Statement of the U.S. Pharmacopeia

Submitted to the House Energy and Commerce Subcommittee on Health

For the Hearing "Made in America: Strengthening Domestic Manufacturing and the Health Care Supply Chain"

June 11, 2025

The United States Pharmacopeia (USP) is pleased to submit the following statement for the record on the hearing "Made in America: Strengthening Domestic Manufacturing and the Health Care Supply Chain."

USP is an independent, scientific, global non-profit organization founded in 1820 when eleven physicians took action to protect patients from poor-quality medicines. Convening in the old U.S. Senate Chamber, they published a national, uniform set of guidelines for medicines called the U.S. Pharmacopeia. Today, USP employs 1300 staff, most of whom are scientists, and works with nearly 800 scientific experts who volunteer their time to establish quality standards for medicines. In addition, USP offers a range of programs to help ensure the supply of quality medicines for Americans, including the USP Medicine Supply Map which tracks the upstream supply chain of medicines and their ingredients, verification programs to confirm the quality of ingredients in medicines, and initiatives to accelerate adoption of advanced pharmaceutical manufacturing technologies, which can support more domestic manufacturing.

These programs reflect a core pillar of USP's work to help strengthen the global supply chain so that the medicines, dietary supplements, and foods that Americans rely on for their health are available when needed and meet quality standards as expected and required. In addition to the scientific experts on USP standard-setting committees, USP is governed by more than 500 organizations, including scientific, healthcare practitioner, consumer, and industry communities,

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as well as dozens of government agencies, who together comprise the USP Convention.[1] Working with this broad base of knowledge across health care, USP creates standards for quality and safety for medicines, food ingredients, and dietary supplements.

Safe and effective medicines, consistently manufactured according to established quality standards, are essential to preventing disease, treating illness, and saving lives. USP's standards and resources are indispensable to innovation and access, providing shared, foundational platforms for industry to help accelerate the development of new technological solutions for the American marketplace. USP has over 6,000 standards for active pharmaceutical ingredients, drug products, and inactive ingredients used throughout the supply chain. USP creates these standards through an open, transparent process, offering the ability to adjust standards to adapt to new industry practices and keep up with evolving science and technology. USP also works closely with the U.S. Food and Drug Administration (FDA) and other government agencies to help ensure the quality and safety of products sold to Americans.

In addition to our work on standards, USP is an active participant in many public-private partnerships on supply chain-related issues. This includes work with the Department of Defense (DoD), the Advanced Research Projects Agency for Health (ARPA-H), the Administration for Strategic Preparedness and Response (ASPR), the Biomedical Advanced Research and Development Authority (BARDA), and the FDA.

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

End-to-end medicine supply chain mapping and analytics are essential for building resilience and supporting domestic manufacturing

The global medicine supply chain is a complex marketplace of manufacturers, suppliers, and distributors from many countries. While the globalization of the medicine supply chain has helped increase access to quality medicines at a lower cost, supply chains have grown longer, more complex and fragmented, leading to a lack of visibility and an increase in the risk to resilience. Moreover, market conditions for the production of some of the nation's generic medicines have become increasingly unsustainable. Unique market dynamics often drive procurement prices for these essential generic medicines below the cost of manufacturing. Under these circumstances, reliable manufacturers, particularly those operating in the United States, 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.[2] Likewise, these circumstances influence incentives to invest in new manufacturing in the United States. 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 disruptions. This can have lasting impacts on patients, health systems, and national security.

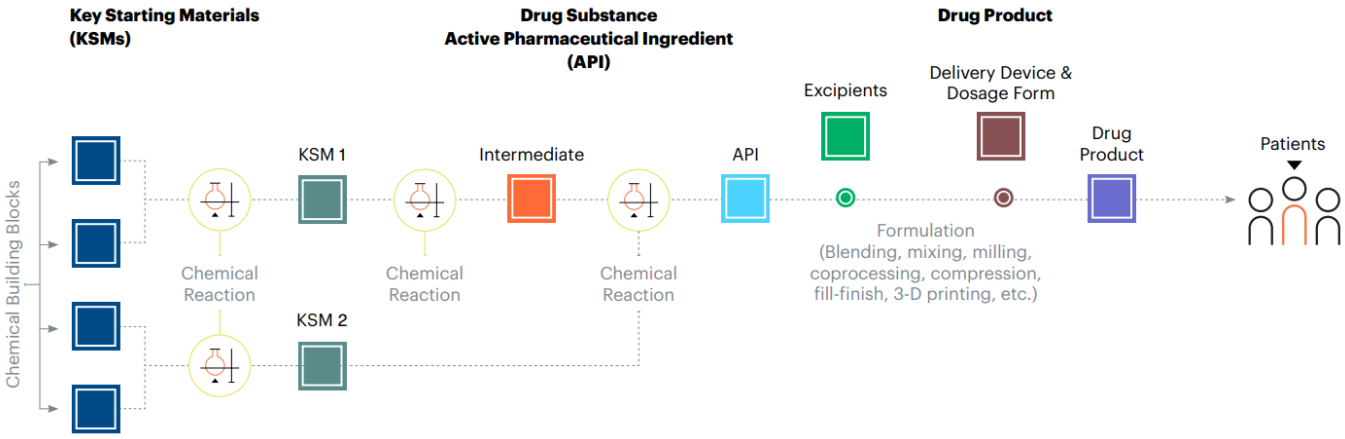
Historically, there has been little insight available into the upstream supply chain for medicines, including for key starting materials (KSMs), active pharmaceutical ingredients (APIs), and finished dosage forms (FDFs). Figure 1 is a simplified schematic depicting some of the complexity involved in the drug supply chain that begins with the KSMs needed to manufacture

[2] 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.

APIs, which in turn are necessary, along with excipients 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 mapping of entire supply chains for medicines.

Figure 1: Simplified pharmaceutical manufacturing supply chain schematic.[3]



USP's Medicine Supply Map[4] – 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 – can analyze and quantify factors linked to supply chain disruptions for drug ingredients and finished drug products. Using the Medicine Supply Map, USP analyzed the location of API manufacturing facilities as well as the manufacturing volume of APIs and FDFs to better understand the geographic concentration of production for U.S. prescription medicines. These insights include actionable information for APIs and FDFs; however, blind

[3] U.S. Pharmacopeia. USP Annual Drug Shortage Report: Economic factors underpin 2023 shortages. 2024. The schematic does not provide a complete picture of the supply chain; it does not include, for example, purchasers, distributors, or healthcare providers.
[4] U.S. Pharmacopeia. USP Medicine Supply Map. www.usp.org/medicinesupplymap. 2025.

spots still exist for the excipients[5,6] and KSMs necessary for many medicines since these large data sets are not readily available. USP experts can provide end to end risk assessment analysis of specific drugs and drug classes.

Location of API manufacturing facilities

To understand the existing concentration of manufacturing for API, USP analyzed API Drug Master Files (DMFs). API DMFs identify existing geographic locations that are manufacturing APIs and can suggest other locations that may be likely to have additional capacity.[7] Not all drug products utilize APIs referencing DMFs, but the geographic analysis of DMFs can provide a perspective on where API manufacturing capacity might be trending.

Based on this data, India maintains the greatest API manufacturing capacity with roughly 50% of API DMF filings in 2023.[8] Additionally, China's API manufacturing capacity has shown a striking rise in recent years. Between 2021 and 2023, the number of DMF filings in China increased 63%, amounting to almost one-third of all filings, 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

[5] Despite being called "inactive" ingredients, excipients play a critical role in drug development, delivery, effectiveness, and stability. Excipients comprise up to 90 percent of a medicine's volume and serve important functions, including as binders, disintegrants, coatings, preservatives, colors and flavorings. Excipients are sourced from suppliers around the world and are used for more than just the manufacture of medicines. The reliance of the pharmaceutical industry on the global excipients supply chain presents challenges for supply chain resiliency as well as quality and regulatory oversight. As such, breakdowns of critical excipient supply chains can have significant downstream effects including drug recalls and patient health impacts. For example, magnesium stearate is included in 32,060 drug products according to NIH DailyMed, including those to treat high cholesterol, high blood pressure, diabetes, and bacterial infections.

[6] U.S. Pharmacopeia. USP Global Policy Position: Excipients: A Blind Spot in Ensuring Medicine Quality and Supply Chain Resilience. 2024.

[7] 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.

[8] U.S. Pharmacopeia. USP Quality Matters Blog: Global manufacturing capacity for active pharmaceutical ingredients remains concentrated. 2024.

EU, rather than a decrease in its own API DMF filings. Meanwhile, the U.S. remained at 4% of API DMFs in 2023 as it did in 2021.

Manufacturing volume of API

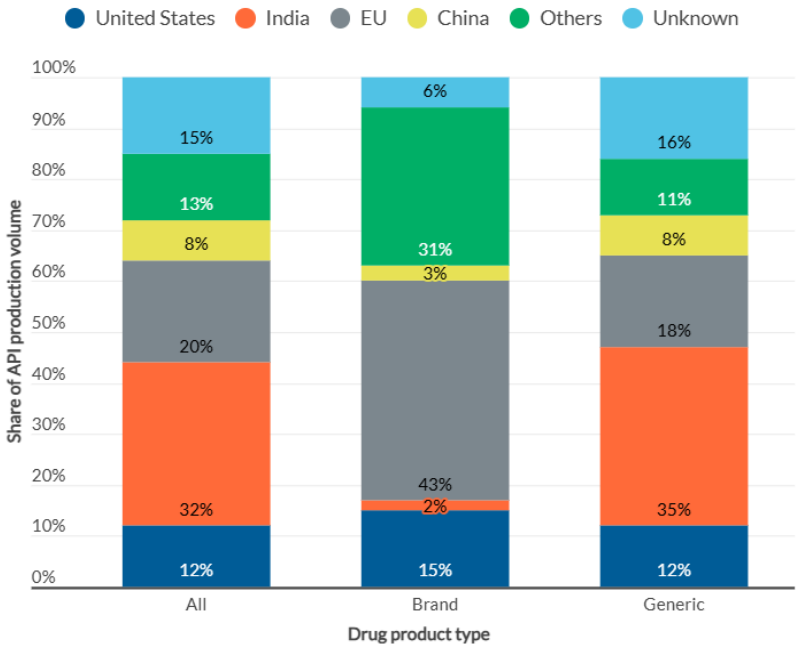
Although API DMF analysis can clarify where manufacturing facilities are based, two facilities could be producing different volumes of medicines. The USP Medicine Supply Map also determines the production volume of APIs from different geographic locations to provide a picture of where current production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

In 2024, the analysis shows:

- Half of the API for prescription medicines in the United States come from India and the EU.
- Generic drugs, which make up 90% of U.S. prescription volume, primarily come from India.
- 43% of branded pharmaceutical API comes from the EU.
- The United States accounts for 12% of total API volume analyzed.[9]
- China contributes 8% of the total volume of API analyzed.
- There is evidence of significant dependence on China for KSMs, the building blocks of API, but further work is necessary to fully understand the supply chain of KSMs.

[9] The analysis excluded IV fluids, such as saline. If those had been included, the U.S. contribution would have been significantly higher.

Figure 2: API manufacturing landscape (excluding IV fluids) in 2024.[10]



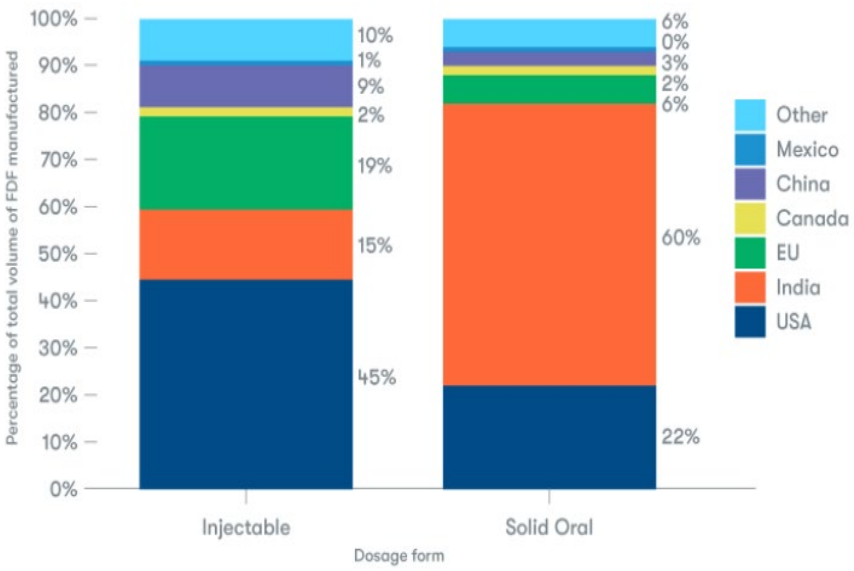
Manufacturing volume of FDF

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.

[10] U.S. Pharmacopeia. 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. 2025.

Figure 3: Manufacturing footprint of prescription pharmaceutical FDF in 2024.[11]



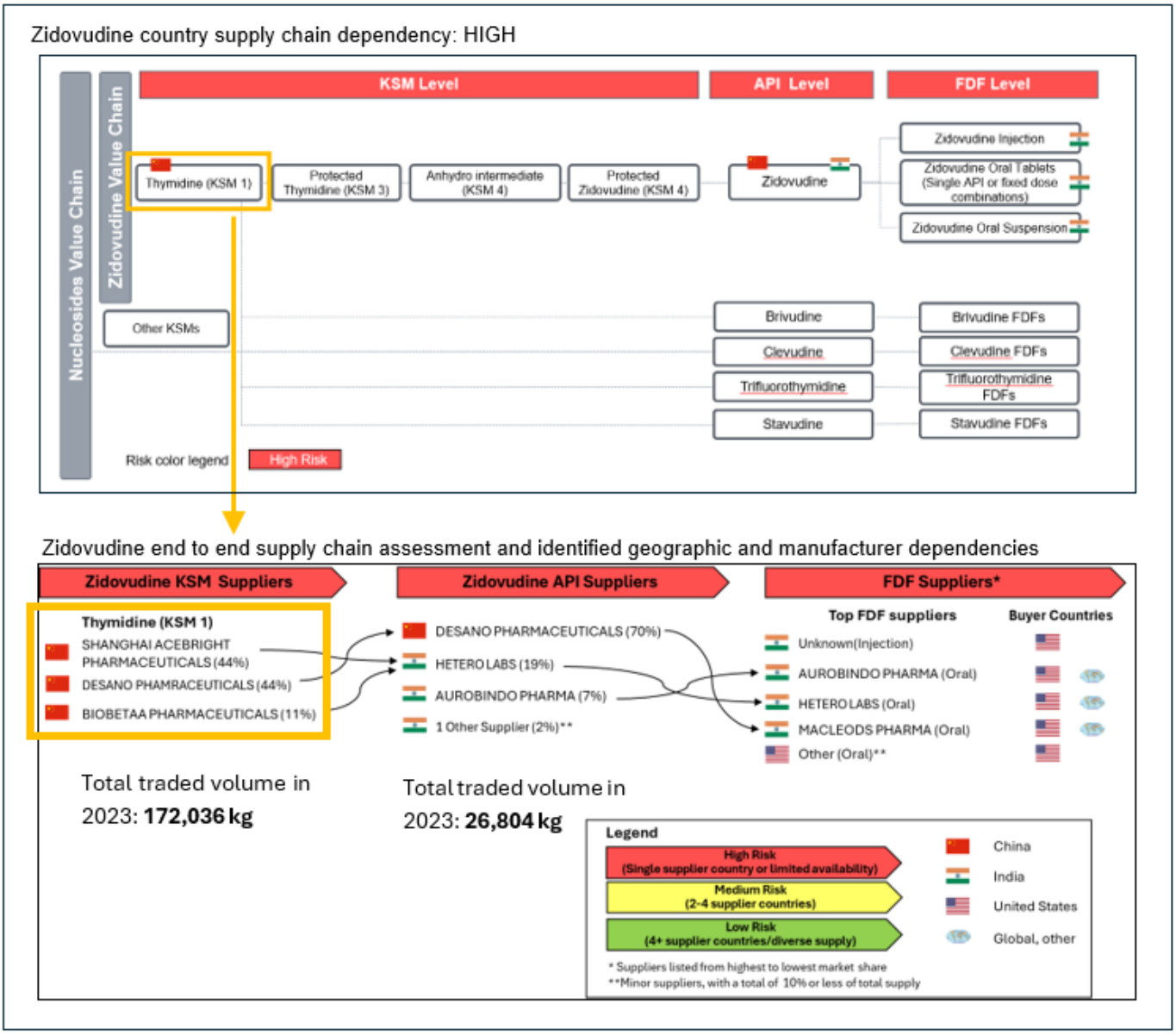
Risk assessment analysis

In addition to the comprehensive, data-driven view of the upstream pharmaceutical supply chain provided by the Medicine Supply Map, USP is also deploying scientific experts to better understand critical blind spots that remain in our knowledge of medicine supply chains. This risk analysis can inform strategic decisions and the development of solutions. This analysis includes an evaluation of the KSM and API manufacturing pathways to identify manufacturing challenges and production bottlenecks; a geographic and technoeconomic risk analysis to assess regional vulnerabilities, economic feasibility, and supply dependencies, enabling a structured evaluation of risk potential; and resulting risk information that is specific to drugs or drug classes. For example, using zidovudine (a nucleoside-based antiviral medicine) as an example, analysis found a critical dependency on one KSM (thymidine) produced only in China, which indicates a

[11] U.S. Pharmacopeia. USP Quality Matters Blog: India and the United States manufacture most finished medicines for the U.S. market. 2025.

high vulnerability risk not just for zidovudine, but for several nucleoside-based antiviral medicines (Figure 4).

Figure 4. Zidovudine (and other nucleoside-based antiviral) supply chain components and geographic vulnerability risk analysis.



While the data presented above provides important insights into the U.S. medicine supply chain, neither a single government agency nor any industry entity currently has a complete view of the upstream pharmaceutical supply chain (including FDFs, APIs, and KSMs), which contributes to a limited understanding of the risks affecting the U.S medicine supply. USP is working toward more complete visibility in the Medicine Supply Map with the inclusion of additional data and insights on KSM dependence. Greater insight is needed to ensure effective deployment of resources, to strengthen our supply chain economy, and national security interests. Failing to account for upstream root causes of supply chain vulnerability paints only half the picture and leaves us susceptible to bottlenecks and geopolitical disruption.

Efforts must continue to understand supply chain risk via initiatives like the Medicine Supply Map data and analytics coupled with extensive expertise in unraveling complicated supply chain maps to provide risk assessment and intelligence.

USP is helping to strengthen our supply chain and economy and mitigate national security risks by identifying vulnerabilities with tools and resources. Our Medicine Supply Map and experts can currently:

- Analyze and quantify factors linked to supply chain disruptions for drug ingredients and finished drug products.
- Identify risks, including from KSMs or APIs that are made in few locations or in countries prone to supply disruption.
- Identify and characterize shortage risks at product, company, facility, and geographic levels.
- Provide end-to-end segmentation and detailed mapping from KSMs through APIs to FDFs for all U.S.-approved small molecule APIs.
- Map commercially available KSMs linked to specific APIs.

- Identify countries of origin, top suppliers, and manufacturers across each segment of the supply chain.

Only through a comprehensive, end-to-end understanding of the pharmaceutical supply chain can we truly unlock the targeted, cost-effective interventions to help make domestic manufacturing in the U.S. sustainable. This approach should cover all U.S. medicines, starting with the most critical products, and expand analysis beyond individual APIs to include related chemical and therapeutic classes. Doing so provides a holistic understanding of supply chain dependencies.

Data- and evidence-informed policy reforms and investments can promote domestic production of medicines

Insights from USP's Medicine Supply Map demonstrate that geographic concentration of pharmaceutical manufacturing anywhere in the world increases the risk of vulnerability to disruption and drug shortages.[12,13]

A disruption in a single region can rupture multiple elements of the supply chain should it impact the reliable supply of APIs and the key 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. While some disruptions are caused by natural events including weather or even earthquakes, some can be driven by intentional actions including trade disruptions or the potential to weaponize trade in medicine.

[12] United States Pharmacopeia. USP Annual Drug Shortages Report: Longstanding drug shortages persist in 2024. 2025.
[13] U.S. Pharmacopeia. USP Annual Drug Shortages Report: Economic factors underpin 2023 shortages. 2024.

Promoting geographic distribution of the manufacturing base[14] of U.S. drug products, APIs, and KSMs can help to reduce supply chain vulnerabilities and support a more reliable, resilient supply chain for these products. Multiple strategies can help to enable geographic distribution of the supply chain, such as various approaches to shoring (onshoring and near shoring), as well as exploring other considerations manufacturers assess when evaluating operation and production sites including strategic locations, regulatory risks, and economic opportunity.

In particular, USP encourages the Committee to consider the following recommendations:

1. **Identify medicines with a vulnerable supply chain using the USP Vulnerable Medicines List**
2. **Enable alternate pharmaceutical manufacturing processes in the United States**
3. **Incentivize resilience with a Drug Supply Chain Resilience Initiative**

Identification of medicines with a vulnerable supply chain will help target interventions

USP recently published the USP Vulnerable Medicines List (VML),[15] which consists of medicines derived from an assessment of their essentiality, demand, and supply chain vulnerabilities and can be used to identify medicines at risk of supply chain disruption.[16,17]

Leveraging Medicine Supply Map and additional data, USP conducted an analysis to identify 100 vulnerable medicines – 49 used to manage chronic conditions and 51 for acute care – to

[14] U.S. Pharmacopeia. USP White Paper: Building geographic diversity in the medicines supply chain. 2023.
[15] United States Pharmacopeia. 2024-2025 Vulnerable Medicines List for the United States: A data-based approach to identify risks and enable interventions to increase reliability of supply. 2025.
[16] United States Pharmacopeia. USP Global Public Policy Position: Identifying and addressing vulnerabilities in the upstream medicines supply chain to build resilience and reduce drug shortages. 2023.
[17] USP's approach borrows from the framework proposed in the article: Wosinska, M., Mattingly, T., & Conti, R. A Framework for Prioritizing Pharmaceutical Supply Chain Interventions. 2023.

inform dialogue related to bolstering medicine supply chain resilience.[18] This data-driven approach accounts for the level of use by the U.S. population, the vulnerability of the medicine to supply chain disruptions, and the availability of alternative therapies. The resulting list includes a wide range of therapeutic classes of medicines, as well as a variety of product types.

The USP Vulnerable Medicines List is a practical list intended to complement other resources to identify potential drugs at risk of supply chain disruption in the United States. **USP encourages the Committee to use the Vulnerable Medicines List to help prioritize the most critical products, target investments, and inform initiatives to bolster the U.S. pharmaceutical supply chain and national security interests.**

Alternate manufacturing processes will better enable domestic production of pharmaceuticals and pharmaceutical ingredients

As noted, the upstream pharmaceutical supply chain is complex and intricate, with myriad ingredients used commercially. Effective policy requires a deep understanding of suppliers and manufacturing locations. Additionally, the upstream pharmaceutical supply chain is a fragmented and interdependent manufacturing ecosystem, prone to unexpected vulnerabilities and often lacking efficiency and sustainability.

Enabling economically viable domestic production of prioritized APIs and KSMs is an important element of a comprehensive effort to enhance medicine supply chain resiliency. Scalable solutions to support onshoring and location production of essential drug candidates, APIs, and KSMs, and bolster rapid response capabilities within the U.S. medicine supply chain include:

- Alternative manufacturing routes: Designing economically viable alternate synthesis pathways, using KSMs that are capable of being sourced in the U.S. or allied countries.

[18] United States Pharmacopeia. 2024-2025 Vulnerable Medicines List for the United States: A data-based approach to identify risks and enable interventions to increase reliability of supply. 2025.

This work requires analysis of new ways to make a medicine that do not rely on ingredients sourced from a single country. USP has undertaken such analysis for various agencies, and urges the U.S. government to expand work on identifying alternative manufacturing routes and provide incentives for drug makers to utilize them;

- Advanced manufacturing technologies (AMTs): Emerging technologies offer promising avenues for reducing our dependence on overseas supply chains. Incentivizing acceleration of innovative approaches like continuous manufacturing and flow chemistry, are key to modernizing, localizing, and stabilizing production; and
- Scale-up and tech transfer: Supporting the transition from lab-scale innovation to commercial-scale implementation.

These innovations in manufacturing processes and technology can help to rapidly scale manufacturing capabilities, shorten supply chains while increasing manufacturing resilience, provide new ways to address drug shortages, and accelerate the development and availability of new therapies.

Many of the structural and chronic challenges with chemical manufacturing, especially chemical pharmaceutical manufacturing, have been due to low efficiency – among the major chemical industry sectors (oil refining, bulk chemicals, fine chemicals, and pharmaceuticals) pharmaceutical manufacturing generates the least product output, with about 1 kilogram of API obtained on average from a total of 25 to 100 kilograms of raw materials input.[19] Other complexities are associated with the hazardous conditions to produce chemical products at scale. Due to these complexities, over the past few decades, the manufacturing of upstream ingredients and bulk APIs has been outsourced to lower cost and less regulated countries rather

[19] Fortunak JM. Current and future impact of green chemistry on the pharmaceutical industry. Future Med Chem. 2009 Jul;1(4):571-5. doi: 10.4155/fmc.09.60. PMID: 21426025.

than tackling and solving the challenges. Therefore, today we witness these structural and chronic challenges along with dependencies on these countries.

For these reasons, a re-imagining of the traditional chemistry processes used along the supply chains of necessary materials is essential. To advance the application of new technologies that help to mitigate identified supply chain risks, new solutions must be explored and funded.

Building on the example of zidovudine (a nucleoside-based antiviral medicine) discussed above that found a found a critical dependency on the KSM thymidine, a key recommendation to reduce reliance on one country is to onshore API and KSM manufacturing of thymidine. This can be accomplished by leveraging continuous manufacturing technology to produce the necessary KSM thymidine. Additional AMTs can then be utilized to locally produce zidovudine more efficiently and other necessary nucleoside-based antiviral medicines while using the domestically produced thymidine. USP chemists have identified an alternate pathway to synthesize thymidine and work to optimize the new process using the AMT flow chemistry is underway.

Through a new Advanced Technologies Lab,[20] USP is supporting the development and application of AMTs, such as those for thymidine and its APIs, to foster more efficient and expanded production of quality medicines. USP will accelerate its work with industry and regulators to advance the application of new technologies and alternate manufacturing processes including developing alternate routes of synthesis for pharmaceutical KSMs and APIs and using AMTs such as pharmaceutical continuous manufacturing. These alternate manufacturing processes will help to mitigate identified supply chain risks, and this work can

[20]United States Pharmacopeia. USP announces new Advanced Technologies Laboratory to accelerate and scale pharmaceutical manufacturing innovations. 2025.

help bring quality-assured products to market more efficiently, strengthen domestic manufacturing capabilities, and build national security.

Another recent example of work to re-imagine the supply chain of pharmaceutical ingredients is the ARPA-H funded Wheat-based High-efficiency Enzyme and API Technology (WHEAT) project. The consortium of partners working on the WHEAT project aim to establish a new way to make API by leveraging cell-free protein synthesis with the aid of wheat germ extract (WGE), a key raw material derived from abundantly available agricultural wheat. This project uses WGE, in conjunction with other advanced technologies to circumvent challenges associated with traditional chemical manufacturing, such as low throughput and long, multi-step complex chemical synthesis. If successful, the team will have demonstrated a paradigm shift in domestic API manufacturing.[21] USP will support this work through USP's new Advanced Technologies Lab.

An initiative to incentivize investment in drug supply chain resilience

In addition to the technical considerations discussed above, efforts to bolster domestic manufacturing and increase supply chain resilience must include a comprehensive assessment of the underlying market factors that influence investments in infrastructure and resilience. Economic factors play a considerable role in leading to medicine supply chain vulnerabilities and subsequent shortages of medicines.[22] Generic medicines account for nearly 90% of the medicines relied on by Americans and less than 20% of the U.S. expenditure on medicines. Yet current generic drug payment policies and practices encourage purchasers to choose manufacturers largely based almost solely on lowest price. Contracts are routinely broken, which also disincentivizes generic manufacturers to invest. This can undermine initiatives to

[21] U.S. Pharmacopeia. USP and Ginkgo Bioworks announce ARPA-H project to support production of essential medicines using innovative cell-free expression systems. 2025.
[22] U.S. Pharmacopeia. USP Annual Drug Shortages Report: Economic Factors underpin 2023 shortages. 2024.

strengthen supply chain resilience by limiting the ability of manufacturers to invest in new, alternate manufacturing processes, domestic production, manufacturing updates and necessary facility maintenance, quality assurance and management, or to build redundancy into supply chains. A fundamental shift in the market is needed to align supply and demand forces to create a more predictable, sustainable, and quality supply chain that can reliably provide medicines to American patients.

The current purchasing and payment systems, however, lack a coordinated and collaborative means to evaluate resilience and reliability and therefore minimize and mitigate risks that affect the U.S. supply of medicines. There is a need for deliberate incorporation of quality, resilience, and reliability, in addition to price, in contracting, purchasing, and inventory decisions.

USP encourages the Committee to consider the development of a Drug Supply Chain Resilience Initiative (DSCRI),[23] which aims to foster stability in the drug supply chain by providing criteria to value the resilience and reliability of manufacturers, promoting sustainable prices for generic medicines, and incentivizing changes in purchasing practices with the goal of better meeting patients' needs through a reliable, safe, and resilient medicine supply chain. A DSCRI must include two distinct elements:

- A data-driven system to differentiate suppliers based on reliability and resilience, such as the development of an assessment or benchmark to enable purchasers to identify resilient manufacturers.
- Establishment of meaningful value-based payment and contracting reforms to incentivize supply chain resilience and reliability.

A manufacturer benchmark metric should function as a tool for decision making and consist of resilience measures, reliability measures, quality measures, as well as the base vulnerability of

[23] U.S. Pharmacopeia. A drug supply chain resilience initiative will better support patients. 2025.

a drug product, which includes understanding the concentration of domestic and non-domestic manufacturing locations. Key benchmark attributes could include:

- Experts to advise on initiative details and benchmark criteria
- A menu of well-established measures that are predictive of reliability
- The ability of manufacturers to choose measures and combine values to reach the resilience benchmark
- A resilience determination per molecule, per manufacturer
- Leveraging partnership with the USP Medicine Supply Map Vulnerability Assessment and the USP Vulnerable Medicines List

Several measures are currently known and available that could be utilized, including those from the USP Medicine Supply Map; publicly available metrics from the FDA; manufacturer measures of product production, inventory, and delivery; and reputable product level quality testing data, among others.

Without significant market and policy interventions, current medicine supply chain vulnerabilities and drug shortage trends will likely continue or worsen. A solution to bolster resiliency can be facilitated by measuring and valuing reliability and quality using a comprehensive framework like the DSCRI.

Conclusion

The USP thanks the Committee for this hearing and for the bipartisan, careful consideration of approaches to support domestic production of essential medicines and health care products. We look forward to working with the Committee and Congress to achieve practical solutions that will strengthen our supply chain, economy, and national security interests.