciates the opportunity to review and comment on this draft report.

Over the last 5 years, drug shortages in the United States have steadily and dramatically grown, tripling from 61 in 2005 to 178 in 2010. Since at least the founding of the Food and Drug Administration's (FDA) drug shortage program in 1999, the agency has been mindful of the hardships and adverse health consequences that drug shortages impose on patients, and has taken an active and responsive role in mitigating and preventing drug shortages. FDA has worked relentlessly to avoid disruptions in patient care by preventing and mitigating drug shortages, making tremendous contributions to the lives of American patients and improving their healthcare outcomes. Since 2010 through September 2011, FDA prevented 137 drug shortages.

Recognizing that drug shortages pose a serious and growing threat to public health, on October 31, 2011, President Obama issued an Executive Order, *Reducing Prescription Drug Shortages*. The Executive Order acknowledges FDA's diligent efforts to prevent and mitigate drug shortages, and emphasizes that the early disclosure of shortages is extremely important to their prevention and mitigation. The President's Executive Order supports, enhances, and amplifies FDA's efforts and charges FDA to take the following actions:

- use all appropriate administrative tools to ensure that manufacturers provide adequate advance notice of manufacturing discontinuances that could lead to shortages of drugs that are life supporting or life sustaining, or that prevent debilitating disease;
- take steps to expand its current efforts to expedite regulatory reviews, including reviews of new drug suppliers, manufacturing sites, and manufacturing changes, whenever it determines that expedited review would help to avoid or mitigate existing or potential drug shortages; and
- 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 so that DOJ may determine whether these activities are lawful and take any appropriate enforcement actions.<sup>1</sup>

FDA appreciates the attention and visibility that this Executive Order provides to the agency's ongoing work on drug shortages. As a reflection of FDA's concern and attention regarding drug shortages, and the high priority FDA places on this issue, in January 2011, the agency began a review of medical product shortages in the four medical product centers of the agency. Based on this review, FDA has released a report, *A Review of FDA's Approach to Medical Product Shortages*, that analyzes the problem and identifies the following findings:

<sup>1</sup> <http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-reducing-prescription-drug-shortages>

**GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "DRUG SHORTAGES: FDA'S ABILITY TO RESPOND SHOULD BE STRENGTHENED" (GAO-12-116)**

- Of the 127 studied drug shortages in 2010-11, sterile injectables accounted for the majority. The major therapeutic classes of drugs in shortage were oncology drugs, antibiotics, and electrolyte/nutrition drugs.
- The leading reasons for the shortages were problems at the manufacturing facility, delays in manufacturing or shipping, and active pharmaceutical ingredient shortages.
- Manufacturing quality problems that have resulted in shortages can be serious, including findings of glass shards, metal filings, and fungal or other contamination in products meant for injection into patients.
- Sterile injectable drugs have unique manufacturing and market features which make shortages of these products more likely to occur and harder to prevent or mitigate.<sup>2</sup>

The review also reveals that the most common FDA action to prevent a drug shortage was expediting review of new manufacturing sites, new suppliers, and specification changes, followed by exercising regulatory flexibility and discretion. Once FDA is notified of a shortage, the agency has many options to mitigate the drug shortage, and in many cases, takes more than one action. In the shortages studied, the agency's four most common actions were:

- asking other firms to increase production,
- working with manufacturers to identify ways to reduce the dangers of products with quality issues,
- expediting review of regulatory submissions, and
- exercising regulatory discretion regarding controlled importation of similar products approved abroad but not approved in the United States.

Furthermore, in order to understand what is causing drug shortages and to enable the evaluation of potential solutions, HHS conducted an analysis of the underlying factors that lead to periods of shortage in the prescription drug market.<sup>3</sup> This report complements the FDA's report on the current drug shortage problem.

No single or simple solution can resolve the problem of medical product shortages. Consequently, efforts to address the problem must be multifaceted, sustained over the long-term, and involve the engagement of all parties involved in the manufacture and distribution of these products. To contribute to such efforts, FDA has actively explored and implemented measures within its purview to improve and maximize its efforts toward the prevention and mitigation of drug shortages:

- FDA created a drug shortages task force within its Center for Drug Evaluation and Research (CDER) to enhance intra-center activities on drug shortages.
- FDA created a dedicated recalls and shortages branch within CDER that helps manage drug shortages.

<sup>2</sup> <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm275051.htm>

<sup>3</sup> <http://aspe.hhs.gov/sp/reports/2011/DrugShortages/ib.shtml>

**GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "DRUG SHORTAGES: FDA'S ABILITY TO RESPOND SHOULD BE STRENGTHENED" (GAO-12-116)**

- FDA's CDER developed a Drug Shortages Action Plan to enhance communications with manufacturers and stakeholders, increase the availability and usability of drug shortages information, and enhance staffing and internal collaborations.<sup>4</sup>
- The FDA Commissioner participated in a stakeholder meeting convened on September 9, 2011 by the Department to discuss and explore solutions to the drug shortages affecting patients in the United States.<sup>5</sup>
- FDA sponsored a public workshop on September 26, 2011 to provide information for, and to gain additional insight from, professional societies, patient advocates, industry, consumer groups, health care professionals, researchers, and other interested persons about the causes and impact of drug shortages, and possible strategies for preventing and mitigating drug shortages.<sup>6</sup>
- FDA developed a database to analyze the epidemiology of drug shortages in real time. This database will be used to track all current drug shortages, and will eventually also be populated with data from past years. It will allow the agency to analyze trends in drug shortages, as well as to assess its performance in mitigating and preventing shortages, through the use of some potential metrics that were included in the FDA report referred to earlier. FDA appreciates GAO's comments on this database and will consider them as the agency moves forward with implementation.
- In coordination with the President's Executive Order, FDA sent a letter to manufacturers on October 31, 2011 reminding them of their legal obligations, under certain circumstances, to notify FDA of the discontinuation of any sole source drugs, and encouraging them to voluntarily notify FDA of any disruptions that could lead to drug shortages.<sup>7</sup>

FDA is committed to ensuring that patients have access to safe and effective medicines and our work to prevent and mitigate drug shortages is no exception. FDA's Drug Shortage Program highlights this commitment, and the agency anticipates its workload will increase as we endeavor to enhance our ability to prevent and ease shortages. FDA has started expanding its drug shortages workforce, and we look forward to their help in tracking shortages, analyzing trends, and establishing clear guidelines and procedures to enhance internal collaborations and communications.

The Congress also has shown interest in drug shortages, and on September 23, the House Committee on Energy and Commerce's Subcommittee on Health held a hearing to examine the increase in drug shortages. Bipartisan legislation (H.R. 2245 and S. 296) supported by the Administration also has been introduced in Congress to address the growing problem of drug shortages.

<sup>4</sup> <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm277732.htm>

<sup>5</sup> <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm271417.htm>

<sup>6</sup> <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM275801.pdf>

<sup>7</sup> <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm277675.htm>

**GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "DRUG SHORTAGES: FDA'S ABILITY TO RESPOND SHOULD BE STRENGTHENED" (GAO-12-116)**

The steadily growing number of drug shortages and their effect on the health of American patients compel all relevant stakeholders to seek solutions, and FDA is committed to participating in robust and effective collaboration to help resolve this critical problem. The causes of drug shortages are extremely complex and have economic, regulatory and legal underpinnings that will require the long-term engagement and thinking of many relevant stakeholders, including manufacturers and other participants along the drug supply chain, regulators and legislators. Although many of the issues that contribute to drug shortages lie outside of FDA's legal authorities, FDA long has been, and will continue to be, vigorously engaged in contributing to the resolution of this urgent public health concern.

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# Appendix IV: GAO Contact and Staff Acknowledgments

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## GAO Contact

Marcia Crosse, (202) 512-7114, [crossem@gao.gov](mailto:crossem@gao.gov).

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## Acknowledgments

In addition to the contact named above, Geraldine Redican-Bigott, Assistant Director; Nick Bartine; Zhi Boon; Emily Goodman; Cathleen Hamann; Yesook Merrill; Lisa Motley; and Patricia Roy made key contributions to this report.

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# Related GAO Products

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*Drug Pricing: Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement.* [GAO-11-836](#). Washington, D.C.: September 23, 2011.

*Drug Safety: FDA Faces Challenges Overseeing the Foreign Drug Manufacturing Supply Chain.* [GAO-11-936T](#). Washington, D.C.: September 14, 2011.

*High-Risk Series: An Update.* [GAO-11-278](#). Washington, D.C.: February 2011.

*Food and Drug Administration: Response to Heparin Contamination Helped Protect Public Health; Controls That Were Needed for Working With External Entities Were Recently Added.* [GAO-11-95](#). Washington, D.C.: October 29, 2010.

*Food and Drug Administration: Opportunities Exist to Better Address Management Challenges.* [GAO-10-279](#). Washington, D.C.: February 19, 2010.

*Food and Drug Administration: FDA Faces Challenges Meeting Its Growing Medical Product Responsibilities and Should Develop Complete Estimates of Its Resource Needs.* [GAO-09-581](#). Washington, D.C.: June 19, 2009.

*Human Capital: Key Principles for Effective Strategic Workforce Planning.* [GAO-04-39](#). Washington, D.C.: December 11, 2003.

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*Agency Performance Plans: Examples of Practices That Can Improve Usefulness to Decisionmakers.* [GAO/GGD/AIMD-99-69](#). Washington, D.C.: February 26, 1999.

*Managing for Results: Critical Issues for Improving Federal Agencies' Strategic Plans.* [GAO/GGD-97-180](#). Washington, D.C.: September 16, 1997.

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