House Oversight and Government Reform Subcommittee on Health Care, District of Columbia, Census and the National Archives

Hearing on

Drug Shortage Crisis: Lives are in the Balance

November 29, 2011

Statement for the Record

Submitted by the

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Good morning and thank you Chairman Gowdy, Ranking Member Davis, and distinguished Members of the Subcommittee, 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 the impact shortages are having on the ability of healthcare providers to care for our patients.

For the last 10 years, ASHP, in collaboration with the University of Utah drug information program, has been tracking and studying drug shortages, and making that information available to the public on our Web site. Since that time we have seen the number of shortages increase, almost tripling since 2006. As a result, hospital pharmacists and other healthcare providers have had to go to heroic lengths to find needed medications, spending time tracking down the product, rather than caring for patients. In some cases, we are told why there is a shortage, for example, there may be a quality issue with the production of the product, in other cases, we simply have no idea. Our analysis of shortages over the last 10 years has shown that most drug shortages are the result of quality issues in the manufacturing process, however, we recognize that there is no one cause of this problem, nor is there one solution. For example 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 do not currently have the data to confirm that this is the case. We do know that drug shortages are not confined to oncology medications. Other significant shortages affect anesthesia, pain management, and nutritional support medications. These other drug classes have experienced increases since 2006 as well. This suggests multiple reasons for drug shortages, both quality assurance and economic. We are pleased, however, to see that other facets of drug shortages, including economic factors, are being considered, but would warn against rushing to any conclusions given the limited data. It would be important to learn from other stakeholders in the supply chain in order to fully assess these causes and solutions to this public health crisis.

Fortunately, the Food and Drug Administration has been able to take steps to address drug shortages when they had access to certain information from drug manufacturers. For example, in 2010 FDA was able to prevent 38 shortages when drug manufacturers notified the agency when a product was discontinued or a manufacturing problem occurred. That number has increased to 101 shortages averted for 2011. For this reason, ASHP supports legislation in both the House and Senate that would require manufacturers to confidentially notify the agency when they experience production problems or discontinue a product. We know that confidential notification by drug manufacturers to the FDA is not a complete solution, nor does it prevent shortages from occurring, but it is a proven solution based on FDA's experience that can be implemented immediately while we look to examine other potential contributory causes of drug shortages.

Hospital and health-system pharmacists have been collaborating with other clinicians and members of the supply chain to work with FDA to address the problem. For example, we believe FDA should have and dedicate the necessary resources to speed up the regulatory processes that help resolve drug shortages. Other alternatives include improved communication between FDA field personnel and the drug shortages program to assess the comparative risk of public harm when a potential enforcement action will cause or worsen a drug shortage; exploring incentives for manufacturers to continue or re-enter the market; a generic user fee program to speed approvals; and last, ensuring the agency has the funding it needs to carry out its mission.

In conclusion, drug shortages continue to be a very serious public health threat, not just for oncologics, but also for pain medications, anesthesia drugs, and nutritional products. 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 health care system. 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 aspects of the manufacturing process. These manufacturing issues are compounded by substantial industry consolidation 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. It 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.

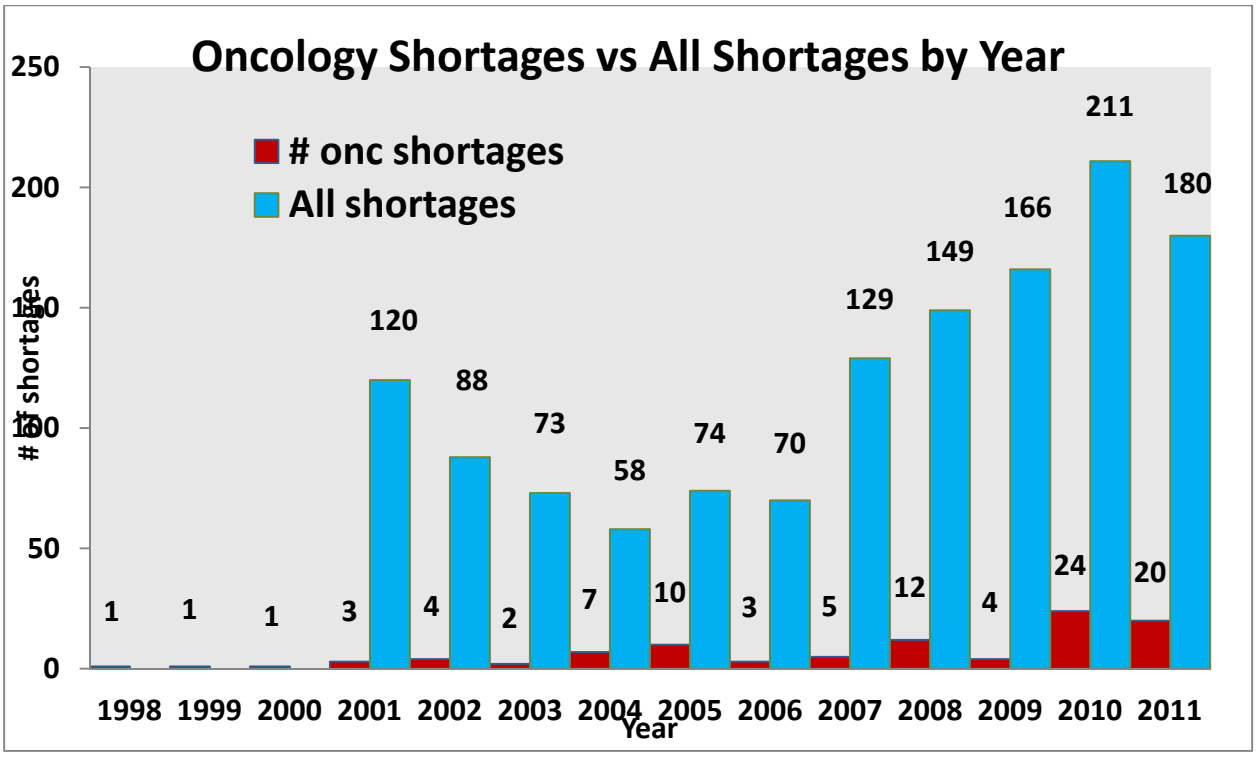
FDA must find a way to abbreviate and prioritize approval processes for existing therapies that are unapproved, but widely used and essential for patient care. For these drugs, the agency should work with manufacturers to fast track their approval for the U.S. market, especially in cases where the

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.


Oncology Shortages vs All Shortages by Year
onc shortages
All shortages
# of shortages
Year
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200
150
100
50
0
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