July 7, 2023

The Honorable Cathy McMorris Rodgers
Chair
House Energy and Commerce Committee
Washington, D.C. 20510

The Honorable Mike Crapo
Ranking Member
Senate Finance Committee
Washington, D.C. 20510

Dear Chair McMorris Rodgers and Ranking Member Crapo:

The Healthcare Leadership Council (HLC) thanks you for the opportunity to submit comments on the drivers of the current drug shortage and ideas on potential solutions.

HLC is a coalition of chief executives from all disciplines within American healthcare. It is the exclusive forum for the nation's healthcare leaders to jointly develop policies, plans, and programs to achieve their vision of a 21st century healthcare system that makes affordable high-quality care accessible to all Americans. Members of HLC – hospitals, academic health centers, health plans, pharmaceutical companies, medical device manufacturers, laboratories, biotech firms, health product distributors, post-acute care providers, homecare providers, group purchasing organizations, and information technology companies – advocate for measures to increase the quality and efficiency of healthcare through a patient-centered approach.

As you explore mechanisms to increase drug supply resiliency, please consider the following background and policy solutions:

What is the scope and impact of recent and ongoing drug shortages?

The U.S. is facing a nearly ten-year peak in drug shortages, with oncology patients particularly severely impacted. As of April 2023, 301 drugs were in shortage, the highest number since 2014.[1] There are concerning shortages across clinical care, including oncology treatments, local anesthetics and basic hospital drugs, asthma medications, ophthalmic medication, attention deficit hyperactivity disorder (ADHD) treatments, and others.

Generic drugs comprise the majority of drug shortages, with generic sterile injectables (GSIs) – including older platinum oncology drugs in current shortage – accounting for the lion's share of generic shortages. The FDA reports that generics comprise 70 percent of drug shortages, and 62 percent of the drugs on the FDA shortage list in January 2023 were GSIs.[2] While GSIs are

[1] Drug Shortages Statistics, American Society of Health System Pharmacists (ASHP), (accessed July 5, 2023), https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics.
[2] Drug Shortages: Root Causes and Potential Solutions, U.S. Food and Drug Administration, (2019), www.fda.gov/media/131130/download and Federal Policies to Address Persistent Generic Drug Shortages, Brookings' Hamilton Project, (June 2023) www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.

used in a variety of treatments, oncology patients are currently experiencing the most severe and detrimental consequences in the midst of an ongoing shortage of chemotherapy drugs.[3]

As the shortages continue, providers are making difficult decisions, including providing alternative treatments and rationing, with potential adverse outcomes for patients. Hospitals regularly experience drug shortages. A 2019 Vizient survey found that all hospitals experienced shortages in 2018, with two-thirds experiencing 20 or more shortages at a given time.[4] Hospitals routinely work with prescribers to offer therapeutically equivalent alternatives; however, these alternatives may be less familiar to the provider or have unfamiliar side effects for the patient. In more extreme circumstances, when faced with a shortage of oncology medications in particular, hospitals engage their ethics departments to make difficult allocation decisions. Evidence of efficacy and tolerability are considered in tandem with ethical principles including beneficence, non-maleficence, transparency, fairness, distributive justice, responsible stewardship, and others. Allocation decisions prioritize patients with potential for cure over those receiving the drug for palliation. These devastating decisions may hasten the end of life – potentially by many months — or, in some cases, years for palliative patients who may achieve unexpected benefits with the drug.

The likely substantial impact this shortage of chemotherapy drugs is having on patients is yet to be measured. For example, a 2009 shortage of mechlorethamine which led providers to use cyclophosphamide as an alternative in treating Hodgkin's lymphoma in children, was associated with a decrease of the two-year survival rate from 88 percent to 75 percent.[5]

While direct patient treatment is the most critical consequence of drug shortages, research and development (R&D) and healthcare costs are also impacted. Clinical trials take years to meticulously develop. The results of a clinical trial may be affected if researchers must substitute another drug or otherwise alter the design of the clinical trial at the onset or during the course of the study period in response to a drug shortage. Shortages are costly both for manufacturers working to increase supply and for hospitals that must purchase alternative medications and otherwise compensate for drugs in scarcity. Shortages increase pharmaceutical spending for hospitals by 6 percent on average.

How do innovative drug manufacturers support a resilient global supply chain?

Globally resilient supply chains are critical to ensure continuous supply of innovative medicines to meet patient needs. Innovative biopharmaceutical companies have extensive measures, including risk management plans (RMPs) and business continuity plans (BCPs), in place to help prevent and mitigate potential drug shortages. On-site RMPs evaluate risks day-to-day across the entire end-to-end supply chain. RMPs are detailed, time consuming, and resource intensive. Robust BCPs that were in place before the COVID-19 pandemic were critical in adapting to disruptions in supply chains and mitigating shortages. Manufacturers maintained critical inventory at distribution centers, worked with external suppliers to support preparedness plans, and maintained a geographically dispersed supply chain with the ability to adapt as countries

[3] How the Shortage of a $15 Cancer Drug Is Upending Treatment, The New York Times, (June 26, 2023) https://www.nytimes.com/2023/06/26/health/cancer-drugs-shortage.html.
[4] New Study Shows Drug Shortages Have a Large Impact on Hospitals, Pharmacy Times, (July 2, 2019), https://www.pharmacytimes.com/view/new-study-shows-drug-shortages-have-a-large-impact-on-hospitals.
[5] The Impact of Drug Shortages on Children with Cancer — The Example of Mechlorethamine, New England Journal of Medicine, (December 27, 2012), https://www.nejm.org/doi/10.1056/NEJMp1212468.

implemented restrictions to contain the spread of the virus. Innovative manufacturers also have internal processes to test and maintain BCPs. Throughout the year, risk assessments, scans, and surveys are performed by the business and/or risk management functions to identify internal and external events.

What is driving current drug shortages?

The current drug shortages are most acute in the GSI market, which is experiencing a confluence of drivers of the persistent shortage. Chief among them is the low profit margins in GSI markets, which limits supply chain resilience. Moreover, production of GSIs requires robust quality control measures. Lack of supply chain resilience results in manufacturers pausing production for long periods of time or exiting the market. Other factors contributing to shortages include workforce shortages and lingering supply chain disruptions from the COVID-19 pandemic, among others.

Because GSIs are injected directly into the body and thus not aided by the digestive system that destroys microorganisms, GSI manufacturing facilities must follow meticulous protocols to ensure the products are sterile. A contamination can shut down a facility for a long period of time. This was the case in December when Intas Pharmaceuticals shut down a production facility of certain oncology platinum drugs in Ahmedabad, India, following an FDA inspection that revealed serious quality issues.[6]

In contrast to extensive RMPs and BCPs that innovative drug manufacturers have in place, low profit margins in generic markets leave little room to react to and manage shocks to the supply chain, such as quality issues or increased demand. Because adhering to quality control in manufacturing sites is such a challenge for GSI products, new manufacturers tend not to enter the market. When a facility is shut down, there are too few manufacturers in the market to meet the increased demand.

Current trends of manufacturers exiting the generics market due to low profits leave our supply chain vulnerable to even worse shortages in the future. Moreover, drug price setting in the Inflation Reduction Act is likely to worsen drug shortages as the law is implemented. As former FDA Commissioner Scott Gottlieb, MD, warned, government price setting contributes to underinvestment in safe and sustainable generic supplies.[7] Price setting provisions will also result in fewer additional brand medicines in a therapeutic class, further exacerbating vulnerabilities in the supply chain.

Recommendations to address drug shortages

As Congress explores mechanisms to address drug shortages, HLC recommends the following potential solutions:

- **Target any increase in transparency and reporting.** Drug manufacturers already work closely with the FDA to share information in order to avoid and mitigate drug shortages. FDA's Center for Drug Evaluation and Research (CDER) credits collaboration with

[6] How the Shortage of a $15 Cancer Drug Is Upending Treatment, The New York Times, (June 26, 2023) https://www.nytimes.com/2023/06/26/health/cancer-drugs-shortage.html.
[7] America's Drug Shortages Reach New Heights, (March 22, 2023), Axios, https://www.axios.com/2023/05/22/americas-drug-shortages-reach-new-heights.

manufacturers for preventing 222 drug shortages during calendar year 2022.[8] A certain level of targeted transparency that protects proprietary information is necessary between the FDA and manufacturers to ensure a resilient supply chain. We urge Congress to avoid any measures that add unnecessary burdens, duplicate existing collaborations, or put innovators' proprietary information at risk. Blanket reporting requirements risk inundating the FDA with data without adding value. Any additional reporting requirements should be developed incorporating stakeholder feedback, be limited in scope, and be targeted at identified problems in the supply chain.

- **Review and enhance recent FDA supply chain resilience efforts.** Before creating new reporting requirements, we urge Congress to review and build upon recent efforts undertaken by the FDA to support a resilient supply chain. Recent measures include expedited reviews of new drug and biologics applications, expedited requests to facilitate expanded manufacturing capacity, and exercising regulatory flexibility and discretion to increase supplies of critically needed medications.[9] Congress should build upon these efforts by allowing the FDA to fast-track abbreviated new drug applications (ANDAs) and expedite manufacturing inspections and approvals for drugs facing a critical shortage.

- **Update the FDA Essential Medicines list.** HLC supports more transparency from the FDA regarding the process and data sources used to develop the FDA's Essential Medicines list. We also urge the FDA to work with stakeholders, including group purchasing organizations (GPOs) and distributors, to update the Essential Medicines list and make use of other lists in shortage prevention efforts.

- **Fund incentives for generic manufacturers to meet quality management maturity (QMM).** We urge Congress to provide funding for the FDA to develop incentives for generic/biosimilar drug manufacturers to achieve QMM. These incentives should be developed with industry stakeholder input. Congress should also allow the FDA to share generic manufacturers' QMM-related information with various entities in the supply chain, including GPOs, distributors, and hospitals, to help inform purchasing and contracting decisions.

- **Support a resilient global supply chain.** Global, diversified supply chains are important to enable a consistent response to external stressors, including natural disasters, health emergencies, or supplier disruptions. HLC supports the following three policy approaches to streamline global supply chain collaboration: (1) the free flow of goods to support robust BCP processes, strong partnerships, and the ability to actively monitor end-to-end supply chain using digital tools; (2) improved country-to-country global cooperation within supply chains to enhance resiliency and flexibility and reduce over-reliance on any one market for any aspect of manufacturing or supply; and (3) accelerated adoption of Fourth Industrial Revolution technologies to digitalize supply chains, allowing for better information sharing and enabling better signals of disruption.

- **Create onshoring and manufacturing incentives.** Significant investment is needed to bring more pharmaceutical manufacturing back to the U.S. High costs of labor and environmental regulations as well as tax incentives abroad have contributed to an

[8] Drug Shortages CY 2022, U.S. Food and Drug Administration, (June 2023). www.fda.gov/media/169302/download?utm_medium=email&utm_source=govdelivery.
[9] Ibid.

offshoring trend in production in recent decades. As moving significant pharmaceutical, biopharmaceutical, and active pharmaceutical ingredient (API) manufacturing to the U.S. will require companies to completely transform existing operations and make massive financial, operational, and personnel investments, the stability of any onshoring incentive is paramount to its success. HLC supports the following three permanent tax incentives to shift manufacturing back to the U.S.:

1. **Investment incentive.** We support a 60 percent tax credit for the construction or expansion of a U.S. facility for the production or manufacture of pharmaceuticals, biopharmaceuticals, API, or medical equipment or supplies.
2. **U.S. manufacturing incentive.** Income from the U.S. production or manufacture of pharmaceuticals and biopharmaceuticals, API, or medical equipment or supplies should receive a deduction equal to 50 percent of such U.S. production or manufacturing income.
3. **Locate IP with associated U.S. manufacturing**. As companies develop and locate manufacturing in the U.S., they should be permitted to locate or relocate the associated intellectual property (IP) in the U.S. at no tax cost. Going forward, profits generated by the IP would be taxed in the U.S.

- **Offer low-interest loans for manufacturing infrastructure upgrades.** A core recommendation of a June 2023 Brookings report proposing federal solutions to the GSI shortage aims to address low profitability of GSI manufacturing. The report proposes HHS invest $2 billion in targeted low-interest loans for facility upgrades or expansions. Part of the loans would be eligible for forgiveness if manufacturers meet certain quality measures.[10]

- **Invest in a robust government stockpile**. HLC took a leadership role on disaster readiness even before the pandemic. HLC worked with the Duke-Margolis Health Policy Center and a broad array of organizations to develop recommendations focused on three key areas: improving data and evidence generation, strengthening innovation and supply chain readiness, and innovating care delivery approaches. This initial report was released in February 2021. While many of these recommendations have been implemented through legislative or administrative action, as Congress considers reauthorization of the Pandemic and All Hazards Preparedness Act (PAHPA), we once again partnered with the Duke-Margolis Center for Health Policy and other organizations to release updated recommendations in May 2023 specific to PAHPA reauthorization. One key recommendation we make is to substantially and consistently fund the Strategic National Stockpile (SNS). It is also critical to engage manufacturers in longer-term committed contracts with frequent, scheduled ordering rather than occasional bulk purchases. Guaranteeing a reliable market of a certain level for goods that may have more episodic demand in commercial or other markets ensures ready availability of drugs and medical goods that are certainly needed sometimes, though otherwise too seldom to justify steady production.

- **Create a targeted buffer inventory.** The Brookings report also recommends HHS purchase GSI products and hold a buffer inventory. Unlike an emergency stockpile, the

[10] Federal Policies to Address Persistent Generic Drug Shortages, Brookings' Hamilton Project, (June 2023) www.brookings.edu/wp-content/uploads/2023/06/20230621_ES_THP_GSI_Report_Final.pdf.

buffer inventory would be held by a wholesaler and immediately disbursed when production is disrupted. Criteria to hold a drug in the buffer inventory would include lack of substitutes, unavailability would lead to immediate and significant adverse health outcomes, and vulnerable supply chains. Oncology GSIs meet each criterion.[11] As a first step, we support an essential medicines stockpile pilot program which would cross reference with FDA's Essential Medicines list. We recommend transparency and close coordination with the private sector.

- **Provide reimbursement incentives.** HLC suggests that Congress and CMS consider payment adjustments (i.e., N95-like policy and/or add-on payments) for generic essential medications frequently in shortage, such as GSIs, where the manufacturer agrees to certain supply chain mitigation and resiliency requirements.

Thank you for your efforts to increase the drug supply chain resiliency. HLC looks forward to working with you on our shared priorities. If you have any questions, please do not hesitate to contact Debbie Witchey at (202) 449-3435 or dwitchey@hlc.org.

Sincerely,

Mary R. Grealy
President

[11] Ibid.