

Senate Finance Committee

Hearing on

“Drug Shortages: Why They Happen and What They
Mean”

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Statement for the Record

Submitted by the



pharmacists advancing healthcare[®]

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Good morning and thank you Chairman Baucus, Ranking Member Hatch, and distinguished Members of the Committee, for holding this hearing. My name is Kasey Thompson and I am Vice President of Policy, Planning and Communications for the American Society of Health-System Pharmacists (ASHP). I am here today to talk about the problem of drug shortages and how shortages are affecting patients and the ability of healthcare providers to care for them.

For the last 10 years, ASHP, in collaboration with the University of Utah drug information program, has been tracking drug shortages, and making that information available to the public on our Web site. We provide a list of shortage drugs, which are defined by the FDA as those for “which the total supply of all clinically interchangeable versions of an FDA-regulated drug is inadequate to meet the current or projected demand at the patient level.” In the past five years, shortages have rapidly escalated, increasing from 70 in 2006 to 231 as of this November, and there appears to be no end in sight.

Generic injectable drugs, which are commonly used in hospitals, comprise the majority of drug shortages. Many drugs fundamental and essential to care are in scarce supply, including anesthetics and pain medications, antibiotics, life support drugs for emergency care, and intravenous nutrition.

Because shortages affect our hospitalized and most vulnerable patients, patient safety and quality of care is our primary concern. Without access to the preferred drug treatment, clinicians must use alternatives, which may be less effective or associated with increased risk of adverse outcomes.

Examples of these events are described in detail in the Institute for Safe Medication Practices survey in September 2011. In this survey, 1800 respondents reported over 1000 adverse drug events caused by shortages. Twenty-five percent of these reports were medication errors; another 20% were adverse drug reactions. A survey conducted by the American Hospital Association in July 2011 also identified suboptimal care, indicating that 82% of hospitals reported delayed treatment and more than half said they could not provide some patients with the recommended therapy.

Drug shortages also add to the cost of providing care. A study by Premier in March of this year suggested the cost of purchasing alternative therapeutic products to those in shortage to be \$200 million. In addition, a survey conducted by ASHP and the University of Michigan indicated that hospital pharmacists are spending 8-12 additional hours per week dealing with shortages. Further, the study estimated that additional annual labor costs to hospitals of managing shortages to be \$216 million. Every minute spent dealing with a drug shortage is time taken away from patient care.

In some cases, we are able to determine why there is a shortage, in other cases, we simply have no idea. As a first step we support the passage of the current bipartisan legislation in the House and Senate that would help the FDA prevent some shortages from occurring if they were notified about a manufacturing problem or planned discontinuation. FDA data indicate that 54% of drug shortages are related to product quality problems followed by lack of capacity or other manufacturing issues. About half the time manufacturers do not disclose the reason for a shortage. Our analysis over the last 10 years has shown that many drug shortages are the result of quality issues in the manufacturing process, loss of a manufacturing site, delays and capacity issues, shortages of raw materials-- particularly a single source of an Active Pharmaceutical Ingredient, product discontinuations, and secondary shortages of a therapeutic alternative resulting from a primary shortage. We recognize that there is no one cause of drug shortages, and therefore no one solution.

We are pleased to see that other facets of drug shortages, including economic factors, are being considered, but we are not currently in a position to draw any conclusions given a lack of sound data. A recent report by the Assistant Secretary for Planning and Evaluation describes the economic analysis of drug shortages. It identified a number of possible factors that influence drug shortages and noted that "Shortages have been concentrated in drugs where the volume of sales and drug prices were declining in the years preceding a shortage, suggesting that manufacturers are diverting capacity from shrinking

lines of business to growing ones.” It has been suggested that Medicare reimbursement policies may be partially to blame for drug shortages. While we believe this is an area that should be explored further, we are hesitant to focus on any one potential cause given the limited data and the numerous factors that contribute to shortages. It will be important to learn from other stakeholders in the supply chain including pharmaceutical manufacturers, wholesalers, group purchasing organizations, and others in order to fully assess these causes and solutions to this public health crisis.

Other incentives for manufacturers to stay or re-enter the market should be examined. For example, tax credits awarded to companies for developing new technologies in the production process should be explored. We believe that any incentives should be geared toward increasing production capacity and upgrading facilities in order to meet demand for critically important generic injectables.

In conclusion, drug shortages continue to be a very serious public health crisis, and compromise our ability to treat adult and pediatric cancer, to feed newborns intravenously who cannot eat, to relieve pain, to battle serious infections, and provide care when the most appropriate drug is unavailable.

While some causes are known, others are not quite as clear. ASHP supports more examination of these other factors to help identify additional causes of drug shortages currently plaguing our healthcare system. We look forward to working with Congress, the FDA, and other stakeholders to ensure an adequate supply of critical, life-saving medications. Again, thank you Mr. Chairman, ranking member, and all members of the committee for the opportunity to provide input on this urgent public health crisis.

Drug Shortages Background and Policy Options

Shortages of prescription drugs in the United States have gained increasing attention in recent years due to the scope and severity of the drugs in short supply. The majority of these shortages occur in drugs that are generic injectables, often administered in a hospital or clinic setting. The shortages have been occurring for anti-cancer drugs, anesthetics, pain, and nutritional drugs, all of which play crucial roles in the care of patients. The result of drug shortages is that caregivers must scramble to find the drug, or use an alternative if one is available. Many caregivers have expressed concern that even if a therapeutic alternative exists, it is likely an older drug which may have more severe side effects or negatively interact with other medications the patient is taking. Further, drug shortages have caused widespread fear among caregivers who are deeply concerned that care could be delayed, rationed, or is provided in a suboptimal manner to stretch doses and preserve scarce supplies.

According to a study conducted in partnership between ASHP and the University of Michigan Health System, labor costs associated with managing drug shortages have an estimated annual impact of \$ 216 million nationally, and more than 90% of respondents agreed that drug shortages were associated with an increased burden and increased costs today compared to two years ago.

Causes of drug shortages are many and complex. Manufacturing issues that lead to drug shortages include product quality issues that result in production halts or recalls, product discontinuations, and unavailability of active pharmaceutical ingredients (APIs) or other raw materials. Secondary shortages—or shortages that occur based on shifts in market demand caused by an initial shortage of another drug—are also common. Other contributing causes to drug shortages include quality issues that arise from the ever-increasing reliance on foreign ingredient and manufacturing sources and a lack of FDA resources to expedite approval of supplemental new drug applications and conduct foreign inspections.

While not a cause of drug shortages, just-in-time inventory practices by product distributors and practice sites have removed the buffer previously provided by larger inventories and resulted in an immediate impact of drug shortages on patient care.

While information on the root cause of each drug shortage is not always publicly available, the cause of many shortages can be traced back to a manufacturing processes or facilities that result in substandard end products. These manufacturing issues are compounded by constraints on capacity over the last few years that has resulted in fewer manufacturers producing critical drugs. When one manufacturer experiences a production interruption, other companies must ramp up production of their product to meet market needs. This increased production is sometimes, but not always, possible. In the case of sole-source drugs, this situation almost instantly results in a shortage situation.

ASHP continues to work with FDA, other health care provider groups and members of the supply chain to address the issue. However, we also believe Congress can help us as well. ASHP supports bipartisan legislation (S. 296, H.R. 2245) that would require drug manufacturers to notify the Agency when they experience an interruption in the production of a drug product potentially resulting in a shortage situation. According to FDA, in 2010 the Agency was able to avoid 38 drug shortages when they were made aware of production interruptions ahead of time, and so far this year, 101 shortages were avoided. However, we believe other steps can be taken as well, for example, require confidential notification of the disruption in supply of single source active pharmaceutical ingredients (API), require manufacturers to develop continuity of supply plans, establish incentives for manufacturers to remain or re-enter the market, and urge FDA to develop expedited approval pathways for pre-1938 (unapproved) drugs. Finally, ASHP believes that FDA must have adequate resources devoted to alleviating and preventing drug shortages.

Notification System

Under current law, manufacturers are not required to report to FDA when they experience an interruption in the production of their products, unless that drug is deemed medically necessary by the agency. The same holds true for manufacturer plans to discontinue a product. Even in cases where the drug is deemed medically necessary and reporting is required, FDA has no enforcement mechanism to penalize a drug maker for failing to report these problems. This information could be extremely useful to FDA in the case of drugs with multiple suppliers where the agency could urge alternate suppliers to step up production of a product to offset the decrease in supply due to the interruption or discontinuation of the initial product. In some instances, FDA is not told there is a problem, or the nature of the problem. This information could be useful in determining the duration and severity of the interruption and may allow the agency to implement countermeasures to help ensure supply.

The importance of notification is highlighted by quality concerns associated with the increased globalization of pharmaceutical manufacturing. A number of drug shortages can be traced back to quality concerns with foreign-produced APIs. An extreme example was the heparin contamination that occurred in 2007, which resulted in a recall, and a subsequent product shortage that was immediate and continued for an extended duration of time. While FDA has increased foreign inspections, it still lacks the resources necessary to fully address this issue. Therefore, drug shortages precipitated by recalls caused by substandard APIs will continue and likely increase.

Legislation (S. 296/H.R. 2245) in Congress would mandate that companies confidentially notify FDA of the interruption in production of any product six months in advance, or as soon as possible in the event of an unplanned stoppage. Manufacturers that fail to report this information would be subject to civil monetary penalties. This early warning system would allow the agency to communicate more effectively

with manufacturers and others in the supply chain to plan for pending supply interruption. The early warning system should be the cornerstone of congressional action to address drug shortages.

Confidential Notification for Single-Source API

In addition, information that can make drugs vulnerable to shortages, such as a single API source, is also frequently unknown beyond the manufacturer. This information is, and should be considered proprietary, but this lack of transparency hinders the development of contingency plans for vulnerable drugs. A requirement that manufacturers confidentially notify FDA when there is a single source of API may help the Agency work with manufacturers to identify backup sources should supply issues arise.

Continuity of Supply Plans

Related to the reporting or an early warning system, FDA could work with manufacturers to develop continuity of supply plans. The current lack of transparency acts as a significant barrier to this type of collaboration. With increased information exchange, contingency plans could be developed that include countermeasures such as manufacturing redundancies or backup supplies; more effective communication among FDA, manufacturers and others in the supply chain; and finally, development of plans that utilize production capabilities of other manufacturers either here in the United States or abroad to ensure availability of a drug in short supply.

In 2010, FDA worked with APP Pharmaceuticals to help alleviate a shortage of propofol, a widely used anesthetic preferred by anesthesiologists because of its excellent safety profile compared to other available drugs. By enabling the company to work with its German counterpart to import the drug, FDA was able to substantially improve product availability after the shortage occurred. Using this example, if an acceptable foreign alternative could be identified before a shortage occurs through establishment of

continuity of supply plans for vulnerable drugs, then importation could be expedited and the negative impact of a specific shortage on patient care could be minimized or averted. Importation represents an extreme example of contingency planning. In its simplest form, manufacturing strategies that include collaborating with other manufacturers, establishing back-up suppliers of raw materials and APIs, and creating alternative production capabilities that can be used as countermeasures would be a significant step forward to combating drug shortages. Contingency planning by companies producing drugs critical to patient care must be a standard of practice. S. 296/H.R. 2245 support the development of contingency plans for drugs that are vulnerable to shortages.

Incentives

Further, shortages are occurring overwhelmingly among generic injectable drugs, where production processes tend to be more complex than their solid dosage counterparts. Low margins for these expired patent products coupled with complex manufacturing processes may lead some manufacturers to abandon production of these drugs altogether in favor of products with higher profit margins, thus reducing the number of potential suppliers of products critical to patient care. A way to offset this problem may be to explore incentives to encourage manufacturers to either stay in the market or enter the market with a new product line. More study needs to be conducted to validate the need for incentives. In addition, other stakeholders in the supply chain need to provide input on the economic factors that influence production capability.

Require development of an expedited approval pathway for pre-1938 drugs.

FDA must find a way to abbreviate and prioritize approval processes for existing therapies that are unapproved, but widely used and essential for patient care. For these drugs, the agency should work with manufacturers to fast track their approval for the U.S. market, especially in cases where the

potential exists for those drugs to fall in short supply. Barriers to manufacturing and marketing these drugs must be minimized in order to foster production and availability of these drugs.

Conclusion

Unfortunately, there is no single solution that can prevent the occurrence of all drug shortages. The complexity of manufacturing processes, the requirement for safe and high-quality products, and globalization of the pharmaceutical supply chain all contribute to fluctuating product supplies that may never be entirely eliminated. However, there are critical steps that Congress, FDA and other stakeholders can implement to ensure that patient care remains available, safe, and effective. While the adjustments and compromises required from all stakeholders are difficult, the need for change is critical. First and foremost is the need for increased communication and transparency.

ASHP, along with several other stakeholder groups has been working collaboratively with Congress and supply chain stakeholders to develop solutions to the drug shortage problem. As indicated before, there is bipartisan legislation in both houses of Congress. Passage of legislation that provides additional authority to FDA is a step in the right direction. In the long term, FDA will require additional resources to best address this and other issues that impact the quality and safety of drugs.

Figure 1: Total Shortages and oncologic shortages

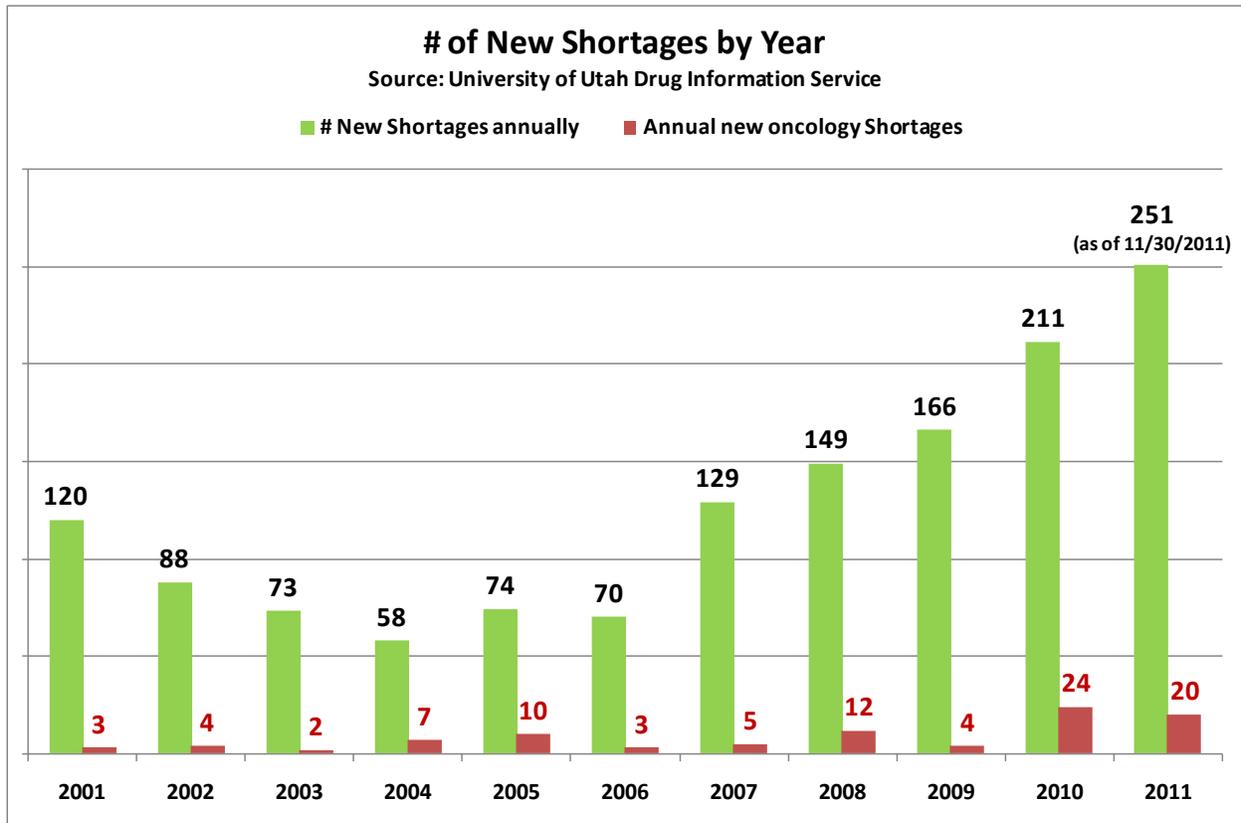


Figure 2: Shortages by drug class

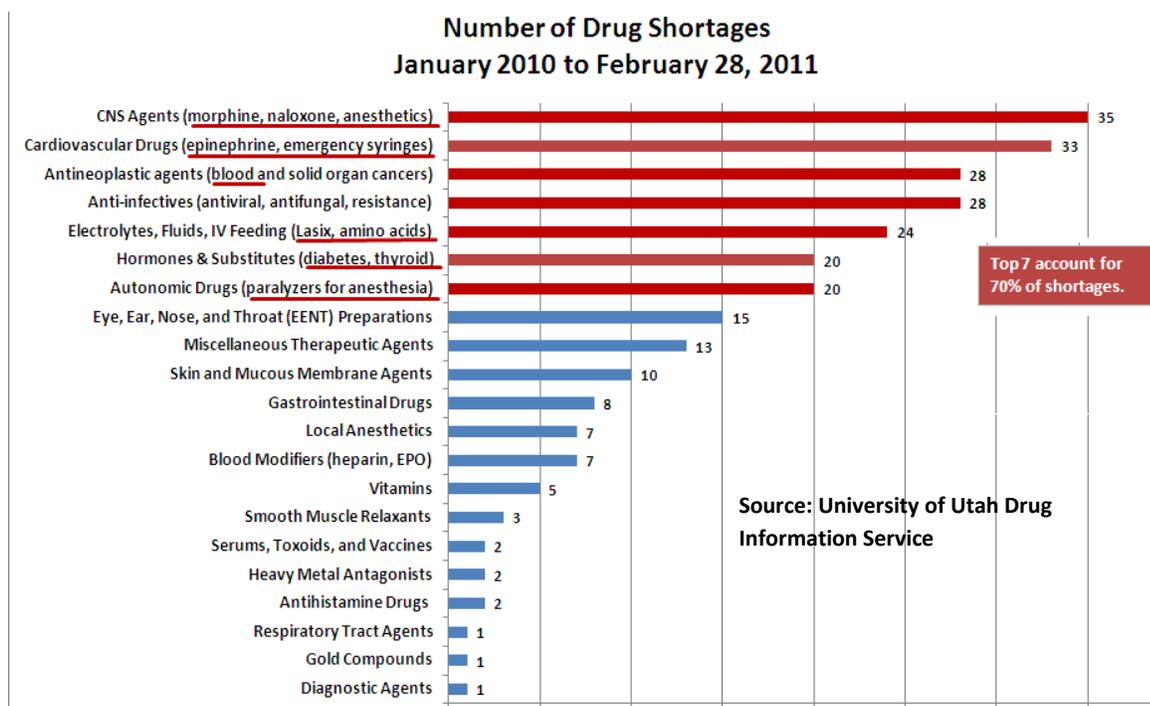


Figure 3: Causes of shortages – FDA data

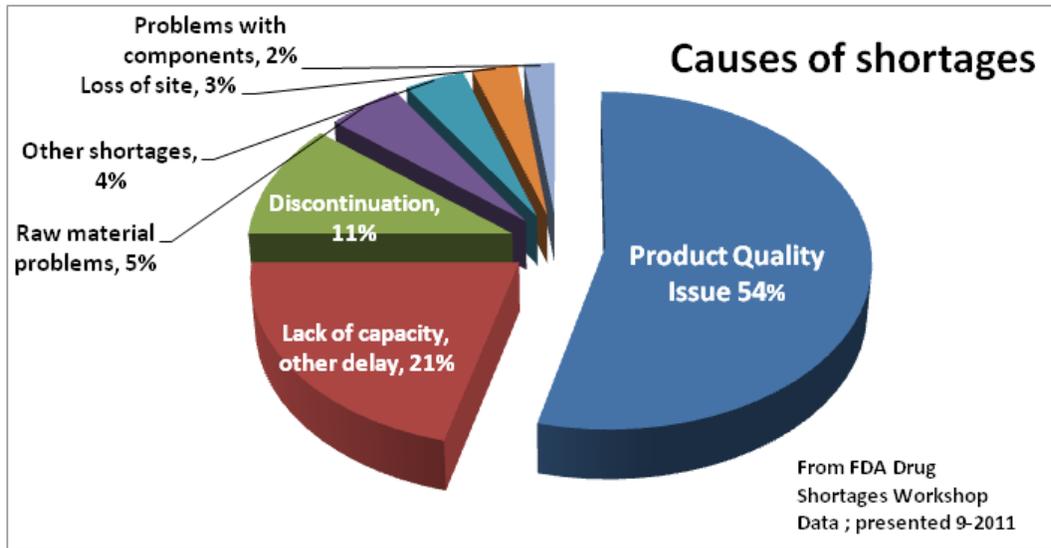


Figure 4: Causes of shortages – University of Utah data

