American Hospital Association™
Advancing Health in America

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The Honorable Cathy McMorris Rodgers
Chair
Committee on Energy and Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Mike Crapo
Ranking Member
Committee on Finance
United States Senate
Washington, DC 20510

Dear Chair McMorris Rodgers and Ranking Member Crapo:

On behalf of our nearly 5,000 member hospitals, health systems and other health care organizations, our clinician partners — including more than 270,000 affiliated physicians, 2 million nurses and other caregivers — and the 43,000 health care leaders who belong to our professional membership groups, the American Hospital Association (AHA) appreciates the opportunity to respond to your request for information on drug shortages.

The AHA applauds your leadership to address this critical issue. Hospitals and health systems have long been concerned about chronic and increasing drug shortages that have serious consequences for patient safety, quality of care and access to therapies. Addressing drug shortages is complex and costly to hospitals and health systems in terms of staff time and other resources required to manage the shortages.

Our detailed responses to your questions follow.

QUESTION: How would you define the scope and impact of the recent and ongoing U.S. (United States) drug shortages? What are the impacts of recent and recurring shortages of generics and other critical medicines on patient care?

America's hospitals and health systems have long been gravely concerned about shortages of a wide range of drugs to treat patients. The COVID-19 pandemic, with its record surge in demand due to large numbers of critically ill patients, exacerbated such shortages and called attention to increasing concerns about the stability and security of U.S. and global medical supplies. Shortages of essential medications continue to rise — especially shortages of generic sterile injectable drugs used in hospitals. In recent months, the situation has worsened, with the abrupt shutdown of Akorn Pharmaceuticals, which made about 100 essential hospital medications, such as albuterol used in children with breathing difficulties, as well as Accord Pharmaceutical's temporary suspension of manufacturing of certain cancer drugs (methotrexate, carboplatin and cisplatin) due to serious quality issues at Intas, their contract manufacturer in India.

According to the American Society of Health-System Pharmacists (ASHP), the U.S. health care system currently is experiencing the most drug shortages since 2014. The number of active drug shortages in the U.S. reached a new peak of 301 in the first quarter of 2023. Shortages of local anesthetics and basic hospital drugs, albuterol solution, common oral and ophthalmic products, and attention-deficit/hyperactivity disorder treatments are affecting large numbers of hospitals and health systems and patients. Chemotherapy drugs, often without alternatives, are increasingly in short supply and have returned to the list of top-five drug classes affected by shortage.[1]

Of particular concern to hospitals are the cascading impact of drug shortages on patients and the heightened stress on scarce hospital resources. Shortages can adversely affect patient care, causing delays in treatment, increasing the risk of medication errors, and requiring the use of less effective alternative treatments. As a result, diseases, such as childhood leukemia, that are curable or manageable for most patients may not be able to be treated effectively.

Hospitals also have experienced increased strain on their workforce and increased costs directly attributable to their efforts to try to obtain needed pharmaceuticals or suitable substitutes.[2] Pharmacists are part of the health care workforce that is known to already be under a great deal of stress and experiencing burnout.[3] Additional stress associated with having to try to track down critically needed medications or find and manage alternatives exacerbates the situation. A 2019 survey[4] from Vizient, Inc. found that, on average, hospitals in the U.S. dedicate more than 8.6 million hours of additional labor hours annually to manage drug shortages. The financial impact adds up to approximately $360 million annually in labor costs for time spent seeking supply and implementing mitigation strategies that enable continuity of patient care.

QUESTION: What market and economic conditions undermine pharmaceutical supply chains or the availability of drugs? Please discuss any specific barriers in public payment programs.

A strong and reliable pharmaceutical supply chain is a critical and integral component to delivering safe and effective high-quality care to patients. However, it has become increasingly clear that our national pharmaceutical supply chain is fragile, and that fragility poses significant risk to the patients and communities served by America's hospitals and health systems.

Various businesses make up the pharmaceutical supply chain, including suppliers, manufacturers, distributors, and group purchasing organizations (GPOs). A disruption anywhere in the chain can create prolonged difficulties in pharmaceutical supply acquisition for providers, which can directly affect their ability to treat patients. Exacerbating these difficulties

[1] https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics
[2] https://www.hsgac.senate.gov/wp-content/uploads/2023-06-06-HSGAC-Majority-Draft-Drug-Shortages-Report.-FINAL-CORRECTED.pdf
[3] https://www.washingtonpost.com/wellness/2023/03/30/pharmacy-shortages-staffing/
[4] https://newsroom.vizientinc.com/Drug-Shortages-Labor-Cost-Report-Vizient-pdf

is the “lean” or “just-in-time” framework of supply chain operations. There is effectively little buffer when disruptions occur. Distributors, manufacturers and even health care providers have pursued this just-in-time supply chain approach with the goal of lowering costs so that health care is more affordable; however, during large scale emergencies and other disruptions in supply, the risks — and added costs — of such a strategy became clear. When those disruptions occur, providers often have little-to-no notice and can be left scrambling to acquire products necessary to care for the sick and injured.

To mitigate these challenges, strengthening the supply chain is crucial. A focus on increasing manufacturing redundancy, diversifying where raw materials are sourced and where products are manufactured, and “fattening” the overall supply chain will provide significant improvements, allowing it to withstand expected and unexpected fluctuations in the supply of and demand for pharmaceutical products and protecting the supply chain against future public health emergencies and natural disasters.

A 2019 report from the Food and Drug Administration’s (FDA) Drug Shortages Task Force[5] found there are three major root causes for drug shortages.

Lack of incentives to produce low margin drugs. Manufacturers of older generic drugs, in particular, face intense price competition, uncertain revenue streams, and high investment requirements, all of which limit their ability to invest in resilience.

The market cannot identify and preferentially buy from those with better quality management practices. All manufacturers must meet regulatory requirements for adherence to the FDA’s Current Good Manufacturing Practices (CGMP), which set expectations for company processes to be allowed to do business in the U.S. marketplace. Some companies do more than simply conform to these requirements. They take additional steps intended to ensure a reliable supply of the drugs manufactured at their facilities. Currently, purchasers, including hospitals and health systems, have only limited information to assess the state of quality management of any specific drug manufacturing facility and have little information linking the drug products they buy with the facilities where they were manufactured. The lack of information does not enable the market to reward drug manufacturers for mature quality management, back-up manufacturing capabilities, or risk management plans, nor does it penalize manufacturers that fail to invest in modernization of their equipment and facilities to ensure a reliable supply. Thus, manufacturers are more likely to keep costs down by minimizing investments in manufacturing quality, which eventually leads to quality problems, triggering supply disruptions and shortages. The lack of information does not enable hospitals and health systems to choose to do business with more reliable manufacturers, sending a market-based signal to support a reliable supply chain. Thus, manufacturers may not see the value in making investments in manufacturing quality and reliability. Congress should consider encouraging the FDA to review and improve the CGMP to set an expectation around practices

[5] https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

intended to secure the supply chain for essential medications. It also may wish to consider directing the FDA to provide a report card on different firms' practices to ensure the quality and resilience of their operations in the event of an emergency or disruption in the supply chain.

Logistical and regulatory challenges make it difficult for the market to recover after a disruption. Over the past two decades, the drug supply chain has become longer, more complex, and more fragmented as companies have located more production overseas and increased the use of contract manufacturers. Although typical markets would respond to a shortage by increasing production, the complexity of the supply chain, and logistical and regulatory challenges, can limit the ability of drug manufacturers to do so. When companies wish to increase production, they may have to obtain approvals from multiple different national regulatory bodies and/or find a new source of active pharmaceutical ingredients (APIs). If a new manufacturer wants to enter the U.S. market and start selling a drug in shortage, the manufacturer must first develop and file an application with the FDA and await its approval. Congress may wish to direct the FDA to review its processes considering what it was able to accomplish during the pandemic and find ways to streamline and reduce regulatory impediments to market entry or expansion of production sites.

QUESTION: Given that supply chain issues can trigger manufacturing delays and disruptions that result in shortages, are further incentives necessary to address manufacturing issues?

The COVID-19 pandemic exacerbated many long-standing access and quality issues that threaten the resilience of our nation's pharmaceutical supply chain. It also magnified the dangers inherent in failing to address these gaps and deficiencies. Supply chain issues can adversely impact patient care by delaying treatment, worsening patients' health outcomes or requiring patients to switch to non-optimal treatment regimens. Congress should act to strengthen the ability of the pharmaceutical supply chain to respond when there is an emergency that creates a sudden rise in demand for medications or a significant disturbance in the supply chain that threatens the availability of critical medications. We recommend that Congress provide additional authorities to the FDA to mitigate and prevent drug shortages, such as by developing and disseminating manufacturing quality ratings that could enable hospitals and GPOs to choose to do business with more reliable manufacturers, sending a market-based signal to support a reliable supply chain, and expanding the agency's authority to require manufacturers to notify the agency about unusual spikes in demand of essential medications. Congress should expand the authority of the FDA to require manufacturers doing business in the U.S. to have an emergency response plan that anticipates likely disruptions in the manufacture of critical drugs, describes what steps would be taken to rapidly restore production, and to run drills practicing putting those steps in place. These could be embedded in the CGMP requirements.

Specifically, the AHA urges Congress to enact legislation including:

- **Diversifying manufacturing sites as well as sources of critical raw materials to ensure supply chain sustainability.** Currently, the U.S. relies heavily on both China and India for the API and key starting materials (KSMs) necessary to manufacture pharmaceutical products. Further, many manufacturers of these products utilize manufacturing facilities located in both China and India. The overwhelming reliance on a limited number of countries for these pharmaceutical products necessary to care for patients in the U.S. raises serious concerns and poses significant risks to patients and burden on health care workers should a disruption occur. Congress should encourage redundancy in the supply chain through policy initiatives focused on spurring diverse sites of production, including where possible, onshore or near shore manufacturing of critical API and KSMs.

- **Increasing end-user inventories and incentivizing additional cushion.** The current just-in-time approach to supply chain logistics functions creates a hazard that becomes a reality during a significant supply chain disruption or emergent need to surge care delivery. Steps need to be taken to "feed" the supply chain with the goal of ensuring enough product is available, or capable of being made available, when demand increases. For example, supporting an increase in end-user inventory of critical medications as well as supplies held across the existing manufacturing and distribution infrastructure in the U.S. will help add necessary capacity to deal with interruptions in the availability of a critical drug. These actions may decrease the need for large national and state stockpiles, which can be difficult to manage and maintain and present significant operating costs, product expiration and waste issues.

- **Requiring the FDA to develop ratings** of the quality management processes of drug manufacturers which are predictive of supply chain and manufacturing vulnerabilities and make these quality ratings publicly available.

- **Requiring drug manufacturers to disclose to the FDA the locations where their products are manufactured**, including contract manufacturer locations, as well as the locations from which they source KSMs, API and excipients used in their finished products, in order illuminate the extent of vulnerability for a product and to allow the development of targeted supply strengthening measures.

- **Requiring drug manufacturers to notify the FDA of unusual spikes** in demand of essential drugs to allow the agency to take steps to mitigate or prevent any impacts on availability and prevent potential shortages.

- **Requiring the FDA to identify those essential drugs**, including their KSM, API and excipients and component parts, that should have increased domestic manufacturing capacity to improve the resilience of the U.S. drug and device supply chain and make recommendations to incentivize their production.

QUESTION: What role, if any, has growth in the 340B program played in drug shortage trends?

The 340B drug pricing program is a critical resource for hospitals to stretch scarce resources so that they can provide more comprehensive services to more patients. The savings 340B hospitals achieve through purchasing certain outpatient drugs at a discount allow them to provide a range of programs and services that directly benefit their patients. Examples include services like medication therapy management, diabetes education and counseling, behavioral health services, and the provision of free or discounted drugs.

The program helps 340B hospitals and their patients access drugs that are otherwise unavailable or are placed in limited distribution. As a result, hospitals, through the 340B program, can mitigate drug shortages in two important ways. First, the program allows participating hospitals to leverage their relationships with community and specialty pharmacies (often called contract pharmacies) to access drugs that are in shortage further ensuring patient access. For example, a drug in shortage may be placed in limited distribution and be available through only a select pharmacy. If the 340B hospital has a contractual relationship with that pharmacy, then it may be able to access that drug and provide it to their patients. Second, the program ensures that 340B hospitals can acquire these drugs at a discounted price, mitigating some of the financial impact caused by drug shortages that hospitals are forced to face.

When drugs are in shortage, hospitals must find an alternative drug to provide their patients. This process of finding and procuring an alternative drug can result in significant costs to the hospital. As previously mentioned, a recent study estimated that drug shortages result in $360 million annually in additional labor costs to hospitals.[6] Furthermore, in some cases these alternative drug products are more expensive than the drug in shortage, creating additional unforeseen costs for hospitals. In such instances, participation in the 340B program can allow hospitals to purchase those drugs at a discounted price defraying the high cost of these alternative drug products and mitigating the financial impact of drug shortages.

For these reasons, the 340B program is an important tool for participating hospitals to overcome the operational and financial impact of drug shortages. As a result, it is crucial for Congress to maintain its support of the 340B program so that participating hospitals and their patients can continue to benefit and mitigate against the impact of drug shortages and the ongoing problem of high drug costs.

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[6] https://newsroom.vizientinc.com/en-US/releases/new-vizient-survey-finds-drug-shortages-cost-hospitals-just-under-360m-annually-in-labor-expenses

QUESTION: Would innovative CMS reimbursement models for drugs at risk of shortage status better allow manufacturer of these drugs to meet production and patient demand? What factors should be incorporated into any model seeking to address shortages?

We recognize that there are many factors that contribute to drug shortages including manufacturer consolidation, raw materials shortages, other supply chain disruptions, and increased demand. However, as noted above, this is a complex marketplace in which regulations and other barriers impede what economists might think of as normal market incentives. What is clear is that certain commonly used, off-patent medications currently provide razor thin margins to the generic manufacturers, margins that may not support additional actions to store additional product, sustain surge capacity, or take other steps to ensure the stability of the supply of these drugs. Careful consideration of whether additional supports are needed to shore up the supply chain for these critical generic drugs may be warranted. CMS should continue to explore models that will foster increased competition and improve access to alternatives in areas where there are shortages.

QUESTION: How has consolidation among Group Purchasing Organizations and Prescription Drug Wholesalers led to less redundancies in the drug supply chain? Has this consolidation contributed to drug shortages, especially among generic drugs? Have business practices, such as just-in-time deliveries and limited-source contracts contributed to the drug shortage issue we are seeing?

We are unaware of scenarios where consolidation among Group Purchasing Organizations (GPOs) is leading to increases in drug shortages. However, we are concerned about continued vertical integration efforts employed by commercial payers to acquire pharmacy benefit managers (PBMs) and specialty pharmacies. Insurers' vertical consolidation has intensified in recent years, which has the real potential to undermine competition by reducing patients' choices. The three largest PBMs are all owned by the same parent company that also owns a large health insurance company. Together, these three PBMs control about 80% of the market. If one or more of these PBMs chooses not to include a drug manufacturer's medications on its formulary, it may be so financially devastating to the manufacturer that it is unable to continue to operate.

In the current drug acquisition system, PBMs play the role of an intermediary negotiator between drug manufacturers and payers. However, that negotiation process relies on a series of fees and rebates based on the proposition that these negotiations help to lower the overall cost of drugs. In turn, PBMs collect and retain fees and a percentage of the rebates achieved, which goes toward their bottom line. While PBMs argue that their role lowers the overall cost of drugs, the process actually results in significant incentives to maintain high drug prices and decrease competition.

Specifically, the use of rebates to achieve preferred formulary placement directly inhibits competition. [7] However, the ability of the brand-name drug manufacturers to afford to offer rebates to the PBMs and use direct-to-consumer marketing to enhance requests for their specific product, enables them to achieve preferred formulary placement for their brand-name drugs. Thus, they can induce continued use of high-priced products over lower-priced generics and biosimilars, effectively pushing those generic and biosimilar options out of the market. These actions limit the availability of additional sources of these drugs and contribute to shortages in times of surging demand.

QUESTION: What factors would lead to a generic drug receiving approval but not coming to market?

There are several factors that can lead to FDA approval of a generic drug but unavailability of that generic drug in the market. The following are the most common methods utilized by manufacturers of innovator drugs to keep generics from becoming available:

Evergreening. Some drug manufacturers attempt to minimize or eliminate competition through product "evergreening." A manufacturer attempts to "evergreen" a product when it applies for patent and market exclusivity protections for a "new" product that is essentially the same as the original product, such as extended-release formulations or combination therapies that simply combine two existing drugs into one pill. What generally happens is that, while the older version of the drug is no longer patent-protected and, therefore, generic alternatives may be offered, drug manufacturers promote the newer version as the "latest and greatest." Without important information on the comparative value of the newer drug, many providers and consumers switch to the brand-only "evergreened" product assuming that the newer version is superior. This undercuts the market for the generic and, as a result, may lead the generic manufacturer to decline to make the drug despite having obtained approval. To limit evergreen practices, patents should be denied for those products that are simply modifications of existing products unless the new product offers significant improvements in clinical effectiveness, cost savings, access or safety.

Pay-For-Delay. Some brand drug manufacturers pay generic manufacturers to delay entry into the market. In 2013, the U.S. Supreme Court ruled that such deals could be a violation of antitrust law but declined to declare them presumptively illegal. Subsequently, the Federal Trade Commission (FTC) has reported a significant decrease in pay-for-delay deals but an increase in other "settlements" between brand and generic manufacturers. To successfully eliminate pay-for-delay tactics, federal law would need to be amended to clarify that such practices are presumptively illegal and increase FTC resources to investigate these and other settlements.

[7] https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/generic-competition-and-drug-prices

Manipulating Orphan Drug Designation. Drug manufacturers receive several incentives to develop drugs for rare diseases. These incentives include seven years of market exclusivity and are intended to spur innovation of therapies for which the manufacturer may otherwise not recoup their investment due to low volume. These incentives have contributed to the development of innovative, life-saving drugs where no therapies previously existed. However, in some instances, manufacturers have received orphan drug status for drugs that they subsequently marketed for other, non-rare indications. In these instances, manufacturers are still receiving seven years of market exclusivity for drugs that are broadly used. For example, Humira (adalimumab), which until recently had no generic competition, initially was approved for an orphan drug designation; however, since receiving that designation, Humira also was marketed for a number of other, non-rare indications.

To mitigate these challenges, FDA should collect information on other intended indications for the drug when evaluating eligibility for orphan drug status. FDA also should do a post-market review at regular intervals throughout the market exclusivity period to determine whether the drug should retain its status as an orphan drug. In instances where the manufacturer is promoting the drug for other indications that do not meet the orphan drug status requirements, FDA could levy penalties, such as requiring that the manufacturer pay the government back the value of the tax breaks and waived fees and reducing the market exclusivity period.

Thank you for the opportunity to submit comments on drug shortages. We look forward to continuing to work with you to resolve this issue. Please contact me if you have questions or feel free to have a member of your team contact Aimee Kuhlman, AHA's vice president of advocacy and grassroots, at akuhlman@aha.org.

Sincerely,

/s/

Stacey Hughes
Executive Vice President