



Resolution

Innovations

USP will explore the development of quality standards and other fit-for-purpose solutions to help stakeholders safeguard the quality of promising healthcare innovations that address patient and public health needs.

Year 3 Update

USP standards build trust and confidence in healthcare breakthroughs, support market access, and advance the quality of medical products, strengthening the medicines supply chain. Given the abundance of new medicine modalities and manufacturing advances, the opportunity is enormous for USP standards and related programs to help ensure quality – from product development to manufacturing, distribution, and delivery – in support of supply chain resilience. To achieve this goal and better anticipate and support stakeholder needs, USP has bolstered its ability to identify and evaluate early technologies and prioritize emerging ideas and trends in pharmaceutical development.

Key areas of progress over the past fiscal year include:

Pharmaceutical Continuous

Manufacturing – USP’s approach to identifying and addressing industry barriers to adoption of pharmaceutical continuous manufacturing (PCM) shifted gears from planning to executing on long-term initiatives across all three pillars of the strategy, including consulting, science, and standards.

The goal is to help companies interested in pursuing PCM unlock its potential efficiencies, which can facilitate increased geographic diversity in manufacturing and bolster medicines supply chain resilience.

- ▶ USP opened its Advanced Manufacturing Technology laboratory in Richmond, VA, and launched its analytical lab services offerings (also known as R&D analytical solutions) in December 2022. The analytical lab services provided in Richmond and at USP’s facilities in Rockville, MD, will be used to characterize materials and develop and qualify methods to help ensure the quality of medicines made with PCM. At the same time, the services will help industry contain production costs and optimize efficiencies in staffing and resources.
- ▶ USP collaborated through a strategic alliance to develop new methods for three active pharmaceutical ingredients (APIs), which will be included in the Biomedical Advanced Research and Development Authority (BARDA) Strategic API Reserve for essential medicines.



- ▶ Pharmatech Associates (a USP company) executed three projects to facilitate adoption of PCM by providing organizations with targeted business strategy development support and upskilling staff through customized education and training.
- ▶ USP launched the Continuous Manufacturing Knowledge Center (CMKC) in collaboration with the National Institute for Pharmaceutical Technology and Education (NIPTE), supported in part by funding awarded to NIPTE by FDA. The online platform is intended to help address potential knowledge gaps by providing stakeholders with rapid access to the latest, updated information to help identify and address barriers to adoption of PCM.
- ▶ USP joined the Alliance for Building Better Medicines – a central Virginia regional coalition of municipal and state government, industry, academia, and not-for-profits with the goal of leveraging PCM and other advanced manufacturing technologies (AMTs) to help build medicines supply chain resilience.
- ▶ To ensure that USP's AMT work remains nimble, this year we made two strategic adjustments. First, USP shifted the strategic focus of laboratory services offerings from commercially-focused to a donor and government focus. This allowed USP to develop and advance projects specifically related to strengthening the supply chain through the application of AMTs like PCM. Second, USP launched the U.S. Government Federal Practice. This new department within USP's Global Health and Manufacturing Services division is designed to build relationships across the U.S. government sector to expand USP's

solutions within and beyond our two main partners, FDA and the U.S. Agency for International Development (USAID).

- ▶ USP launched a flow chemistry laboratory in Hyderabad, India, to support industry, governments, and USAID- and other donor-funded projects, including development of new, economically and sustainably viable routes of synthesis for APIs and key starting materials.
- ▶ USP developed the first in a planned series of technical guides for PCM, covering development of control strategies for continuous manufacturing of solid oral dosage form drug products.
- ▶ USP organized a July 2023 workshop on identifying and addressing barriers to continuous manufacturing adoption, convening 150 stakeholders from industry, academia, and FDA, in Rockville, MD.

3-D Printing of Pharmaceuticals – 3-D printing (3DP) initiatives at USP graduated from early evaluation to the formal programming and standards development phase. These initiatives aim to help unlock the potential for 3DP technology to enable production of smaller batches of medicines with tailored dosages, shapes, sizes, and release characteristics to facilitate personalized medicine.

Advanced Technology Evaluations – USP continued to identify, explore, and support advancement of new production and distribution methods, new medicine modalities, emerging analytical technologies, and informatics trends and applications.

- ▶ USP launched new research projects to inform its understanding of imaging analytical technologies and to explore green chemistry and other tools to



improve pharmaceutical environmental impact (such as with per- and polyfluoroalkyl substances).

- ▶ In February 2023, USP hosted its first open forum to engage stakeholders on their needs for improving the pharmaceutical environmental footprint.
- ▶ USP initiated studies to evaluate the potential substitution of solvents to reduce environmental impact.
- ▶ USP initiated a pilot evaluation of algorithmic modeling for data comparability of handheld instruments.
- ▶ USP continued to advance polymer material characterization through applications of light scattering technologies.

Complex Generics – Defined as drug products that have a complex active ingredient, formulation, or route of delivery, or are part of a drug/device combination, complex generics are becoming increasingly common, and generic entry increasingly challenging. This year, through robust engagement strategies, USP advanced initiatives to develop a deeper understanding of gaps and opportunities to meet stakeholder needs, identifying appropriate standards, materials, and solutions. Notable accomplishments include:

- ▶ Development of a plan to introduce new extractable and leachable standards, published as a *Stimuli* article in *Pharmacopeial Forum* in July 2023.
- ▶ Convening a two-day complex injectables roundtable that welcomed over 800 global registrants, including those from industry, regulators, and other stakeholders. As a result, USP is developing a needs-based scientific strategy to support stakeholders in the development of complex injectables. Examples

include creating a general chapter for microsphere complex products and developing application notes or methods for molecular weight determination of complex polymers.

- ▶ USP conducted a global regulatory landscape assessment, charting global regulations impacting complex products, documenting global regulatory pathways, and identifying key opportunities for engagement on complex products.
- ▶ USP further engaged with FDA and the Center for Research on Complex Generics (CRCG) through USP-FDA quarterly meetings and discussions with CRCG on nitrosamines and other topics.

Nuclear Magnetic Resonance

Spectroscopy – USP advanced multiple initiatives leveraging nuclear magnetic resonance (NMR) spectroscopy technology for use in quality assurance.

- ▶ USP revised General Chapters <761> *Nuclear Magnetic Resonance Spectroscopy* and <1761> *Applications of Nuclear Magnetic Resonance Spectroscopy* in response to public comments received and to facilitate use of NMR as an analytical technique for demonstrating quality.
- ▶ USP initiated General Chapter <1762> on solid-state NMR to incorporate modern technologies and contemporary practices of NMR spectroscopy and published a *Stimuli* article on “Consistent Terminology for Advancement of NMR Spectroscopy.”
- ▶ USP sponsored its second quantitative NMR (qNMR) symposium in January 2023 with over 500 global attendees, concluding with a roundtable with the qNMR community in China.

- ▶ USP advanced work on the qNMR Knowledge Hub, which is expected to launch in Fiscal Year 2024.
- ▶ In collaboration with a third-party vendor, USP completed the first Good Manufacturing Practice (GMP)-validated method for NMR-based digital references.
- ▶ USP completed feasibility studies for potential use of NMR to identify diethylene glycol (DEG) in cough syrup and create a digital reference for cannabidiol (CBD) suitable for identity and assay testing.
- ▶ In collaboration with the University of British Columbia Department of Chemistry, USP demonstrated proof of concept for a benchtop NMR process analytical technology (PAT) setup for reaction monitoring leveraging USP's USP-ID NMR analysis software. (See *Digital Transformation of Standards Resolution* update.)

Drug Dissolution – In collaboration with the New Jersey Institute of Technology, USP completed studies focusing on the hydrodynamics of reduced-volume dissolution systems using particle image velocimetry (PIV) technologies. As a result of these studies, USP is preparing a scientific paper addressing the findings for publication in a peer-reviewed journal.

Graph Database and Artificial Intelligence Capabilities – USP continued to accelerate its understanding of graph databases and artificial intelligence (AI) capabilities to uncover hidden connections and anomalies across complex data assets and create data-driven predictions and personalized recommendations to meet stakeholder needs. One example of a use case for graph databases and AI is their ability to enable stakeholders to better understand the interconnectedness of USP standards and

related information and create an “ecosystem” view, potentially enabling increased utilization of a range of USP products and services. By leveraging graph databases and AI capabilities, USP has the potential to innovate and transform our business operations, customer experiences, and strategic insight generation as a more digitally-enabled organization.

- ▶ USP matured its understanding of the operational and business impact of graph databases by developing use cases and proofs of concept to understand requirements for scaling graph databases into an enterprise capability.
- ▶ USP developed an early understanding of AI capability and the current market landscape, specifically around large language models (LLMs). Through collaboration with business owners, USP built several use cases to gain additional insight into the capability.
- ▶ In a cross-functional effort, an AI strategy workshop was conducted in January 2023 to understand the potential benefits and impact of AI tools and capabilities on USP's business and operations. Input gathered at the workshop has been incorporated into the development of an AI strategy that will recommend an enterprise approach to AI.

Planned for Remainder of the Cycle

- ▶ USP will develop a mechanism for gathering earlier stakeholder feedback on its portfolio of new solutions to facilitate industry adoption of innovations.
- ▶ USP will continue to identify, evaluate, and incubate emerging technologies for potential integration into the organization's quality-focused solutions.



- ▶ USP plans to leverage PAT to support expanded adoption of PCM through formation of a PAT Expert Panel and expanded laboratory capabilities for PAT research in live manufacturing systems.
- ▶ USP will develop additional technical guides for PCM best practices.
- ▶ USP will publish data evaluating the hydrodynamics of reduced-volume dissolution systems and determine potential applications for monograph inclusion. USP will also conduct computational fluid dynamics studies to understand hydrodynamics across multiple volumes of dissolution media.
- ▶ USP will consolidate learnings on knowledge graph prototyping, propose a roadmap for enterprise

implementation, and continue to identify use cases for AI to enhance USP's current products and ways of working.

- ▶ USP will strengthen our business case for scaling graph databases enterprise wide and will continue to build our understanding for adoption of AI capabilities, such as LLMs and natural language processing.
- ▶ USP aims to launch the qNMR Knowledge Hub in Fiscal Year 2024.
- ▶ USP will launch the USP-ID NMR software. (See *Digital Transformation of Standards* Resolution update.)

Contact

For additional information on this Resolution, contact Michael Ambrose at MRA@USP.org.

