VIA ELECTRONIC SUBMISSION

June 6, 2024

Senate Finance Committee
219 Dirksen Senate Office Building
Washington, DC 20510

Dear Chairman Wyden, Ranking Member Crapo, and members of the Committee,

The United States Pharmacopeia (USP) appreciates the opportunity to provide comments on the Senate Finance Committee's legislative draft to address shortages of critical medicines entitled "Drug Shortage Prevention and Mitigation Act," which focuses on leveraging the Medicare and Medicaid programs to address the market and economic challenges faced by manufacturers of generic sterile injectables (GSIs).

USP is an independent, scientific, global non-profit organization founded in 1820 and dedicated to building trust in medicines through rigorous science, public quality standards, and a range of programs to help advance the supply of quality medicines.[1] 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.[2] 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.

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 are 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 because lower-margin and lower-price drug products may provide limited incentives for manufacturers to continually invest in quality control systems and build redundancy and resilience into supply chains.

A fundamental shift in the market for lower-priced drugs is necessary to increase predictability of both demand and supply and to increasingly value a drug's supply chain resilience and reliability. USP recently outlined approaches to identify and

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

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address vulnerabilities in the upstream supply chain to build resilience and reduce drug shortages.[3]

Many of the concepts proposed by USP are in alignment with the Committee's proposed approach to addressing drug shortages through the implementation of new demand-side policy reforms. In addition, USP offers some additional thoughts for your consideration:

1. **Identify risks: USP urges the Committee to work with applicable federal agencies and the private sector, including USP, to identify at-risk products eligible for the newly proposed program through the establishment of a vulnerable medicines list.**

2. **Incentivize resilience: USP supports the establishment of a public-private partnership with oversight from the HHS Supply Chain Resilience and Shortage Coordinator to develop a mechanism to reward medicine manufacturers for investments in quality, resilience, and reliability with meaningful payment reforms and committed long-term contracts.**

3. **Incentivize modern manufacturing technologies: USP supports near- and long-term financial incentives and necessary supports to bolster and enable greater adoption of advanced manufacturing technologies (AMTs) by manufacturers and urges further consideration of how and the degree to which the advanced manufacturing provider incentive structure could directly impact generic manufacturers' adoption and utilization of AMTs.**

The proposed reforms, along with our suggestions, can promote a collaborative approach among supply chain stakeholders to prevent drug shortages. We look forward to engaging with the Committee and other stakeholders as the draft legislation continues to be refined.

1. Identify Risks
Identify drugs at risk for shortage to guide decision making

Given the ongoing urgency of this issue and the threat posed to our nation's patients and public health, USP is pleased to see the Committee explore solutions through economic reforms—including payment and contracting reforms—that seek to incentivize quality and reliability throughout the entire pharmaceutical supply chain. Such incentives would apply to certain at-risk GSIs. As noted in the Committee's legislative draft, the risk level of medicines would be determined by the Secretary in consultation with the Food and Drug Administration (FDA) and relevant stakeholders. Determination of these "high risk" medicines that have the most vulnerable supply chains is an integral part of the proposed approach.

To support these efforts, USP recommends the establishment of a vulnerable medicines list in the United States. This list could be a complement to, or a component of, already established essential medicines lists, which would factor in

[3] USP Global Policy Position: Identifying and addressing vulnerabilities in the upstream medicines supply chain to build resilience and reduce drug shortages. 2023; https://www.usp.org/supply-chain/build-resilience-and-reduce-drug-shortages

supply chain vulnerabilities. Such supply chain vulnerabilities should include sole or limited numbers of suppliers, geographic concentration of manufacturers and active pharmaceutical ingredient (API), excipient, and key starting materials (KSM) suppliers, political and geopolitical risks, climate change and vulnerabilities, manufacturing complexity, price, and other factors.

Neither a single government agency nor any industry entity has a complete view of the upstream supply chain risks. This lack of clarity contributes to a limited understanding of the risks affecting the United States' supply of medicines. In response, USP developed a tool called the Medicine Supply Map, which uses multiple sources of information to identify the global sites of pharmaceutical ingredient and finished dose manufacturing. The Medicine Supply Map utilizes more than 40 datasets from USP, FDA, Centers for Medicare & Medicaid Services (CMS), European Medicines Agency, World Health Organization (WHO), and private sector sources. These data are enriched with information about risk drivers such as price and ingredients and cover 92 percent of FDA-approved generic prescription drugs. Notably, the Medicine Supply Map includes over 250 million aggregated datapoints to evaluate indicators of a shortage risk. 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.

These valuable Medicine Supply Map insights can be used to identify high-risk GSIs eligible for the economic incentives outlined in the draft. Recent and ongoing shortages in oncology drugs have made clear that while data signals exist that can help predict upstream pharmaceutical supply chain risk, the data are not integrated in a way that can generate actionable insights to prevent or mitigate drug shortages. For example, USP shared data[4] on vulnerabilities in the supply chains of 20 essential cancer medications, identified in a survey of nearly one thousand oncologists from around the world. All except two of the medicines are on the WHO Essential Medicines List.[5] Four of these 20 essential cancer medicines are currently in shortage in the United States, according to the FDA, and seven of the 20 essential cancer medicines analyzed are three to five times more likely to be in shortage than the average medicine.

Additional analysis leveraging USP's Medicine Supply Map suggests GSIs have inherently vulnerable supply chains and are at greater risk for shortage compared to other generic medicines: the average prescription drug product in the United States has a vulnerability score of 22.8 percent, and the average vulnerability score of GSIs is 40.1 percent as of April 2024.[6] Furthermore, USP recently released an *Annual Report on Drug Shortages* that leverages Medicine Supply Map data. The analysis:

- Identified "severe risk of shortage" for 91 percent of GSI shortages in 2023;

[4]Why cancer medicines are and continue to be vulnerable to drug shortages. 2023; https://qualitymatters.usp.org/why-cancer-medicines-are-and-continue-be-vulnerable-drug-shortages

[5] WHO Model List of Essential Medicines - 23rd list. 2023; https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02

[6] Informed by Medicine Supply Map insights and analysis, the USP Supply Vulnerability Score is calculated based on more than 100 risk factors to predict the likelihood of a shortage for a given drug. The closer the vulnerability score is to 100 percent, the greater the risk for that drug to be in shortage in the next 12 months. The score can help stakeholders, including hospitals, distributors, manufacturers, and the U.S. government, prioritize mitigative actions for the medicines most at risk of drug shortage (e.g., holding additional stock, securing multiple suppliers, and offering long-term contracts). The scores indicate drivers of risk—for example, low price or production concentration—so that targeted actions can be taken.

- Found that more than half, 53 percent, of new drug shortages in 2023 were for GSI medicines;
- Calculated that the average price of GSI medicines in shortage was nearly 8.5 times less than those not in shortage; and
- Identified that over half, 52 percent, of GSIs in shortage cost under five dollars in 2023.

These data highlight the significance and consequences of low prices associated with the "race to the bottom" economics in place. Additionally, in 2023 the United States was the largest producer of finished dosage form GSI medicines with nearly half (48 percent) of the total volume and over half (53 percent) of the total volume production of GSIs newly in shortage, highlighting the risk associated with geographic concentration and the lack of redundancy across the upstream supply chain.[7]

Establishing a list of vulnerable medicines based on Medicine Supply Map information would enable the U.S. government and private sector pharmaceutical supply chain stakeholders to move to a more proactive and informed approach to preventing shortages. Vulnerability information would assist in mitigating the impact of those shortages that do occur and should be considered as part of shortage prevention and mitigation plans in the United States. Medicine Supply Map insights would also 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 particular vulnerabilities of specific medicines. Such visibility needs to be available to all relevant medicine supply chain stakeholders to allow for rapid implementation of the quality and reliability strategies outlined in the draft.

USP applauds the Committee for recognizing the need to evaluate GSIs with a focus on those products most vulnerable to shortage. **We urge the Committee to work with applicable federal agencies and the non-profit and private sectors, including USP, to identify at-risk products eligible for the newly proposed program through the establishment of a vulnerable medicines list.**

2. Incentivize resilience

a. Develop and implement tools to assess supplier reliability, coupled with payment incentives to foster investment in supply chain resilience

Economic factors play a considerable role in leading to shortages. Current drug payment policies and practices encourage purchasers to choose manufacturers largely based on lowest price, which creates adverse market incentives for manufacturers to keep costs down even at the expense of needed investments in supply chain resilience and reliability. A fundamental shift in the market for lower-priced drugs is necessary to increase predictability of both demand and supply and to increasingly value a drug's supply chain resiliency and reliability in addition to its price. Improving and reforming contracting practices to include minimum three-year contracts with manufacturers, meaningful purchase volume commitments, and

[7] USP Annual Drug Shortage Report: Economic factors underpin 2023 shortages. 2024; https://go.usp.org/l/323321/2024-05-31/92zsjg/323321/1717187146zgOpt4vW/GEA_GC_056R_MSM_Report_2024_05_FINAL.pdf?_gl=1*1h1d8o*_gcl_au*NjMzNTA5NzEuMTcxNjkwNjA0Ng..*_ga*MzIxNDMzMTkyLjE2NDA3MDk1NTA.*_ga_DTGQ04CR27*MTcxNzUyMTQ4Ni41NDMuMC4xNzE3NTIxNDg2LjAuMC4w

stable pricing is necessary to ensure that manufacturers can make sufficient investments in quality, resilience, and reliability.

USP is pleased to see that a key element of the policy dialogue, including in the Committee's proposal, has focused on measuring resilience and reliability of the supply chain and necessary payment reforms. Specifically, the policy dialogue to incentivize a resilient and reliable medicines supply includes two distinct elements:

1. The need for meaningful payment reform, including modification of mechanisms within the Medicare and Medicaid payment systems to operationalize a reliability incentive program; and

2. Data to differentiate suppliers based on reliability and resilience, such as the development of a data set, mechanism, or 'score' to enable purchasers to differentiate and identify quality-tested products and reliable manufacturers.

We appreciate the Committee's acknowledgement of the need for a mechanism to differentiate suppliers beyond price and the use of Manufacturer Reliability Agreements for the disclosure of certain supply chain information as dictated by collaboratively developed core standards and, if applicable, advanced standards. This concept is similar to concepts outlined in other proposals, including the recently released white paper, "Policy Considerations to Prevent Drug Shortages and Mitigate Supply Chain Vulnerabilities in the United States."[8] In that white paper, the U.S. Department of Health and Human Services (HHS) outlined two new programs that could help address the broad market issues that are a root cause of drug shortages, specifically focusing on GSIs but acknowledging the solutions outlined can be applicable to other vulnerable medicines.

To promote the quality of medicines, and to drive impactful market changes, USP supports the intent of these programs to bring transparency into the market, link purchasing and payment decisions to supply chain resilience and reliability practices, and incentivize investments in supply chain resilience and diversification in the supply chain, including investments in geographically distributed manufacturing and AMTs. We encourage the Committee to consider how to incorporate measures of quality into the proposed incentives. As quality concerns for some medicines persist, any mechanism for measuring reliability should recognize and reward manufacturers that participate in a pharmaceutical product quality testing program utilizing validated quality testing methods found in the *USP-NF*[9] or other test methods accepted by the FDA.

The Committee could consider the development of a credible and comprehensive mechanism to assess reliability and resilience. This type of tool is considered by many stakeholders, including USP, to be essential to operationalizing payment reform mechanisms.[10] Acknowledgement that a manufacturer's culture of quality, manufacturing quality, and product quality are central determinants of reliability is fundamental to developing solutions. A mechanism to incentivize reliable suppliers

[8] Policy Considerations to Prevent Drug Shortages and Mitigate Supply Chain Vulnerabilities in the United States. 2024; https://aspe.hhs.gov/sites/default/files/documents/3a9df8acf50e7fda2e443f025d51d038/HHS-White-Paper-Preventing-Shortages-Supply-Chain-Vulnerabilities.pdf
[9] USP-NF. 2024; https://www.uspnf.com/
[10] 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%20Quailty%20Management.pdf

of medicines and provide an opportunity to reward medicine manufacturers for quality, resilience, and reliability is a necessary policy reform. However, a fundamental challenge facing the development of this mechanism is a lack of coordinated data to differentiate manufacturers based on these metrics.

The formation of a public-private partnership could be one potential solution to ensure that relevant supply chain stakeholders have an opportunity to participate in the design of a quality assessment mechanism, engage in dialogue, and play a role in the development of a successful tool.

b. Establish public-private partnership(s) with oversight from the HHS Supply Chain Resilience and Shortage Coordinator to develop a mechanism to meaningfully reward medicine manufacturers for investments in quality, resilience, and reliability that would:

1. Underscore the value of drug supply chain resilience and reliability by rewarding participant adherence to long-term, committed volume contracts with manufacturers and penalizing those who break them;
2. Incorporate drug shortage prevention factors, such as backup raw material suppliers, manufacturing flexibilities and redundancies, inventory buffers, domestic and nearshore manufacturing capabilities, and risk management plans;
3. Aggregate currently available metrics such as metrics from the USP Medicine Supply Map, reputable product-level quality testing data that utilizes validated test methods from the *USP-NF* or others accepted by the FDA, publicly available metrics from FDA, and other relevant metrics;
4. Enable product-specific assessments that are useful for drug purchasing agents, such as drug product quality testing utilizing validated test methods; and
5. Function as a tool for decision making tied to financial incentives outlined in the Committee's draft legislation, such as innovative Center for Medicare & Medicaid Services (CMS) payment programs, tax incentives, price supports, federal grants and loans, and other incentives.

The components of this mechanism should also serve as criteria to evaluate and apply new payment benchmarks that reward quality. Further, this tool can be utilized by private purchasers to inform buying decisions based upon quality and reliability.

3. Incentivize modern manufacturing technologies
Support efforts to increase utilization of AMTs and foster geographic diversification of manufacturing

USP is pleased to see concepts related to AMTs included in the Committee's draft legislation. For many years, USP has been supportive of efforts that enable innovative approaches and increased adoption and implementation of AMTs such as continuous, additive, and distributive manufacturing technologies, which can improve manufacturing efficiency, reduce production costs, reduce environmental footprints, and facilitate supply chain resilience. USP has invested in specific laboratory capacity for the development of public quality standards that can be utilized to accelerate adoption of AMT. USP standards for AMT will provide greater regulatory predictability by providing manufacturers with guidance on ensuring product quality through advanced technologies for drug manufacturing.

As written, the program in the draft legislation stipulates providers can receive an additional incentive payment for meeting the advanced manufacturing standard for a substantial portion of the manufacture of the applicable generic or components of such generic. While USP applauds the recognition of the positive potential of AMT, it is important to note that significant up-front capital investments are often required for companies to adopt advanced technologies, which can present a greater challenge for lower margin, lower priced products such as generics with multiple competitors. Adoption of AMTs to produce generic drugs has been lower than for innovator products, with cost considerations and economic factors noted as obstacles to the adoption of new technologies.[11] **To fully recognize the intended benefit of the proposed incentive, USP supports near- and long-term financial incentives and necessary supports to bolster and enable greater adoption of AMT by manufacturers[12] and urges further consideration of how and the degree to which the advanced manufacturing provider incentive structure could directly impact generic manufacturers' adoption and utilization of AMTs.**

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USP thanks the Committee for its attention to addressing drug shortages and improving medicine supply chain resilience. We look forward to working with this Committee and Congress to seek solutions to drug shortages that will ensure patients have access to the therapies they need. In the meantime, if you have any questions or would like additional follow-up, please contact Joe Hill at: Joe.Hill@usp.org for more information.

Sincerely,

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[11] Technology Solutions for Improving the Resilience of Generic Prescription Drug Manufacturing. 2023; https://www.brookings.edu/wp-content/uploads/2023/12/20240110_CHP_Wosinska_WSSummary.pdf

[12] Recognizing Challenges and Opportunities to Support Adoption of Advanced Manufacturing Technologies for Medical Products. 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=