

House Energy and Commerce Committee
Subcommittee on Health

Hearing:

Examining Drug Shortages

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Statement for the Record
Submitted by the



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Summary

Good morning and thank you Chairman Pitts, Ranking Member Pallone, and distinguished Members of the Subcommittee, for holding this hearing. My name is Kevin Colgan and I am Corporate Director of Pharmacy at Rush Medical Center in Chicago, IL. I am here today because I cannot serve my patients or their caregivers due to shortages of medications, some of them critical to patient care.

While there is no single solution that will immediately solve the problem of drug shortages, there are things we can do to help address the issue. First, bipartisan legislation in both houses of Congress would enable FDA to require that drug manufacturers report confidentially to the agency when they experience an interruption in the production of their product. This early warning system will help FDA work with other manufacturers to ramp up production when another company experiences a problem. Moreover, the bills call upon FDA to work with manufacturers to develop continuity of supply plans which could help to identify backup sources of API and produce redundancies in inventory to serve as reserve supplies. While some have argued that the legislation won't have any impact, we disagree. According to FDA, in 2010 38 drug shortages were avoided when the agency was given advance notice. Further, opponents of this approach argue that it will lead to hoarding. We know that hoarding already occurs. How do some find out about shortages before others? We don't know all the answers to this question.

What we do know is that early warning to FDA will help make sure that everyone has the same information at the same time. Simply put, the public benefit of an early warning system far outweighs the risk of hoarding. In other emergency preparedness areas such as terrorism, flu pandemic and natural disasters, we develop action plans and communication channels among necessary responders. Why would we approach drug shortages any differently?

Second, 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 devote necessary resources to speed up the regulatory process to address 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.

Many of you sitting in this room sometime over the next several months is going to receive the news that you, a loved one or a friend, has been diagnosed with cancer, needs surgery, has been admitted to an intensive care unit, has a serious infection that requires intravenous antibiotics or antiviral medications, or has a premature baby or grandbaby that requires nutritional support. The last thing you want to hear is that we don't have first-line medication to treat you; that the medication we have may not work as well and

could cause heart damage, but it is all we have to offer; or that we are delaying your treatment until we are able to obtain drugs that are in short supply. These are all situations, I, my clinical pharmacy staff, and the physicians, nurses, and respiratory therapists that we work with have had to manage over the past year. From our perspective, drug shortages represent a national health care crisis. We don't have one single solution, but we have offered a number of solutions that together can help resolve this crisis.

Again, thank you Mr. Chairman, ranking member, and all members of the committee for the opportunity to provide input on this problem.

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 an 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 most 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. 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. By FDA's own account, in 2010 the agency was able to avoid 38 drug shortages when this type of notification was made available.

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 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 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 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. There are several ways this could potentially be accomplished: 1) explore tax incentives for manufacturers to produce a drug in short supply or one deemed “vulnerable” to a shortage; 2) grant temporary exclusivity for a new product line of a drug in shortage or deemed “vulnerable” to one; 3) if a generic user fee program is created within the next reauthorization of the Prescription Drug User Fee Act (PDUFA), FDA could explore reduced user fees for drugs in short supply or deemed “vulnerable.”

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 and safe. 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 legislation in both houses of Congress as well as broad bipartisan support in the Senate for action. 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.