AMERICAN SOCIETY OF HEALTH-SYSTEM PHARMACISTS STATEMENT FOR THE RECORD

"Legislative Proposals to Prevent and Respond to Generic Drug Shortages"

U.S. House Committee on Energy and Commerce Subcommittee on Health

September 14, 2023

Dear Chair Guthrie, Ranking Member Eshoo, and Members of the Subcommittee on Health:

Introduction: The American Society of Health-System Pharmacists (ASHP) has monitored national drug shortages for over two decades. Current data indicate severe and persistent shortages of generic drugs, including sterile injectable medications often used in hospitals, clinician offices, and other healthcare settings.[1] Most recently, severe shortages of chemotherapy agents used to treat a wide variety of cancers have been in critically short supply.[2] While the causes of drug shortages are complex, several summits, hearings, and reports have identified root causes of drug shortages.[3] [4] [5] Solutions targeted at these root causes include promoting quality and transparency, ensuring diversity in the manufacturing base, and directly incentivizing new manufacturing.

Overview of ASHP's Role in Monitoring Drug Shortages: ASHP is the largest association of pharmacy professionals in the United States, representing 60,000 pharmacists, student pharmacists, and pharmacy technicians in all patient care settings, including hospitals, ambulatory clinics, and health-

[1] https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics
[2] https://www.ashp.org/-/media/assets/drug-shortages/docs/ASHP-2023-Drug-Shortages-Survey-Report.pdf
[3] https://www.fda.gov/media/131130/download?attachment
[4] https://nap.nationalacademies.org/catalog/26420/building-resilience-into-the-nations-medical-product-supply-chains
[5] https://academic.oup.com/ajhp/article/78/6/511/6009025

system community pharmacies. Our members manage drug shortages in hospitals, ambulatory clinics, and various other healthcare settings.

We collect public reports of drug shortages from clinicians, patients, and caregivers. Through a partnership with the University of Utah Drug Information Service, ASHP maintains a Drug Shortages List that includes active and resolved drug shortages.[6] We post every prescription drug shortage report we receive to our database as soon as it is investigated and confirmed with the manufacturer, usually within 24-72 hours. The ASHP Drug Shortages List includes information down to the individual manufacturer and national drug code (NDC) level and reflects any supply interruption that affects how a pharmacy prepares or dispenses a drug product. The FDA shortage list is developed based on reports from manufacturers and from the public, but a shortage is determined by comparing overall market availability to historical demand of a drug.[7] Because of the detailed tracking down to the NDC level, our list is often considered to be comprehensive and reflective of drug availability on the front lines.

We also provide practitioner-focused resources to help the healthcare community manage shortages. Examples include general guidelines for managing drug shortages and specific recommendations for therapeutic alternatives, comparisons within individual drug classes, and safety information.

[6] https://www.ashp.org/drug-shortages/current-shortages/drug-shortages-list?page=CurrentShortages
[7] https://www.healthaffairs.org/content/forefront/shortages-going-down-not-interpreting-data-fda-and-university-utah-drug-information

Drug Shortages: As of July 2023, ASHP's Drug Shortages List included 309 active, ongoing drug shortages — the highest number in nearly a decade and close to the all-time high of 320 shortages.[8] Most of these medications are low-cost generics. A recent ASHP member survey found that 99% of respondents are experiencing drug shortages, with 57% reporting critical shortages of chemotherapy drugs causing rationing, delaying, or canceling treatment.[9] While the number of newly reported shortages each year has generally decreased since 2011, the number of long-term shortages has been increasing. Some drugs have been on the ASHP Drug Shortages List for over ten years.

The causes of drug shortages can range from raw material availability to natural disasters disrupting infrastructure. Most often, shortages are caused by a manufacturing delay or declines in manufacturing quality.[10] [11] [12] The root causes behind these shortages come from a lack of incentive to produce older, generic drugs with slim profit margins, and from a lack of market recognition of manufacturers with more reliable supply chains or better quality systems.[13]

Several recent, highly impactful shortages can be attributed to insufficient manufacturing quality management. The current shortage of some injectable chemotherapy drugs stemmed from several deficiencies in good manufacturing practices.[14] These problems are not limited to overseas

[8] American Society of Health-System Pharmacists. Drug shortages statistics. https://www.ashp.org/drugshortages/shortage-resources/drug-shortages-statistics (accessed 2023 July 28).
[9] https://www.ashp.org/-/media/assets/drug-shortages/docs/ASHP-2023-Drug-Shortages-Survey-Report.pdf
[10] https://nap.nationalacademies.org/catalog/26420/building-resilience-into-the-nations-medical-product-supply-chains
[11] https://academic.oup.com/ajhp/article/78/6/511/6009025
[12] https://www.fda.gov/media/131130/download?attachment
[13] Ibid
[14] https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/intas-pharmaceuticals-limited-652067-07282023

manufacturing. A 2018 inspection of a manufacturing facility in Kansas also found deficiencies in manufacturing quality and resulted in a severe shortage of injectable opioid medications used to manage pain in hospitals and surgical centers and as sedatives in patients in intensive care units.[15]

Repeated quality issues can apply further economic pressure on manufacturers, resulting in business decisions to shut down facilities or even file for bankruptcy. A domestic manufacturer in Illinois ceased business operations and filed for Chapter 7 bankruptcy in February after years of quality deficiencies.[16] A large generic manufacturer closed a site in California after years of attempting to address quality concerns. That same manufacturer has expressed interest in reducing its generic drug portfolio in favor of manufacturing more profitable medications.[17]

Without a way for purchasers to identify manufacturers with strong quality systems, there is no financial incentive for manufacturers to invest in quality management. The current system of FDA approval and pass/fail inspections does not provide purchasers with any distinction among drug products other than the price, overly emphasizing the cost in purchasing decisions and contributing to a "race to the bottom" in generic drug prices. A healthcare practitioner's expectation of quality is that a drug is available when needed, has expected potency without contamination or impurities, and is not subject to recall. ASHP supports FDA's Quality Management Maturity (QMM) assessment protocol practice areas for quality evaluation: management commitment to quality, business continuity,

[15] https://www.fda.gov/media/120632/download
[16] https://www.fiercepharma.com/manufacturing/akorn-pharma-bankrupt-calls-it-quits-closes-all-us-sites-and-cuts-entire-workforce
[17] https://www.bloomberg.com/news/articles/2023-05-18/teva-plans-cuts-to-generic-drug-production-amid-shortages

advanced pharmaceutical quality system, technical excellence, and employee engagement and empowerment.[18]

Solutions: ASHP commends the work of the FDA Drug Shortage Staff and their efforts to prevent and mitigate the impact of drug shortages. Each year, the shortage team at FDA works behind the scenes to resolve problems and prevent hundreds of drug shortages. However, the FDA cannot force any manufacturer to make any product, no matter how life-saving it may be. FDA also cannot address all of the root causes of these shortages, and additional policies must be adopted to address the underlying causes.

A diverse base of high-quality manufacturers and suppliers is critical to solving the drug shortage crisis and ensuring our nation's healthcare security. This requires solutions in two areas: transparency of quality information and resiliency of production.

Transparency of Important Quality Information: Providing transparency through reporting of critical information is vital to enabling providers to select from reliable sources of generic drugs. The current system assumes that all generics are equal, even while some manufacturers may differ in quality. Enforcement of existing manufacturing location and volume reporting requirements for both active pharmaceutical ingredients (API) and finished dosage form (FDF) facilities will allow providers and

[18] https://www.fda.gov/media/171705/download?attachment

suppliers to evaluate the reliability of manufacturers. However, these reporting provisions should apply to all API suppliers, rather than being limited to certain suppliers.

Inspection reports and warning letters should be made available quickly and without redactions so that purchasers can make decisions based on full transparency of manufacturer quality and supply chain risks.

Manufacturing Diversity and Redundancy: ASHP supports efforts to expand domestic manufacturing, but this will not reduce shortages if it comes at the expense of reliable foreign suppliers. Manufacturing diversity and redundancy is needed to strengthen our supply chain and prevent shortages. Without diversity of production, a disruption either domestically or abroad can result in severe shortages. Domestic manufacturing is not immune from disruptions that lead to shortages. Hurricane Maria devastated the island of Puerto Rico in 2017, resulting in shortages of small-volume parenteral solutions (SVPs) like saline or dextrose.[19] Pfizer's North Carolina plant was recently struck by a tornado, damaging 40,000 pallets of packaging supplies and finished products.[20] [21] Manufacturing diversity and redundancy, including geographic diversity, should also be prioritized to ensure manufacturing resilience and to reduce shortages.

[19] https://www.fda.gov/drugs/drug-safety-and-availability/fda-works-help-relieve-iv-fluid-shortages-wake-hurricane-maria
[20] https://cdn.pfizer.com/pfizercom/Rocky-Mount-Update-31JUL23.pdf
[21] https://www.ashp.org/-/media/assets/advocacy-issues/docs/GRD-Letter-to-EC-on-SVP-Shortages; https://www.reuters.com/business/healthcare-pharmaceuticals/pfizer-says-supply-some-drugs-may-be-disrupted-after-nc-tornado-2023-07-24/

503B Compounding: ASHP supports flexibilities for compounding by 503B outsourcing facilities to mitigate the impact of shortages. We recommend allowing 503B outsourcers to compound bulk medications based on shortages identified in ASHP's drug shortage list, in addition to the list identified by FDA. As previously discussed, ASHP's list is more inclusive and better able to detect frontline disruptions in supply. We also encourage Congress to allow a sufficient period for outsourcing facilities to sell their inventory when a shortage ends.

Shelf-life Extension: Extended shelf-life studies also provide short-term relief during shortages. ASHP supports proposals to encourage manufacturers to identify the maximum, safe shelf life of their products. However, proposals should include shelf-life extensions of generic products, not just branded products that are still under market exclusivity. Nearly 90% of the drugs on the ASHP Drug Shortages List are generic. ASHP also encourages FDA to directly conduct shelf-life extension studies if companies are unwilling to do so.

Provisions that Do Not Solve, or May Worsen, Drug Shortages: Proposals that seek to increase generic manufacturer profitability by cutting their obligations under Medicaid and the 340B Drug Pricing Program will not improve drug shortages and may inadvertently contribute to shortages. These proposals are problematic because they do not require that manufacturers use savings to increase production or invest in quality. This would benefit manufacturer shareholders without addressing the quality issues at the root causes of drug shortages. In fact, these proposals may actually exacerbate

shortages by incentivizing manufacturers to delay recovery from a shortage in order to avoid their obligations under these programs.

ASHP is not aware of any link between drugs frequently in short supply and discount or rebate programs. In fact, the most significant savings from the 340B program come from high-priced, brand-name drugs that are very rarely in shortage. The drugs on our shortage list are mostly generic drugs, which provide relatively small 340B discounts. Inpatient medication use is excluded from the 340B program, and many of the sterile generic injectable medications responsible for critically impactful shortages are used in the inpatient setting. ASHP does not believe any changes to the 340B program will reduce drug shortages and would divert patient care resources from safety-net providers.

Lastly, many of the proposals around reimbursement fail to recognize that the drugs in shortage are often older generic drugs that are not separately reimbursed in many healthcare settings. Payment for these medications is bundled with other patient care services. This increases the pressure to purchase medications based on the lowest price, rather than the reliability of their manufacturing and supply chain.

ASHP's Recommendations to Reduce Drug Shortages: To effectively address drug shortages through quality, transparency, and direct economic incentives, we recommend:

- **Enforce Existing Drug Shortage Requirements:** Congress should amend section 510(j) of the Food Drug and Cosmetic Act (FDCA) to include meaningful penalties for manufacturers that fail to

develop risk management plans or report manufacturing and supply chain data as required by this section.

- **Improve Transparency into Manufacturer Quality:** Congress should require FDA to finalize, and make public, metrics of quality management maturity (QMM) so that purchasers can buy from manufacturers less likely to experience a shortage. In the absence of publicly reported QMM metrics, FDA should make unredacted manufacturing inspection reports publicly available so that purchasers have a better understanding of supplier manufacturing challenges and which products are made at facilities with records of manufacturing quality and compliance problems.
- **Encourage New Manufacturers and Manufacturing Sites:** Congress should give FDA authority to waive generic drug user fees for drugs described in 506C(g) of the FDCA, for which FDA may prioritize and expedite review of an abbreviated new pharmaceutical drug application (ANDA) or related supplement to mitigate a shortage. The fee waiver would apply only to manufacturers that commit to promptly market their generic pharmaceutical drug if it is approved.
- **Encourage Long-Term, Guaranteed-Volume Contracts:** Congress should authorize the Centers for Medicare & Medicaid Services to provide an add-on payment to providers for critical generic pharmaceutical drugs determined by HHS to be at risk of experiencing a shortage, if those providers certify that they have entered an agreement to acquire at least 50% of their historical purchase volume for those products via long-term contracts. To ensure investment in supply chain stability and quality, the agreement must include a requirement that manufacturers maintain a six-month buffer supply of finished product as well as meaningful penalties for failure to supply contracted products, including when manufacturing disruptions result from regulatory violations or

supplier disruptions. To be eligible for pass-through payments providers must demonstrate that their suppliers participate in FDA's QMM program and voluntarily make their QMM metrics publicly available.[22]

- **Diversify the Manufacturing Base:** Congress should require the federal government to use its purchasing power to encourage greater diversity and redundancy in the supply chain by spreading purchase volume from federal agencies across at least three different manufacturers with approved ANDAs for any critical generic pharmaceutical drug determined by the Department of Health and Human Services to be at risk of experiencing a shortage. Federal purchasers should require that manufacturers do not rely on the same contract manufacturers, as this would not actually diversify the manufacturing base. Federal contracts should require manufacturers to maintain a six-month buffer supply of finished product, and include meaningful penalties for the failure to supply, including when manufacturing disruptions result from a regulatory violation or supplier disruption. As noted earlier, to ensure quality and transparency, federal agencies should give preference to manufacturers that participate in FDA's QMM program and voluntarily make their QMM metrics publicly available.[23]

ASHP greatly appreciates the House Energy and Commerce Committee's leadership in working to ensure Americans have access to safe and effective drugs without hindrance or delay. Such efforts are

[22] Recommendations from ASHP and other healthcare providers in 2021 called for FDA to make these metrics public. https://news.ashp.org/news/ashp-news/2021/12/16/healthcare-groups-release-drug-supply-chain-recommendations
[23] Recommendations from ASHP and other healthcare providers in 2021 called for incentivizing the creation of private sector reserves of essential medicines, medical devices, and supplies not adequately provided by the Strategic National Stockpile. (https://news.ashp.org/news/ashp-news/2021/12/16/healthcare-groups-release-drug-supply-chain-recommendations)

critical to ensuring patients have continuity of care. We look forward to working with the Committee to provide greater transparency into the drug supply chain and ensure patients and providers have ready and uninterrupted access to safe and effective drugs required to ensure optimal patient care.

Sincerely,

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