

VIA ELECTRONIC SUBMISSION

April 22, 2024

Office of the United States Trade Representative
600 17th Street NW
Washington, DC 20001

Re: Request for Comments on Promoting Supply Chain Resilience (USTR-2024-0002)

Dear Sir/Madam:

The United States Pharmacopeia (USP) appreciates the opportunity to provide comments on the Office of the United States Trade Representative's (USTR) Request for Comments on Promoting Supply Chain Resilience ("Request"). USP is an independent, scientific, global non-profit organization founded in 1820 and dedicated to building trust in medicines through rigorous science and public quality standards. We are governed by more than 500 organizations, including scientific, healthcare practitioner, consumer, and industry communities, as well as dozens of government agencies, who together comprise the USP Convention.¹ A core pillar of USP's mission is to help strengthen the global supply chain so that medicines are available when needed and meet quality standards as expected and required.

Safe and effective medicines, consistently manufactured according to established quality standards, are essential to preventing disease, treating illness, and saving lives. To that end, pharmacopeias develop public quality standards that establish benchmarks to ensure that specific medical products have the quality attributes required by regulatory agencies. Manufacturers and regulatory agencies rely on clearly defined quality expectations for medicines and their ingredients, as well as methods to validate that they meet these expectations. USP's public quality standards help guide quality assurance across multiple aspects of a medicine's lifecycle, including development, manufacturing, storage, distribution, preparation, administration, and use.

A resilient supply chain can withstand acute disruptions so that safe, effective, and quality medicines can be supplied to patients, in adequate quantities, when they are needed. Manufacturing quality and product quality are central determinants of reliability, and fundamental to the development of solutions that support a resilient supply chain. These considerations also demand a comprehensive assessment of the underlying market factors that can influence investments in infrastructure.

¹ USP's governing bodies, in addition to the Council of the Convention, include its Board of Trustees and Council of Experts.

Many drugs that are at risk of supply chain disruptions are off-patent medicines that have lower margins compared to products on patent.² Lower-margin and lower-price drug products may provide limited incentives for manufacturers to continually invest in quality control systems and attract redundancy and resilience into supply chains. Therefore, a fundamental shift in the market is necessary for lower-priced drugs to guarantee more certainty and predictability of both demand and supply and to increasingly value a drug's supply chain resiliency and reliability.

Please see our comments below to specific questions from the USTR's Request, with a specific focus on the pharmaceutical and medical goods supply chain.

Measurement and policy tools to support supply chain resilience.

Question 2: What existing or new tools could help ensure that growth in domestic manufacturing and services does not undergo the same offshoring that we have experienced over the past few decades?

Question 11: How can supply chain be measured, including the costs of insufficient resilience, and the impacts of trade and investment policy on resilience? What are appropriate quantitative or qualitative data to consider?

While the globalization of the medicines supply chain has generally facilitated access to medicines at a lower cost, geographical concentration in portions of the supply chain has increased the risk of unreliable supply following sudden or unexpected shocks in specific locations, including those caused by natural disasters, trade wars, domestic or geopolitical strife, or global public health emergencies. When such disruptions occur, the quality, safety, and adequate supply of medicines, particularly those used for critical treatments, become a national security issue, and can have unintended and dire consequences for public health infrastructure and the health of the American public. USP's Medicine Supply Map³ data show that geographic concentration anywhere – including within the United States – increases the risk of drug shortages. Policymakers are increasingly concerned about a fragmented global trade network that could further accelerate drug shortages. To ameliorate these risks, stakeholders must diversify where products are manufactured.

Currently, no single government agency or industry entity has a comprehensive view of the medicine supply chain. Some trade data, such as import-export declarations data, may be useful to help to understand the upstream supply chain for certain chemicals and pharmaceutical products. While current trade data may not show a complete picture of

² U.S. Food and Drug Administration. Drug Shortages: Root Causes and Potential Solutions. (2019). Accessed at <https://www.fda.gov/media/131130/download?attachment>

³ More than 40 datasets from USP, U.S. Food and Drug Administration (FDA), the Centers for Medicare & Medicaid Services, European Medicines Agency, World Health Organization, and private sector sources are utilized by the Medicine Supply Map platform. These data are enriched with information about risk drivers such as price and ingredients and cover 92 percent of FDA-approved generic prescription drugs. The Medicine Supply Map includes over 250 million aggregated datapoints to evaluate indicators of drug shortage risk, including geographic concentration, manufacturing complexity, price, and quality. The model is also informed by insights on the use of USP quality standards in over 80 percent of FDA-registered finished dose and API manufacturing facilities.

the manufacturing and supply chain, it can provide insights into the chemicals supply chain, such as supplier country, buyer country, quantity, or volume. These insights support gaining visibility into the complexities of the global commodity and fine chemicals trade and transactions. However, import-export trade data and/or reporting is not globally required and/or harmonized, and countries offer different levels of information.

A critical need exists to invest in early warning capabilities that signal threats to and vulnerabilities within the pharmaceutical supply chain. U.S. Government entities and private sector stakeholders responsible for getting medical products to patients—including manufacturers, wholesalers, and hospitals—need actionable insights that can assist in anticipating and predicting supply chain vulnerabilities and their causes before they result in a drug shortage. Early warning capabilities would help the U.S. Government increase the return on its investments in strengthening the nation’s medicine supply by targeting investments and resources to the vulnerabilities of specific medicines.

In exploring policy reforms to address drug shortages, policymakers are also discussing mechanisms to measure resilience, providing an opportunity to reward manufacturers for quality, resilience, and reliability. Conversations and research to incentivize a resilient and reliable medicines supply chain include two distinct elements: payment reforms and data to differentiate suppliers based on reliability and resilience, such as the development of a data set or ‘score.’ A recently released white paper from the U.S. Department of Health and Human Services (HHS) describes a policy concept, a Manufacturer Resiliency Assessment Program (MRAP), which could measure the resiliency of manufacturers,⁴ and another concept, a Drug Supply Chain Reliability (DSCR) Program, has been proposed as a possible solution to better understand and evaluate resilience and reliability at the product manufacturer level and bring additional transparency to the supplier base.⁵

Such a measurement tool could underscore the value of drug supply chain resilience and reliability and incorporate drug shortage prevention factors that fall outside of quality management maturity programs, such a domestic and nearshore manufacturing capabilities. It could also function as a tool for decision making tied to financial incentives, such as tax incentives, price supports, federal grants and loans, and other incentives.

Question 4: What are examples of trade and investment policy tools that potentially could be deployed in the following sectors (pharmaceutical and

⁴ U.S. Department of Health and Human Services. Policy Considerations to Prevent Drug Shortages and Mitigate Supply Chain Vulnerabilities in the United States. (2024) Accessed at <https://aspe.hhs.gov/sites/default/files/documents/3a9df8acf50e7fda2e443f025d51d038/HHS-White-Paper-Preventing-Shortages-Supply-Chain-Vulnerabilities.pdf>

⁵ Duke Margolis Center for Health Policy. Addressing Drug Shortages Through Quality Management Maturity and Supply Chain Reliability Programs. 2023; <https://healthpolicy.duke.edu/sites/default/files/2023-12/Addressing%20Drug%20Shortages%20Through%20Quality%20Management.pdf>.



medical goods) to enhance supply chain? In these sectors, what features of the current policy landscape are working well, or less well, to advance resilience?

Over the past decades, global medicines supply chains have moved from being vertically integrated—where a drug manufacturer owns or controls most aspects of production (including suppliers)—to horizontally distributed, where many functions in the supply chain, such as the production of both active pharmaceutical ingredients (APIs) and inactive ingredients, are often outsourced to multiple firms around the world. Geographic diversification of the supply chain is one of many potential approaches to rebalance supply chains and reduce risk, and there are ongoing conversations among stakeholders about shoring approaches such as friendshoring/allyshoring, nearshoring, or onshoring as ways to inject resilience and reliability into the medicines supply chain. These approaches may help to unwind consolidation in heavily geographically concentrated areas, drive redistribution of capability, create more flexibility for product manufacturing, and decrease over exposure in any one region.⁶ Additionally, some industry stakeholders have expressed support for proposals to encourage onshoring production, such as grants from HHS to support construction, alteration, or renovation of facilities for U.S.-based manufacture of medicines included on the list of essential medicines.⁷

Furthermore, there is a need to explore system reforms to improve sustainability of the generics marketplace, including incentives or other measures to promote manufacturing diversification, incentives for manufacturing and quality upgrades, and investments promoting the use of new technologies such as advanced manufacturing technologies (AMT) for vulnerable medicines with a higher risk of shortage. Quality concerns are one of four risk categories identified by the USP Medicine Supply Map as correlated with drug shortages, which also include: geographic concentration of manufacturing sites, low drug prices, and higher manufacturing complexity. These four risk factors are often interrelated, and, in combination, can exacerbate economic challenges for manufacturers of low-margin drug products and impact business decisions about whether to continue manufacturing some drug products. Manufacturers of older, lower-margin drugs often have little economic incentive to make needed quality investments due to their slim profit margins. As detailed in the policy position paper *Identifying and addressing vulnerabilities in the upstream medicines supply chain to build resilience and reduce drug shortages*, USP supports economic or other incentive measures that will encourage multiple suppliers for key drugs, geographic diversification of manufacturing facilities, and broader component supply, as well as economic incentives to encourage increased domestic manufacturing of APIs and finished drug products in the United States.⁸

⁶ U.S. Pharmacopeia. Building Geographic Diversity in the Medicines Supply Chain. https://www.usp.org/sites/default/files/usp/document/public-policy/USPWP_GeoDiversification_2023.pdf

⁷ Association for Accessible Medicines. (2021 October). A Blueprint for Enhancing the Security of the U.S. Pharmaceutical Supply Chain. AAM-Blueprint-US-PharmaSupply-Chain.pdf (accessiblemeds.org)

⁸ U.S. Pharmacopeia. Identifying and addressing vulnerabilities in the upstream medicines supply chain to build resilience and reduce drug shortages. (2023) Accessed at <https://www.usp.org/supply-chain/build-resilience-and-reduce-drug-shortages>

Policies that aid in the development and adoption of Advanced Manufacturing Technologies (AMTs) are other potential solutions to bolster supply chain resilience. AMTs such as pharmaceutical continuous manufacturing, distributed manufacturing, and additive manufacturing have the potential to improve manufacturing efficiency, reduce production costs, reduce environmental footprints, help to return some manufacturing to the United States, and allow economies new to pharmaceutical manufacturing to establish manufacturing capacity. The Administration has recognized the need to catalyze investment in novel technologies critical to economic growth and through the U.S. Economic Development Administration, recently designated 31 Regional Innovation and Technology Tech Hubs, including the Advanced Pharmaceutical Manufacturing Consortium based in Richmond, VA. This hub aims to accelerate the growth, innovation, and sustainability of U.S.-based advanced pharmaceutical manufacturing.

Capital allocation and resource investments

Question 9: What factors are driving supply chain and sourcing decisions, and how does trade and investment policy impact them? How do companies factor geopolitical risk into their global and domestic manufacturing and sourcing decisions? How do companies take into account traceability and transparency considerations in supply chain and sourcing decisions?

Question 10: To what extent is supply chain resilience shaping capital allocation decisions among industry and investors?

Financial incentives for manufacturers to accelerate geographic diversification opportunities are inadequate for many generic drug producers. For common medications, especially generic drugs or those drugs that are not produced in large quantities, economic margins are small and returns on any investments are limited and not guaranteed.⁹ Additionally, the “switching costs” and economic resources needed to establish new facilities are often too high for the low return on investment.

In addition to cost, many considerations contribute to a company’s assessment of where to move operations and production. While not an exhaustive list, these additional considerations include:

- *Strategic locations:* Additional partners in regions closer to the final end-users and near target markets allow for more integration from diversification of manufacturing and distribution partners, easier flow of goods, and potential and current multinational trade agreements.
- *Operational considerations:* Identifying who will provide infrastructure investment is a key consideration for geographic diversification. Using traditional pharmaceutical manufacturing technology, many domestic companies are unable to offset labor and other cost advantages that foreign nations can provide. However, infrastructure deficiencies and uncertainty in the electricity and water sectors in some existing manufacturing locations may contribute to supply chain

⁹ Syed, Sanobar. (2023, June 28). 4 Key Considerations For Onshoring Or Nearshoring Of Drug Production. Outsourcedpharma. <https://www.outsourcedpharma.com/doc/key-considerations-for-onshoring-or-nearshoring-of-drug-production-0001>

instability. Investment in new infrastructure, including AMTs, could enable domestic pharmaceutical manufacturing to regain its competitiveness and potentially ensure a stable supply of medicines.

- *Economic Opportunities:* Several economic considerations exist when exploring shoring initiatives closer to end-user markets, such as competitive labor costs, potential tax exemptions, faster time to market, reductions in logistics costs, and more effective planning cycles to free up working capital tied to suppliers and inventory in transit.¹⁰
- *Regulatory Risks:* Challenges in filing for market authorizations, import permits, and manufacturing certifications – including administrative delays – can deter plans to move operations.

Question 6: Across sectors, how does access to capital equipment, manufacturing equipment, and technology support supply chain resilience for U.S. producers, and is there a role for trade and investment policy?

Significant up-front capital investment is often required for AMTs such as pharmaceutical continuous manufacturing, which becomes an even greater challenge for low margin, low priced products. Furthermore, smaller manufacturing companies may not have the technical or resource capabilities to test the feasibility of novel manufacturing approaches. U.S. policymakers and other government leaders could help to overcome barriers to AMT adoption, in part, through a combination of public financing and incentives for private investments, particularly for those medicines identified as vulnerable or essential. Near- and long-term economic incentives and public investments are needed to provide manufacturers with the necessary support to invest in AMT, and clarity with respect to regulatory expectations in the United States and globally for products manufactured using AMTs are needed to further promote the viability of these technologies. Without new incentives and a more predictable regulatory environment, the potential of AMTs is likely to remain underutilized.¹¹ USP is currently engaging with a broad group of stakeholders, including academic research centers and manufacturers, to identify and articulate appropriate standards and practices that will help make advanced manufacturing more accessible and achievable for industry uptake.

USP appreciates the opportunity to comment on the Request and welcomes the opportunity to further engage with the USTR on policy approaches and strategies to support a resilient supply chain for pharmaceuticals and medical goods. For more

¹⁰ Howells, Richard and Overby, Stephanie. (2023). Five Realities About Nearshoring and Reshoring Strategies. SAP. <https://www.sap.com/insights/viewpoints/five-realities-about-nearshoring-andreshoring-strategies.html>

¹¹ U.S. Pharmacopeia. Recognizing Challenges and Opportunities to Support Adoption of Advanced Manufacturing Technologies for Medical Products. (January 2024) https://www.usp.org/sites/default/files/usp/document/public-policy/USP%20AMT_PositionPaper_2024.pdf?utm_source=facebook&utm_medium=&utm_term=&utm_content=&utm_campaign=



information, or if there are questions about these comments, please contact Amy B. Cadwallader, Ph.D., Director, Regulatory and Public Policy Development and USP Quality Institute, at (301) 692-3567 or Amy.Cadwallader@usp.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Anthony Lakavage". The signature is written in a cursive style with a prominent initial "A".

Anthony Lakavage, J.D.
Senior Vice President, Global External Affairs
Secretary, USP Convention and Board of Trustees

