

## VIA ELECTRONIC SUBMISSION

February 4, 2022

The Honorable Patty Murray  
Chair, Committee on Health,  
Education, Labor and Pensions  
Room 154 Russell Senate Office  
Building  
Washington, DC 20510

The Honorable Richard Burr  
Ranking Member, Committee on  
Health, Education, Labor and Pensions  
Room 217 Russell Senate Office  
Building  
Washington, DC 20510

Dear Chairwoman Murray and Ranking Member Burr,

On behalf of the United States Pharmacopeia (USP), I am writing to applaud your leadership on the release of the discussion draft of the “Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act” (“PREVENT Pandemics Act” or draft). This legislation will greatly improve our nation’s pandemic planning and response capabilities, as well as strengthen the pharmaceutical supply chain to help ensure that patients have reliable access to quality-assured medicines they can trust. USP appreciates the opportunity to provide feedback.

USP is an independent, scientific, global non-profit organization founded in 1820 and dedicated to building trust where it matters most: in the world’s medicines, dietary supplements, and foods through rigorous science and public quality standards.<sup>1</sup> A core pillar of USP’s mission is to help strengthen the global supply chain so that the medicines people rely on for their health are available when needed and meet quality standards as expected and required. USP works closely with the U.S. Food and Drug Administration (FDA), other government agencies, and across the health and science communities to develop USP standards (over 6,000 today) that are enforced by the FDA. In addition to our work on standards, USP remains an active participant in many public-private partnerships on supply chain related issues. This includes work with the FDA, the Assistant Secretary for Preparedness and Response (ASPR), and the Biomedical Advanced Research and Development Authority (BARDA). USP is 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.<sup>2</sup> The USP Convention elected the 12 members of the USP Board of Trustees, which oversees our work.<sup>2</sup>

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

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<sup>1</sup> USP standards are developed by Expert Bodies comprised of more than 750 scientific experts. These experts collaborate to develop USP standards through an open, transparent process, offering the ability to adjust standards to confront public health emergencies, adapt to new industry practices, and keep up with evolving science and technology.

<sup>2</sup> USP’s governing bodies in addition to the [Council of the Convention](#) include its [Board of Trustees](#) and Council of Experts.

better for the next one. USP supports the multifaceted approach taken in the PREVENT Pandemics Act to address these risks and vulnerabilities and offers the following general comments on the draft:

- **Improving public health response coordination.** USP commends efforts to improve coordination and clarify roles and responsibilities of departments and agencies in public health and medical preparedness and response activities during a public health emergency. USP also believes that Congress should increase funding for our public health agencies to ensure that they can meet their mission of preparing for and responding to pandemic threats and potential disruptions in the medical supply chain.
- **Strengthening public health communication.** USP strongly supports efforts to counter misinformation during public health emergencies such as developing recommendations for effective communication and dissemination of evidence-based scientific information. USP quality standards remain a trusted source of reliable, science-based information to help ensure that medicines are produced consistently and according to regulatory expectations for quality. In addition, over the course of the COVID-19 pandemic, USP has worked with vaccine manufacturers; federal agencies including CDC, BARDA, and FDA to develop guidance on the handling of vaccines to enable the drawing of additional vaccine doses from vials, to compound quality hand sanitizer when it was in shortage, and to identify falsified medical products. While partnering with stakeholders in each of these areas to develop public guidance, USP's scientific expert committees reviewed and contributed to these guidance resources. In this way, we leveraged the trusted and mission-focused scientific platform of USP to bring critical and credible information to a range of stakeholders in a timely manner. We look forward to more collaborations like these in the future to support informed decision-making.
- **Improving public health data availability and access.** USP applauds efforts to modernize public health data standards and develop best practices to improve the quality of demographic data collection. USP continues our dedication to developing standards and solutions to advance medication safety by increasing interoperability and promoting health equity.
- **Addressing disparities and improving public health emergency responses.** USP supports further study on the effects of health disparities on health outcomes during public health emergencies from the National Academies of Sciences, Engineering, and Medicine (Academies). We aim to help advance health security, health literacy, and health data collection through collaboration with experts and are prepared to support the Academies as it conducts its study.

***In addition, USP provides the following detailed comments on several specific sections of the draft.***

## TITLE IV—MODERNIZING AND STRENGTHENING THE SUPPLY CHAIN FOR VITAL MEDICAL PRODUCTS

The global supply chain for medicines has numerous vulnerabilities that can be challenged by acute disruptions, for example, from natural disasters, public health emergencies, and quality-related disruptions in manufacturing. An FDA analysis of 163 drugs that went into shortage during the five year period from 2013 to 2017 found that quality problems in manufacturing were responsible for 62% of the shortages.<sup>3</sup> 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. Unfortunately, the COVID-19 pandemic brought these impacts into sharp focus.

USP urges Congress to prioritize the identification of upstream supply chain risks, which can enable regulator and industry action to reduce medicine supply disruptions while also providing evidence to inform public investment and policy reforms that build more 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.<sup>4</sup>

USP has invested millions since early 2020 to develop and continuously improve upon an informatics tool, the **Medicine Supply Map**, to help identify, characterize, and quantify vulnerabilities in the upstream pharmaceutical supply chain, deliver insights that can guide risk mitigation strategies and investments, and help inform policy changes that advance supply chain resilience.<sup>5</sup> The *Medicine Supply Map*, the first ever of its kind, uses multiple sources of information<sup>6</sup> to identify the worldwide sites of raw ingredient and medicine manufacturing. These data are enriched with information about risk drivers<sup>7</sup> such as price and ingredients and cover 92 percent of FDA-approved generic prescription drugs. The model is also informed by insights on the use of USP quality standards in nearly 22,000 finished drug product, active pharmaceutical ingredient (API), and excipient manufacturing sites in 150 countries.

To help build a more sustainable supply chain, USP recommends that Congress support efforts to identify and assess the resiliency of drugs and medical products, such as the *Medicine Supply Map*. USP also is pleased to have been in numerous discussions with federal agencies about formally utilizing these tools which have been developed by USP without any external resources as a part of fulfilling our public health mission. Modest federal support to expand this work and formally utilize it to 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 supply chain.

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<sup>3</sup> U.S. Food and Drug Administration, “Drug Shortages: Root Causes and Potential Solutions,” October 2019.

<sup>4</sup> USP. 2021. *Are My Medicines at Risk of a Shortage?* Available at: <https://qualitymatters.usp.org/are-my-medicines-risk-shortage>

<sup>5</sup> USP. 2022. *Medicine Supply Map*. Available at: <https://www.usp.org/supply-chain/medicine-supply-map>

<sup>6</sup> Over 20 datasets from USP, FDA, the Centers for Medicare & Medicaid Services, European Medicines Agency, World Health Organization, and private sector sources are included in the *Medicine Supply Map*

<sup>7</sup> Currently, the *Medicine Supply Map* includes over 250 million aggregated datapoints on risk indicators including manufacturing location, chemical information, price, dosage form, and quality.

## Section 402. Supply chain considerations for the Strategic National Stockpile.

***USP supports amending the Strategic National Stockpile (SNS) Annual Threat-Based Review to include an assessment of the supply chains and any vulnerabilities for products that SNS plans to purchase during the period covered by the Review. USP strongly encourages utilizing the Medicine Supply Map to inform the Review and resulting decisions.***

The SNS, which is a repository of medicines and essential medical supplies, is critical for the protection of the American public. USP supports the Government's building and maintenance of stockpiles of critical medicines and medical products to be prepared to meet the needs of patients and healthcare providers if product shortages result from a crisis. The composition of the essential products in national stockpiles should be continually reviewed and modified to address the most likely shortages of the included products.

The *Medicine Supply Map* is leveraging myriad data in a model to predict and assess the resiliency of drug products based on the expected resiliency of their upstream supply chains. The model also fills knowledge gaps that were highlighted in the 100-day supply chain report from the White House.<sup>8</sup> Simply put, the insights from the *Medicine Supply Map* can be leveraged as part of a proactive effort to identify medicines that require additional investment or policy action to help ensure their supply and determine what medicines to prioritize, especially those medicines purchased for the SNS. USP stands ready to assist authors of the SNS Annual Threat-Based Review with insights from the *Medicines Supply Map* and related data analysis.

## Section 404. Improving transparency and predictability of processes of the Strategic National Stockpile.

***USP applauds the proposal to issue guidance on how stakeholders can access the SNS and other countermeasures. USP also applauds the call to convene stakeholders to share information related to the SNS and supply chain and stands ready to join the conversation and provide important insights related to supply chain vulnerabilities.***

USP, in collaboration with several other organizations, recently developed a series of recommendations to improve the resiliency of the U.S. supply chain and mitigate medical supply shortages.<sup>9</sup> The COVID-19 pandemic highlighted weaknesses in our supply chain, including difficulty in accessing the SNS, as well as deficiencies in the medications and devices included in the SNS. The series of recommendations propose several actions to improve the function, composition, and accessibility of the

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<sup>8</sup> The White House (2021). "Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth: 100-Day Reviews under Executive Order 14017". Retrieved August 20, 2021, from <https://www.whitehouse.gov/wp-content/uploads/2021/06/100-day-supply-chain-review-report.pdf>.

<sup>9</sup> Recommendations from the American Medical Association, American Society of Anesthesiologists, American Society of Health-System Pharmacists, Association for Clinical Oncology, and the United States Pharmacopeia. 2021. Available at: <https://www.ashp.org/-/media/assets/news-and-media/docs/Healthcare-Supply-Chain-Recommendation>

SNS during public health emergencies. USP urges consideration of the following recommendations related to the SNS when drafting the guidance.

- Increasing transparency regarding the specific products and quantities of such products included in the SNS and finalizing and regularly updating a list of medicines necessary to respond to potential national-scale public health emergencies.
- Incentivizing the creation of private sector reserves of essential medicines and supplies not adequately provided by the SNS by implementing systems to help facilitate the communication of inventory and availability in geographic regions so that facilities can share inventory when necessary and able. Additionally, we recommend increasing the use of data from additional sources, such as wholesalers and distributors, to forecast supply rather than requiring regular hospital inventorying of medical supplies.
- Creating a workable process for SNS requests that includes: establishing a process for planned non-emergency distributions from SNS to medical facilities of medications and devices prior to their expiration dates at discounted prices to promote practiced workflows and decrease wastage due to expired and obsolete products; publishing a clear, nationally consistent process for making requests from the SNS, including publication of contact information for key personnel in each agency that has responsibility for managing requests and distributions from the SNS; engaging pharmacists, physicians, other clinicians, and supply chain experts to develop processes for maintaining and refreshing products in the SNS; creating a standard distribution logistics process for medications, devices, and related supplies from the SNS, which incorporates feedback from clinicians and supply chain experts, including clear expectations for how updates to these processes will be publicized, if needed, in the event of a national emergency; and publishing criteria, including an overarching organizational strategy, which will be used to prioritize distribution of products from the SNS, including clear expectations for how updates to these criteria will be publicized, if needed, under both normal operations and in the event of a national emergency.

The ongoing public health crisis has magnified the dangers inherent in failing to address gaps and deficiencies in the pharmaceutical supply chains, including in the SNS. These recommendations are intended to provide a range of potential policy and marketplace changes to improve supply chain quality, SNS process, and overall resilience.

## **TITLE V—ENHANCING DEVELOPMENT AND COMBATING SHORTAGES OF MEDICAL PRODUCTS**

### **Section 501. Advancing qualified infectious disease product innovation.**

***USP supports the expansion of eligibility for the Qualified Infectious Disease Product (QIDP) designation to include biological products.***

A stagnant pipeline for new antimicrobial medicines threatens public health given the global spread of antimicrobial resistance (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.<sup>10</sup> Expanding eligibility for QIDP designation to biological products will help incentivize more options for novel antimicrobial treatments and help combat AMR.

In the United States, more than 2.8 million antibiotic-resistant infections occur each year, resulting in more than 35,000 deaths.<sup>11</sup> Globally, an estimated 700,000 people die each year from AMR<sup>12</sup> and without an immediate, collaborative response at the global level, AMR could lead to 10 million deaths a year by 2050.<sup>13</sup> AMR was one of the world's most concerning public health issues before the emergence of COVID-19, and as we recover from the pandemic, AMR will be an even more urgent issue.

Unfortunately, existing efforts to address AMR have been diverted due to the ongoing pandemic, during which misuse of antibiotics to treat COVID-19 has increased; in many circumstances, patients are receiving antibiotics for COVID-19 although they are entirely ineffective in treating it. For instance, a meta-analysis found that 71.9 percent of patients hospitalized with COVID-19 before mid-April 2020 received antibiotics, even though only 6.9 percent of these hospital admissions were associated with bacterial infections.<sup>14</sup> A similar study by Pew Charitable Trusts suggests that in 96 percent of admissions for patients diagnosed with COVID-19, an antibiotic was given prior to confirmation of a bacterial infection.<sup>15</sup>

In addition to the expansion of QIDP eligibility, we encourage Congress to consider other approaches to address AMR. USP supports a multifaceted approach to addressing AMR, including:

- Prioritizing building resiliency for the supply of antimicrobials.
- Building capabilities among global stakeholders to reduce the proliferation of poor-quality anti-microbials globally, especially in LMIC countries. Ongoing research via the USP Quality Institute<sup>16</sup> and other efforts provide evidence that resistance emerges when pathogens are exposed to substandard antimicrobial medications and that resistance may spread across product classes. So, while it is imperative to incentivize new antimicrobials, it is equally essential to focus on conserving the effectiveness of existing

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<sup>10</sup> USP. 2020. Addressing Antimicrobial Resistance. Available at:

<https://www.usp.org/sites/default/files/usp/document/about/public-policy/policy-position-paper-amr-2020.pdf>

<sup>11</sup> Biggest Threats and Data: 2019 AR Threats Report. CDC website. Accessed August 17, 2020.

<https://www.cdc.gov/drugresistance/biggest-threats.html>

<sup>12</sup> World Health Organization (WHO). Antimicrobial Resistance Global Report on Surveillance. April 2014. Accessed August 17, 2020. <https://www.who.int/antimicrobial-resistance/publications/surveillancereport/en/>

<sup>13</sup> World Health Organization (WHO). New report calls for urgent action to avert antimicrobial resistance crisis. April 29, 2019. Accessed August 17, 2020. <https://www.who.int/news-room/detail/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis>

<sup>14</sup> Langford et al. 2020. Bacterial co-infection and secondary infection in patients with COV/019: a living rapid review and meta-analysis. Available at: [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30423-7/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30423-7/fulltext)

<sup>15</sup> Pew Charitable Trusts. 2021. Could Efforts to Fight the Coronavirus Lead to Overuse of Antibiotics? Available at: <https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2021/03/could-efforts-to-fight-the-coronavirus-lead-to-overuse-of-antibiotics>

<sup>16</sup> USP Quality Institute, at <https://www.usp.org/our-impact/quality-institute>.

medicines. Otherwise, the world will face a continuing cycle of pathogen resistance to each new antimicrobial product.<sup>17</sup>

- Improving antimicrobial stewardship by addressing over- and inappropriate prescribing.
- Improving patient adherence to treatment regimens.
- Implementing steps to fund or incentivize more research and development into the next generation of products.<sup>18</sup>

Approaches to advance incentives and improve reimbursement for priority antimicrobial medicines should consider the impact of poor-quality products on the lifetime of current and future antimicrobial products. A robust and diversified pipeline of new antimicrobial products is critical in anticipation of AMR that spreads faster and further than predicted. At the same time, a concerted global focus, including US leadership, is needed to conserve the effectiveness of existing antimicrobials because, as COVID-19 has shown us, pathogens travel around the world which makes antimicrobial resistance an urgent concern that requires global action.

We urge Congress to prioritize efforts to prevent AMR from becoming the next global public health crisis.

## Section 506. Advanced platform technologies.

***USP applauds the establishment of a designation system for advanced platform technologies “to bring significant efficiencies to the drug development and review process.” This designation will be important for such platform technologies as mRNA, viral vector vaccines, monoclonal antibodies, and antiviral drugs. We do, however, urge Congress to ensure that principles of patient access and fair market competition are maintained as these new technologies are developed.***

We also encourage multistakeholder efforts to address common quality challenges that may arise during the development of these new platform technologies (lack of tools to assess quality have been shown to slow new medicine technology adoption in the past). Since the successful application of platform technology, such as mRNA, is relatively new, there are limited regulatory guidelines and industry standards to guide non-proprietary aspects of mRNA quality during development and manufacturing. These include areas such as verifying the identity of the drug substance, controlling impurities, and measuring content for dosing. Without a common set of methods for assessing quality across these dimensions of product development, researchers and manufacturers of mRNA products must develop their own in-house methods and protocols, which diverts their attention and resources,

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<sup>17</sup> A World Health Assembly resolution adopted in 2015 introduced a [Global action plan on antimicrobial resistance](#) that outlined five objectives, including an increased focus on preventing, detecting, and responding to poor quality antimicrobials as a key tool to conserving the effectiveness of antimicrobial medicines. This resolution was sponsored and supported by the U.S. government.

<sup>18</sup> USP. 2020. Addressing Antimicrobial Resistance. Available at: <https://www.usp.org/sites/default/files/usp/document/about/public-policy/policy-position-paper-amr-2020.pdf>.

and reduces regulatory predictability. This can delay approval/authorization of an mRNA-based product, slowing patient access to it.

To help address this need, USP is developing a set of analytical methods for mRNA quality to support developers, laboratories, manufacturers, and regulatory agencies worldwide. The goal is to create scientifically-validated tools on mRNA quality attributes overall, which aim to help accelerate product development, guide successful scale-up of manufacturing, and fuel confidence that manufacturers are employing best practices and appropriate quality controls when using this new modality. Ultimately, this will yield faster patient access. USP will be calling on industry, academic, and government experts with experience or interest in mRNA vaccines and technology to provide feedback on methods, and we encourage the submission of alternative analytical methods as well as supporting documents (e.g., validation documentation).

### Section 511. Ensuring registration of foreign drug and device establishments.

***USP supports the amendment to clarify that registration with FDA is required for any foreign drug and device establishment “engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device that is imported or offered for import into the United States,”<sup>19</sup> regardless of whether the drug or device undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.***

Limited visibility into the supply chain can create problems for the quality of medicines and supply chain resilience. Further, the more diffuse and fragmented the supply chain is across multiple jurisdictions, the greater the risk that important information about the origin, production volume, distribution chain, and integrity of products can be lost, and with it the ability to identify potential problems and respond appropriately. Increased clarity around the registration requirement supports greater visibility across the drug and device supply chains by helping to ensure that all foreign establishments that manufacture or process drugs or devices intended to be marketed in the United States must register with FDA, even if the establishment does not directly import products into the United States.

### Section 512. Extending expiration dates for certain drugs.

***USP supports efforts to provide additional guidance that would aid in establishing the longest feasible expiration dates supported by stability studies to help mitigate or prevent drug shortages.***

The mitigation and prevention of drug shortages is essential, especially during a pandemic. Guidance that would help extend expiration dates could help prevent supply disruptions that may lead to drug shortages. According to FDA’s drug

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<sup>19</sup> Section 510(i)(1) of the FD&C Act.



shortage report, “Shortages can be exacerbated if drugs must be discarded because they exceed a labeled shelf life based on unnecessarily short expiration dates.”<sup>20</sup>

### Section 518. Advanced manufacturing technologies designation pilot program.

***USP supports the advanced manufacturing pilot program, and we encourage Congress to direct the pilot program to help address the barriers outlined below and explore solutions that involve both the public and private sectors.***

***USP also supports and would be greatly interested in participating in a public workshop on the advanced manufacturing pilot. We encourage Congress and the FDA to include industry and other relevant stakeholders, such as standard setting groups and academia, in the workshop.***

Pharmaceutical continuous manufacturing (PCM) is a promising advanced manufacturing technology (AMT) because it enables continuous use of a production line that can yield significantly more product output per square foot of space. This type of AMT has the potential to improve manufacturing efficiency, reduce production costs, and significantly reduce environmental footprints. 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.

We are pleased to see the proposal for an advanced manufacturing pilot program, and we hope that it will help address some of the barriers to more widespread adoption of AMT. For example, current challenges to increased adoption of AMT include limited experience with this technology across regulators and limited guidance for industry. These challenges lead to uncertainty among manufacturers seeking regulatory approval for products manufactured with AMT.

USP recommends that the pilot program explore ways to bolster relevant regulatory science and enable consistent and efficient regulatory review of finished dose products and API through the use of AMT. This pilot program could also include training of reviewers, inspectors, and other relevant regulatory personnel. The pilot should include input from stakeholders outside of the government who can help address the challenges to greater adoption. For example, USP is actively working in this space, leading research programs in AMT quality and beginning work on developing public standards as well as partnering with other leading organizations, like the Medicines for All Institute at Virginia Commonwealth University, to build analytical laboratory infrastructure and workforce capacity. By working together with committed and experienced stakeholders such as USP and other organizations, the pilot program could help reduce several of the challenges to broader adoption of PCM.

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<sup>20</sup> FDA Report, “Drug Shortages: Root Causes and Potential Solutions.” Available at: <https://www.fda.gov/media/131130/download> (updated Feb. 21, 2020).

## Conclusion

Again, we thank you for releasing this important discussion draft to improve our nation's pandemic planning and response capabilities and strengthen the pharmaceutical supply chain. We are committed to working with you on the advancement of this bill. 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](mailto:Joe.Hill@USP.org) or 202-239-4137.

Sincerely,



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