VIA ELECTRONIC SUBMISSION

May 6, 2025

U.S. Department of Commerce
Bureau of Industry and Security
Office of Strategic Industries and Economic Security
1401 Constitution Avenue NW
Washington, DC 20230

Re: Docket No. 250414-0065; XRIN 0694-XC120; Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients

Dear Sir/Madam,

On behalf of the United States Pharmacopeia (USP), I appreciate the opportunity to offer our comments to the Department of Commerce's (Department) Bureau of Industry and Security, Office of Strategic Industries and Economic Security on the *Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients* (Notice). USP is a private, scientific, non-profit organization founded in 1820 with a mission to improve global health through public quality standards and related programs that help ensure the quality, safety, and benefit of medicines and foods. We work to strengthen the supply chain so that the medicines people rely on for health are available when needed and work as intended.

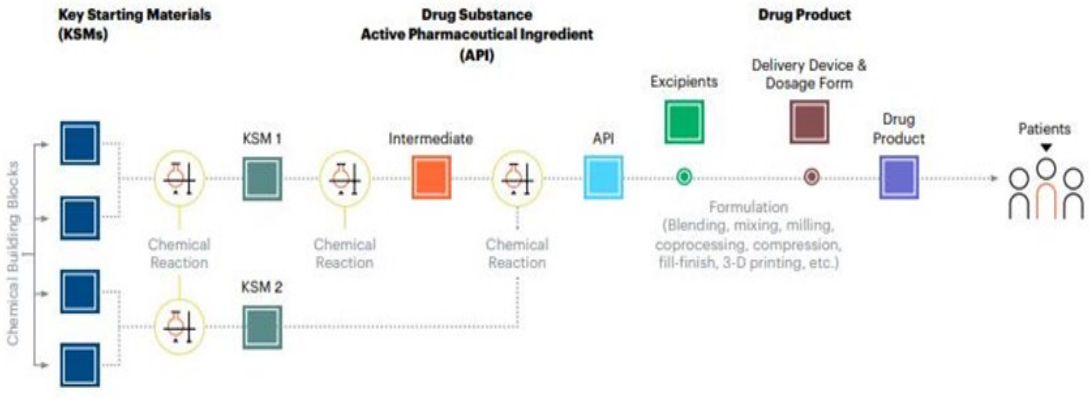
The global medicine supply chain is a complex marketplace of manufacturers, suppliers, and distributors from many countries. The globalization of the medicines supply chain has helped increase access to quality medicines at a lower cost. At the same time, supply chains have grown longer, more involved, and fragmented, leading to a lack of visibility and an increase in the risk to resilience. Moreover, the market for producing some of the nation's most vulnerable medicines has become increasingly unsustainable. Unique market dynamics often drive procurement prices for these medicines below the cost of manufacturing them. Under these circumstances, reliable manufacturers, particularly those operating in the U.S., factor business and economic considerations into whether to maintain production in the United States, move operations outside the United States, or exit the market altogether.[1] These factors combine to reveal the extent of the supply chain's vulnerabilities to supply and demand fluctuation, geopolitical matters, global pandemics, natural disasters and trade restrictions. This can have lasting impacts on patients, health systems, and future innovation.

Generally, there has been little insight available into the upstream supply chain for medicines, including for key starting materials (KSMs), active pharmaceutical ingredients (APIs) and finished dosage forms (FDFs). Figure 1 is a simplified schematic depicting some of the complexity involved in the drug supply chain that begins with the KSMs needed to manufacture APIs, which in turn are necessary, along with excipients (inactive ingredients) and other materials, to manufacture a finished drug product. To anticipate the impacts of policy and market forces, decision-makers need end-to-end data and visibility in the supply chain.

[1] When market conditions limit manufacturers' profitability, this reduces a manufacturer's motivation to maintain a presence in, or enter, the market and to invest in manufacturing quality and redundant capacity.

USP–Rockville
12601 Twinbrook Parkway | Rockville, MD 20852-1790, USA
+1-301-881-0666 | usp.org

Figure 1: Simplified pharmaceutical manufacturing supply chain schematic[2]



Role of foreign supply chains, particularly of major exporters, in meeting United States demand for pharmaceuticals and pharmaceutical ingredients.

Using USP's Medicine Supply Map[3] – a data intelligence platform that maps where 94% of U.S. pharmaceutical drug products and their ingredients are made, and identifies, characterizes, and predicts supply chain risk – USP can analyze and quantify factors linked to supply chain disruptions for drug ingredients and finished drug products.

Location of API Manufacturing Facilities

To understand the existing concentration of manufacturing for API, USP analyzed API Drug Master Files (DMF). API DMF filings identify existing geographic locations that are manufacturing APIs and can suggest other locations that may be likely to have additional capacity.[4] Not all drug products utilize APIs referencing DMFs, but the geographic analysis of DMFs can provide a perspective on where API capability might be trending.

Based on this data, India holds the greatest API manufacturing capacity with roughly 50% of API DMF filings in 2023.[5] Additionally, China's API manufacturing capacity has shown a striking rise in recent years. Between 2021 and 2023, the number of DMF filings of China increased 63%, corresponding to almost one-third of all the filings in 2023, while India's share of new API DMF filings decreased in 2023. The European Union (EU) saw a sizeable decrease in total active API DMF share in 2023, which was likely due to an overall increase in manufacturing activities outside the EU, rather than a decrease in its own API DMF filings.

Manufacturing Volume of API

Although API DMF analysis can clarify where manufacturing facilities are based, two facilities could be producing different volumes of medicines. The USP Medicine Supply Map did further analysis to look at the production volume of APIs for different geographic locations (Figure 2). This analysis gives a picture of where current production comes from.

---

[2] USP Annual Drug Shortage Report: 2024

[3] USP Medicine Supply Map. www.usp.org/medicinesupplymap.

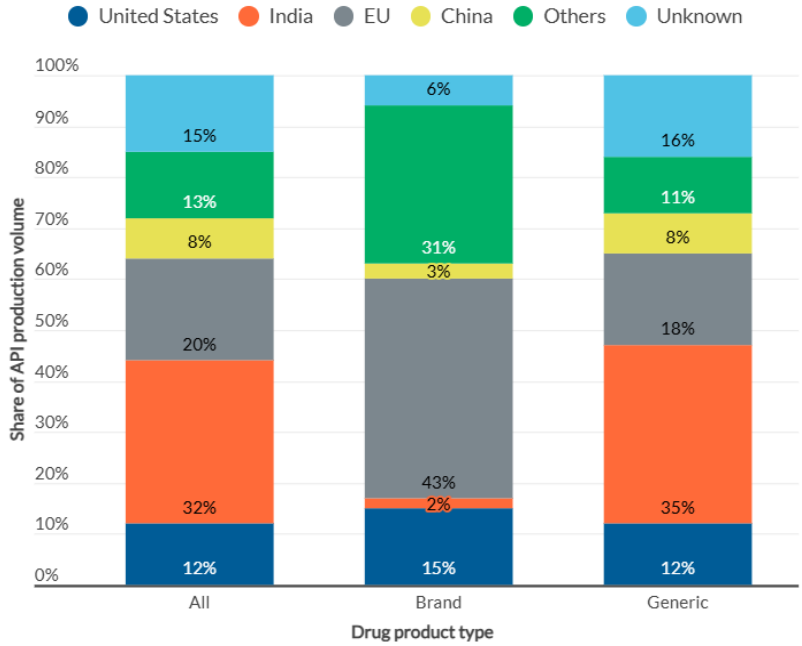
[4] The proportion of DMFs in a particular location should not be interpreted as the proportion of APIs being sourced from that region. Aggregated DMF information is reflective of manufacturer site locations only, and this analysis does not contain information about the quantity produced or geographic distributions of APIs themselves.

[5] USP Quality Matters Blog: USP Quality Matters Blog: Global manufacturing capacity for active pharmaceutical ingredients remains concentrated

The analysis shows half of the API for prescription medicines in the U.S. come from India and the EU. Generic drugs, which make up 90% of U.S. prescription volume, primarily come from India, while 43% of branded pharmaceutical API comes from the EU. The United States accounts for 12% of total API volume analyzed.[6] China contributes 8% of the total volume of API analyzed, however, there is evidence of significant dependence on China for key starting materials, the building blocks of API. Further, the USP Medicine Supply Map identified some API and essential medicines that are exclusively manufactured in China.

Figure 2: API manufacturing landscape (excluding IV fluids), 2024[7]

Volume in extended units

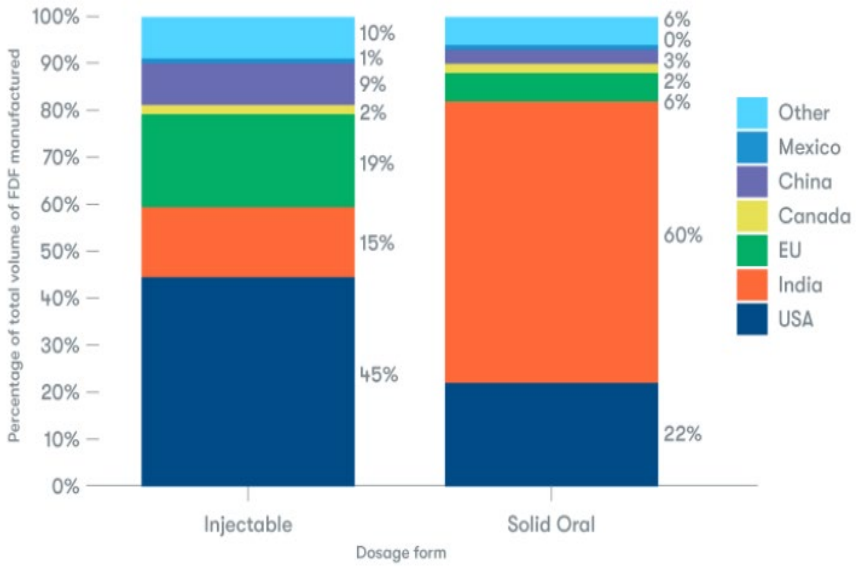


Manufacturing volume of FDF

Using USP's Medicine Supply Map, analysis of the geographic concentration of U.S. prescription pharmaceutical finished dose forms was performed (Figure 3). The United States is the largest manufacturer of injectables with 45% of production volume, followed by the EU with 19% of production volume. For solid oral dosage forms, India has 60% of production volume, followed by the United States with 22% of production volume. Market shares have remained relatively unchanged over 2022 and 2024.

[6] The analysis excluded IV fluids, such as saline. If those had been included, the U.S. contribution would have been significantly higher.
[7] USP Quality Matters Blog: Over half of the active pharmaceutical ingredients (API) for prescription medicines in the U.S. come from India and the European Union

Figure 3: Manufacturing footprint of Rx pharmaceutical finished dose forms (FDF), 2024[8]



Historically, tariffs have been based on the country where the pharmaceutical API was made. The insights from these analyses underscore the complexity of medicine supply chains and the varying factors that should be considered when assessing strategies or policies with the intent to increase domestic manufacturing of pharmaceuticals and pharmaceutical ingredients or securing supply chains. It is important that comprehensive, end-to-end data is available when making these decisions. Additional analysis is planned to understand the therapeutic categories of the API produced within each region.

Concentration of United States imports of pharmaceuticals and pharmaceutical ingredients from a small number of suppliers and the associated risks.

Insights from USP's Medicine Supply Map demonstrate that geographic concentration of pharmaceutical manufacturing anywhere in the world, including within the United States – where pharmaceutical manufacturing has been especially impacted by weather and natural disasters – increases the risk for drug shortages. A disruption in a single region can rupture multiple elements of the supply chain should it impact the reliable supply of APIs and the starting materials essential for their synthesis, excipients, packaging materials, and other supplies. Drugs in which the API and/or FDF are made in a single or few locations are at a higher risk of shortages. The risk of drug shortages is particularly acute when a single facility is responsible for producing the entire U.S. market supply for a particular drug.

Promoting geographic diversity of the manufacturing base[9] of U.S. drug products, including domestic manufacturing, can help to reduce supply chain vulnerabilities and support a reliable, resilient supply chain for these products. Multiple strategies can help to enable geographic diversity of the supply chain, such as various approaches to shoring (onshoring and near shoring), as well as exploring other potential considerations manufacturers assess when evaluating operations and production sites including strategic locations, regulatory risks, and economic opportunity.

[8] USP Quality Matters Blog: India and the United States manufacture most finished medicines for the U.S. market

[9] USP White Paper: Building geographic diversity in the medicines supply chain

The extent to which domestic production of pharmaceuticals and pharmaceutical ingredients can meet domestic demand and the feasibility of increasing domestic capacity for pharmaceuticals and pharmaceutical ingredients to reduce import reliance.

Market dynamics in response to external shocks, including those caused by new tariffs or trade policy, can be highly drug-specific and have the potential to disproportionately impact certain products that are more vulnerable to supply chain disruptions. USP encourages policymakers to address the underlying incentives for production and consider a range of reforms to foster security in the manufacturing base for U.S. drug products to reduce the risk of disruptions and shortages, including those that support expansion of current domestic manufacturing capabilities.[10] This includes:

- Economic or other incentive measures that will encourage multiple suppliers for key drugs, geographic diversification of manufacturing facilities, and manufacturing location and component supply redundancies;
- Mapping of current global KSM suppliers, as well as identifying alternative sources and routes of synthesis for essential products with vulnerabilities;
- Economic incentives to encourage increased domestic manufacturing of APIs, finished drug products, and KSM in the United States, prioritizing specific medicines or ingredients that are most vulnerable to supply disruptions;
- Market-based incentives that encourage utilization of excess domestic manufacturing capacity: up to 50% of manufacturing capacity in the U.S. is currently unutilized;
- Financial incentives to provide manufacturers with the necessary support to build facilities supporting advanced manufacturing technologies on U.S. soil; and
- Development of a drug supply chain resilience benchmark initiative to foster resiliency in the drug supply chain, promote sustainable prices for generic medicines, and incentivize changes in purchasing practices.

***

Thank you again for the opportunity to comment. For more information about the information provided or if you have any questions, please contact Amy B. Cadwallader, PhD, Director, Regulatory and Public Policy Development at Amy.Cadwallader@usp.org or by phone at (301) 692-3567.

Sincerely,

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

[10] USP Global Public Position Paper: Identifying and addressing vulnerabilities in the upstream medicines supply chain to build resilience and reduce drug shortages. https://www.usp.org/supply-chain/build-resilience-and-reduce-drug-shortages