VIA ELECTRONIC SUBMISSION

August 2, 2024

The Honorable Diana DeGette
U.S. House of Representatives
2111 Rayburn House Office Building
Washington, DC 20515

The Honorable Larry Bucshon, M.D.
U.S. House of Representatives
2313 Rayburn House Office Building
Washington, DC 20515

Dear Representatives DeGette and Bucshon,

The United States Pharmacopeia (USP) appreciates the opportunity to provide comments to your request for information (RFI) regarding policies, initiatives, and proposals that build on the successes of the 21st Century Cures Act and the objectives of the proposed Cures 2.0 Act. We applaud your leadership on these issues and your commitment to advancing modern approaches to the development of life-saving cures and health care improvement.

USP is an independent, scientific, global non-profit organization founded in 1820 and dedicated to building trust in medicines through rigorous science-based public quality standards. We are guided by approximately 500 organizations, including scientific, healthcare practitioner, consumer, and industry communities, as well as dozens of government agencies, who together comprise the USP Convention. A core pillar of USP's mission is to help strengthen the global supply chain so that medicines are available when needed and that they meet quality standards as expected and required. USP's public standards and related programs are created by our expert committees and have helped to protect and improve the health of billions of people around the world. As medicines and other therapies evolve, we believe it is critical to continue to assure the quality of these products in order to realize their full life-saving potential. Although there are many components to the regulatory framework to safeguard medicine quality, public quality standards and adherence to them are foundational.

In addition, standards are indispensable to innovation, providing shared platforms for industry participants to work together to bring new technological solutions to the marketplace. Securing the integrity of fair and broad-based frameworks that establish accurate and workable standards for technology adoption and interoperability is therefore critical for accelerating innovation. Standardization creates a foundational framework from which innovators can design specific solutions, providing a set of parameters to work within so that they can focus their energies on creating tailored and impactful solutions. Standards are also critical in the commercialization of new technologies, building trust and supporting the creation of new markets.

As described in the RFI, you seek to bolster existing policies, identify new policies and initiatives that can help to advance innovative therapies, and further enhance the goals of the 2016 Cures legislation and Cures 2.0. **As part of these efforts, USP urges you to consider concepts and policies that increase adoption of advanced manufacturing technologies (AMTs) and ensure a resilient supply chain for quality medicines as part of your proposals.** These approaches promote an environment that supports the evolving landscape of therapeutic

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development and helps ensure that patients have access to high-quality critical and routine medicines they need, when they need them.

AMTs can speed production of drug products, improve medicine quality, mitigate drug shortages, and facilitate pharmaceutical supply chain reliability

When effectively and appropriately applied to the production of certain drug products, AMTs such as continuous, additive, and distributive manufacturing can help strengthen manufacturing of medicines, provide more flexibility to innovate, reduce lifetime costs of manufacturing, and provide enhanced ability to understand, control, and measure quality of the product through the process. Independently or combined with traditional manufacturing methods such as batch manufacturing or as part of broader technology modernization efforts, AMTs can help to improve drug quality, help to address drug shortages and speed time-to-market.

AMT represents a paradigm shift in pharmaceutical production with unique technical and practical considerations. We are pleased that the Consolidated Appropriations Act, 2023 includes a provision directing the Department of Health and Human Services (HHS) to create national centers of excellence in advanced and continuous pharmaceutical manufacturing. Grants provided to the centers of excellence will support technology development, stakeholder collaboration, best practices, and implementation of the technology. However, USP urges Congress to ensure that the Centers of Excellence in Advanced and Continuous manufacturing are adequately funded. While the 21st Century Cures Act appropriated $100 million to five centers of excellence over a 5-year period, USP supports additional appropriations to build and expand the work of the centers.

In addition to funding the national centers of excellence, we encourage you to consider including support for adoption of AMTs through near- and long-term financial incentives and other policies that will help to bolster and enable greater adoption of AMT by manufacturers. These incentives may be particularly important for lower margin, lower priced products such as generics for which the up-front capital investments required present a significant barrier to adoption.

For many years, USP has been supportive of efforts that enable innovative approaches and increased adoption and implementation of AMTs, including mechanisms to incentivize increased utilization and adoption of AMTs, and has invested in specific laboratory capacity for the development of public quality standards that can be utilized to accelerate adoption of AMT. Standards for AMT may provide greater regulatory predictability by providing manufacturers with guidance on ensuring product quality through advanced technologies for drug manufacturing. USP is actively engaged with a broad range of stakeholders to identify and articulate appropriate public quality standards and practices that will make AMT more accessible and industry uptake more achievable. **We welcome the opportunity to discuss insights gained from these efforts and ways these learnings can inform future initiatives or policy decisions.**

A robust pharmaceutical supply chain is critical to public health

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. The medicine supply chain is complex and vulnerabilities in the upstream supply chain can manifest as shortages of critical and life-sustaining drugs if not mitigated. Shortages are systemic and may have a long-lasting impact on future

innovation. Shortages may occur with many classes of drugs, including oncology drugs, with far-reaching implications for patients and health systems. When oncology drugs are in shortage, health care providers may be forced to make challenging treatment decisions when there are no other reasonable alternatives to first-line therapeutics. Shortages of cancer drugs also slow clinical trials of new treatments when those trials rely on the drugs in short supply as the standard of care. **To advance the next generation of breakthroughs, it is imperative we strengthen the resilience of the supply chain and prevent and mitigate potential shortages of critical medicines, both for patients who need them today and for patients in the future who may depend on new treatments informed by today's standards of care.**

Policymakers and stakeholders, including USP[1], continue to highlight the need for comprehensive actions to prevent and mitigate shortages, including potential programs to measure and incentivize the resilience and reliability of the supply chain, enhancement of public and private collaborations, and geographic diversification within the supply chain. **We encourage you to actively engage those involved in this work to align the goals of a resilient supply chain with the goals and objectives of Cures 2.0 and 21st Century Cures.**

Additional areas of consideration

Antimicrobial Resistance

Cures 2.0 highlights the need to increase antimicrobial innovation. Combating antimicrobial resistance (AMR) necessitates enhanced collaboration, communication, and coordination across stakeholders. Misuse and overuse of antimicrobial medicines are the main drivers of AMR. Poor-quality antimicrobials also contribute to the emergence and spread of AMR because exposure to moderate amounts of the antimicrobial may kill weaker, less-resistant strains, but not stronger ones. The more resistant strains thrive and reproduce at a greater pace. **USP recommends a multifaceted approach to addressing AMR, including:**

- **strengthening the resiliency of the global antimicrobial supply chain, including fostering broader geographic distribution (less concentration) and more sources of APIs which are currently highly concentrated in a few locations;**
- **improving antimicrobial stewardship by addressing over- and inappropriate prescribing, improving patient adherence to treatment regimens, and addressing the impact of antimicrobials in the environment;**
- **building capabilities to reduce the proliferation of poor-quality antimicrobials by strengthening regulatory authorities and surveillance capabilities; and**
- **incentivizing more research and development into the next generation of antimicrobial drug products.**

Cell and Gene Therapies

The development of cell and gene therapies (CGTs) is a growing field that faces regulatory and manufacturing issues as it develops. CGT scientific advancements

[1] Solving drug shortages: A call to action. 2024; https://www.usp.org/supply-chain/drug-shortages

can outpace the speed at which regulatory frameworks are established and despite some flexibility from regulatory agencies, challenges remain. **Cures 2.0 calls for a report on the current state of cell and gene therapy regulation and foreseeable regulatory challenges. USP supports and encourages future iterations of Cures to include updates to this report**. While CGTs have shown exceptional efficacy in treating long-standing unmet medical needs across a spectrum of inherited and other disorders, the challenges facing developers are numerous, diverse, and encompass every aspect from patient identification to administration and follow-up. **USP supports policies that foster the development of innovative CGT products and promote solution-oriented and dynamic resolutions to challenges.**

Increasing Health Literacy

Cures 2.0 recognizes the importance of encouraging and promoting greater health literacy. Approximately 90 million American adults (47%) have limited health literacy, putting them at a higher risk for adverse medication use.[2] Limited understanding of how to use medications can worsen health outcomes and increase costs for patients, as well as the healthcare system. Healthcare professionals play a pivotal role in providing individuals with **clear, understandable, and accessible** health information. USP works with experts and stakeholders to develop dynamic, patient-centered health literacy related standards, tools and solutions for healthcare professionals that promote visual, audio, and written patient understanding and mitigate medication errors, reinforcing our commitment to improve health care quality, patient safety, and the patient experience within the electronic health care system.[3] **We urge you to continue encouraging initiatives and soliciting feedback from a variety of stakeholders to increase health literacy and improve patient outcomes.**

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USP is committed to working with you to advance therapeutic innovations and ensure the quality of the medicine supply for American patients. If you have any questions or would like additional follow-up, please contact Joe Hill at Joe.Hill@usp.org.

Sincerely,

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[2] Gutierrez KM, Cohn LD. Medication Competence, Numeracy, and Health Literacy. Health Lit Res Pract. 2019 Aug 8;3(3):e181-e186. doi: 10.3928/24748307-20190625-01. PMID: 31428735; PMCID: PMC6690220.
[3] See https://www.usp.org/healthcare-quality-safety/health-literacy.