VIA ELECTRONIC SUBMISSION

March 29, 2023

Senate Committee on Health, Education, Labor, and Pensions
428 Senate Dirksen Office Building
Washington, DC 20510

Re: Pandemic and All-Hazards Preparedness Act Reauthorization Request for Information

Dear Senators Sanders, Cassidy, Casey and Romney:

The United States Pharmacopeia (USP) is pleased to provide a response to the Senate Committee on Health, Education, Labor, and Pensions (HELP) Request for Information on policies related to the Pandemic and All-Hazards Preparedness Act (PAHPA) reauthorization. USP is an independent, scientific, global non-profit organization founded in 1820. A core pillar of USP's work is to help strengthen the global supply chain so that the medicines that people rely on for their health are available when needed and meet quality standards as expected and required. USP is governed by more than 500 organizations, including scientific, healthcare practitioner, consumer, and industry organizations, as well as dozens of government agencies, who together comprise the USP Convention.

The COVID-19 pandemic has highlighted risks and vulnerabilities in our pandemic preparedness response infrastructure and medicines supply chain, which need to be addressed to respond more effectively to the ongoing pandemic and to prepare better for the next one. USP supports a multifaceted approach to address these risks and vulnerabilities and offers the following comments for the Committee's consideration during the PAHPA reauthorization process.

Additional Data and Insights Are Needed to Guide Policy Reforms to Strengthen the Resilience of the Medicine Supply Chain

We commend Congress for the inclusion of several provisions in the Omnibus spending bill signed into law in December 2022 that aim to bolster the medicines supply chain and prepare for future public health emergencies. Among these provisions, support for the development and implementation of advanced and continuous pharmaceutical manufacturing technologies and investments in supply chain resilience were important initial steps to improving and building a more sustainable supply chain.

As the Committee considers how it might further build on these efforts, USP recommends that the Committee prioritize the identification of upstream supply chain risks. Early disruptions during the pandemic occurred within this part of the supply chain, where raw chemicals, active pharmaceutical ingredients (APIs), and finished dosage forms are produced, refined, and packaged. Disruptions and vulnerabilities in the upstream supply chain continue to present risk to the resilience of the medicines supply chain. Improved visibility into and analysis of the vulnerabilities of the upstream medicines supply chain can help target potential policy reforms and inform U.S. government investments to enhance resilience. Neither a single government agency nor any industry entities have a complete view of upstream supply. This lack of clarity can lead to a poor understanding of the risks impacting the U.S. medicines supply.

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

To address these challenges, USP proposes that the Committee consider the establishment of and investment in a public-private partnership to support supply chain resilience. A centers of excellence model could be an appropriate construct for such partnership, although other models could be effective as well. Activities undertaken through the partnership could include:

- Monitoring the pharmaceutical supply chain for disruptions, shortages, and quality issues;
- Coordinating among the Department of Health and Human Services, Department of Commerce, Department of Defense, Department of Veterans Affairs, other federal and state agencies, global and multilateral organizations, allied trading partners, academic research institutions, non-profits, and private sector entities to identify, assess, and respond to supply chain challenges;
- Building predictive capabilities to inform stakeholders, including the U.S. Government, manufacturers, wholesalers and hospitals, of the risk of supply chain disruption with enough notice that mitigative action can be taken;
- Informing decisions made by the Strategic National Stockpile on medicines to include; and
- Periodically issuing public recommendations and reports on ways to prevent supply chain disruptions, shortages and quality issues.

The USP *Medicine Supply Map* could be utilized in such a partnership. The USP *Medicine Supply Map*, which is a data intelligence platform designed to identify and assess the resiliency of drugs and medical products (www.usp.org/medicinesupplymap), uses multiple sources of information to identify the worldwide sites of pharmaceutical ingredient and finished dose medicine manufacturing. More than 40 datasets from USP, 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 covers 92 percent of FDA-approved generic prescription drugs. Notably, 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 active pharmaceutical ingredient (API) manufacturing facilities.

Efforts like the *Medicine Supply Map*, which inform decision making with insights on vulnerabilities in the upstream supply chain, would make an important and unique contribution to targeting US government investments where they can be most effective in fortifying the drug supply.

Additional Investments and Incentives Are Needed to Overcome Barriers to Adoption of Advanced Manufacturing Technologies (AMT)

Manufacturers have long produced pharmaceuticals using a method known as “batch manufacturing.” Advances in manufacturing technologies – collectively referred to as advanced manufacturing technologies (AMT) – could help to strengthen supply chain resilience, but significant hurdles must be addressed to foster broader adoption.

Traditional batch manufacturing will remain an essential pillar of global medicine manufacturing strength, and any discussion related to onshoring must consider existing capacity for batch manufacturing. Recent studies suggest up to 50 percent of manufacturing capacity in the U.S. is

not utilized. Implementing market-based incentives that encourage utilization of this excess domestic capacity would enhance the resilience of the U.S. medicines supply chain.

At the same time, AMT, including pharmaceutical continuous manufacturing (PCM), can be phased into unutilized manufacturing sites in some cases. PCM can provide efficiencies for many medicines and their ingredients and could facilitate expansion of domestic manufacturing in the U.S., particularly for the manufacture of critical medicines.

PCM is highly automated and involves a continuous flow of materials in a single facility, from inputs to process outputs, such as an active pharmaceutical ingredient or finished drug product. It can enable flexibility and efficiency, lower production costs, cut the environmental footprint, accelerate production and scale-up in response to emergencies and reduce potential quality issues through real-time monitoring. In contrast, in traditional batch manufacturing, the raw materials that are eventually transformed into the final product (e.g., a tablet) are processed in different machines at different times and potentially in different locations. This process naturally requires many starts and stops in manufacturing.

Continuous manufacturing provides a set of technologies that can help bring manufacturing back to U.S. soil and may allow economies that are new to pharmaceutical manufacturing to establish production plants of quality medicines and APIs. However, substantial challenges stand in the way of broader adoption of PCM. These obstacles can include knowledge about the areas where PCM use could be the most impactful and how to best implement it; workforce capacity challenges with an industry-wide shortage of PCM expertise; considerable capital and start-up costs associated with establishment of new facilities; lack of clarity on the return on investment; and ongoing uncertainties regarding regulatory reviews and approvals of medicines made with PCM around the world.

USP is working with partners to address PCM knowledge gaps through educational programs; the creation of an online continuous manufacturing Knowledge Center in collaboration with the National Institute for Pharmaceutical Technology and Education (NIPTE) and funded by FDA; and the launch of a flow chemistry research and development (R&D) laboratory to investigate novel routes of synthesis for API using PCM and develop new analytical techniques to help ensure product quality. To build upon these efforts, USP supports the authorization of appropriations to fund workforce training on AMT.

However, not all drug manufacturers have the financial resources necessary to invest in AMT; this is especially true for manufacturers of low-margin drug products. Addressing these economic and market factors will be fundamental to fostering broader uptake of these promising advanced manufacturing technologies for lower margin medicines.

Efforts Must Be Made to Prevent Antimicrobial Resistance from Becoming the Next Global Public Health Crisis

USP supports a multifaceted approach to addressing antimicrobial resistance (AMR) which includes prioritizing building resiliency in the antibiotics supply chain. A stagnant pipeline for new antimicrobial medicines threatens public health given the global spread of AMR. Recent trends, such as unpredictable market dynamics and the inability to recover high investment costs, have discouraged the research into, and development of, new antibiotics and novel AMR products, including biologics. The Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB), codified into legislation through the Pandemic and All-Hazards Preparedness and Advancing Innovation Act in 2019, serves as a valuable resource to provide

advice, information, and recommendations related to US government activities aimed at combating AMR. The efforts of PACCARB underscore the multidimensional factors that contribute to AMR and the need for a coordinated approach to address AMR.

USP supports the funding of research into vulnerabilities in the antibiotic supply chain and strongly encourages including investigation of antibiotic quality as a risk factor. Additionally, approaches to advance incentives for the development of novel antimicrobial medicines should consider the impact poor-quality products have on pathogens' ability to develop resistance and render products ineffective. Ongoing research via the USP Quality Institute (Quality Institute | USP) and other efforts provide evidence that antibiotic resistance emerges when pathogens are exposed to substandard antimicrobial medications and that resistance may spread globally across product classes. While it is imperative to consider the geographic distribution of antimicrobial medicine manufacturing to ensure access, it is equally essential to focus on conserving the quality and effectiveness of all antimicrobial medicines in the supply chain to help reduce the risk of a continuing cycle of pathogen resistance to each new antimicrobial product. As COVID-19 has shown us, pathogens travel around the world quickly, which makes antimicrobial resistance an urgent concern.

***

USP appreciates the opportunity to engage with the HELP Committee, and we look forward to continued collaboration as we seek innovative solutions to improve our nation's pandemic planning and response capabilities and strengthen the pharmaceutical supply chain. Again, thank you for the opportunity to comment on the Request for Information. Should you need additional information about USP's comments or wish to further discuss ways in which we can work together, please do not hesitate to reach out to Joseph M. Hill, Director, U.S. Government Affairs at Joe.Hill@USP.org or 202-239-4137.

Sincerely,

Anthony Lakavage, J.D.
Senior Vice President, Global External Affairs
Secretary, USP Convention and Board of Trustees
APL@usp.org
(301) 816-8334