IV

Resolution

Access to Biologics

USP will develop standards and other solutions to support innovation in the efficient development and manufacturing of quality biologics and advanced therapies to increase access to these medicines.

Year 3 Update

USP continues to expand its portfolio of standards, best practices, and tools to support the quality and consistency of biologics, a fast-growing segment of medicine such as recombinant therapeutic proteins including monoclonal antibodies, vaccines, peptides, oligonucleotides, tissues, and cell and gene therapies. This year, USP continued to develop tools and solutions to support emerging modalities, including mRNA and viral vector-based vaccines as well as cell and gene therapies. These efforts help build a common understanding of relevant quality attributes and test methods for biologics to support quality and consistency, thereby strengthening the integrity of the global supply chain for biologics. In addition, these tools offer greater efficiency to industry in the development process and support regulatory reviews. USP also continued to explore advanced manufacturing technologies and analytics that have the potential to increase the supply of biologics and enable more decentralized manufacturing, which remains a key principle of supply chain resilience.

Key areas of progress over the past fiscal year include:

Monoclonal Antibodies – USP expanded its portfolio of solutions to support quality assessment of monoclonal antibodies (mAbs) and collaborated with FDA to evaluate new analytical tools that can accelerate biosimilars development.

- USP was awarded a two-year, $1.5 million grant under the FDA Biosimilars User Fee Act Research Program to enhance biosimilars development and regulatory science. The research focuses on assessment of the multi-attribute method (MAM), an emerging analytical method that has the potential to provide more detailed information on product quality, thereby increasing the efficiency of biosimilars development.
- The MAM Expert Panel completed a draft of *USP* General Chapter <1060> *Best Practices for Mass Spectrometry-Based Multi-Attribute Method for Therapeutic Proteins*, which will be published in

Pharmacopeial Forum (*PF*) in September for public comment.

- USP published the "Monoclonal Antibody (mAb) Analytical Guide," which outlines mAb testing needs at various phases of development and provides links to USP resources to support mAb quality.
- USP expanded its standards and tools for assessment of host cell protein impurities in biologics. Activities included publication in *PF* of new *USP* General Chapter <1132.1> *Residual Host Cell Protein Measurement in Biopharmaceuticals by Mass Spectrometry*, and release of a new reference material.

Advanced Manufacturing and Analytics – USP responded to stakeholder feedback on challenges implementing pharmaceutical continuous manufacturing and in-line/at-line analytics for biologics.

- USP held a hybrid workshop on Biopharmaceutical Continuous Manufacturing in December 2022 at USP headquarters in collaboration with BioPhorum. The workshop was well attended by industry, vendors, academia, and regulators. A publication summarizing the key themes from the workshop was published in *Pharmaceutical Engineering* (July/August 2023 issue).
- USP initiated a new Expert Panel on the topic of in-line/at-line monitoring and real-time release testing to develop a new general chapter that will provide guidance on the application of process analytical technology (PAT) and provide a summary of related technologies, including their strengths and weaknesses.

Vaccine Quality – USP continued its efforts to support quality and consistency of vaccines through publication of new tools and educational offerings and continued its engagement with global stakeholders.

- USP expanded its vaccine quality toolkits to include DNA, virus-like particle, and attenuated virus vaccines.
- USP published a second edition of the Analytical Procedures for mRNA Vaccine Quality: Draft Guidelines, which incorporates feedback and more than 15 new methods received from stakeholders.
- USP expanded engagement efforts, developing new educational materials and trade articles, and presenting over 15 talks on vaccine quality.

Advanced Therapies – USP continued to advance development of standards and tools to support the quality of advanced therapies, with particular focus on adeno-associated virus (AAV)-based gene therapies and lentivirus-based cell therapies.

- USP, the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), and the National Institute of Standards and Technology completed a multi-laboratory study comparing analytical techniques for analysis of empty and full AAV capsid gene therapy. Preliminary results were presented at the NIIMBL national meeting and prepared for publication.
- The AAV Expert Panel continues to advance a new chapter on best practices for manufacturing and quality control of AAV-based gene therapies.
- USP initiated a new Expert Panel on lentiviral cell therapy. The panel is drafting a new general chapter on best practices for the design, manufacturing, and quality control of lentivirus-based cell therapies.

Analytical Reference Materials – USP worked to introduce a new class of products called analytical reference materials (ARMs). These products complement USP's reference standard portfolio by providing materials for use during development and characterization of biotherapeutics. The first ARM, which launched in June 2023, consists of a common host cell protein impurity found in biological products derived from a common bioproduction cell line. ARMs in development aim to support other modalities, including peptides, vaccines, and cell and gene therapies.

Raw and Starting Materials – USP advanced both documentary and physical reference standards and materials to support quality assessments of raw and starting materials.

- The Plasmid DNA Expert Panel completed a draft of *USP* General Chapter <1040> *Quality Considerations of Plasmid DNA as a Starting Material for Cell and Gene Therapies*, which will be published in *PF* in November 2023 for public comment.
- USP released five new reference standards for DNA phosphoramidites, which are critical raw materials for oligonucleotide therapeutics. Additional raw material standards are in development to support other types of oligonucleotides.
- To provide guidance on quality starting materials in the production of oligonucleotide drug products, USP's BIO 1 Expert Committee (EC) recruited expert advisors to draft a white paper in this area as an initial step toward developing a related general chapter.

Stakeholder Engagement – Throughout the year, USP convened stakeholders to help identify and inform solutions that support trust in supplies of quality biologics and to raise awareness of USP solutions that can accelerate quality assessments of biologics. Some highlights in FY23 were:

- The Biologics Sector of the USP Convention collaborated with the FDA Center for Drug Evaluation and Research to develop an infographic to inform dialogue between patients and healthcare providers on the quality of biosimilars. The infographic was launched in September 2022 and was informed by multiple stakeholders, including patient advocacy organizations, innovator and generic manufacturing trade organizations, healthcare societies, and payor and pharmacy benefit manager groups.
- USP held its Asia-Pacific Economic Cooperation (APEC) forum Center of Excellence training in May 2023 for approximately 150 regulators from the APEC region and beyond to address knowledge gaps about quality considerations for chimeric antigen receptor (CAR) T-cell therapies.
- The Fiscal Year 2023 Biologics Stakeholder Forum focused on CAR T-cell chemistry, manufacturing, and control considerations. Based on feedback from attendees, it's clear that additional guidance is needed in this area and input from the event will help the new Lentiviral Expert Panel as they begin their work.
- USP staff delivered approximately 60 presentations at industry conferences and other stakeholder events focused on biologics.
- USP Biologics staff published eight trade journal articles and one peer-reviewed article to raise awareness of solutions supporting the quality of proteins, cell and gene therapies, vaccines, and peptides.

Planned for Remainder of the Cycle

- USP will expand its portfolio of standards and materials for mAbs, with a particular focus on common impurities, functional assessment, and new analytical techniques such as MAM.
- USP will continue to advance draft guidelines for mRNA and viral vectored vaccines based on stakeholder feedback, including evaluating and validating methods. Relevant reference standards and materials will also be identified and developed to support platform methods for these new vaccine modalities.
- USP will continue to expand its portfolio of standards and tools to support cell and gene therapies, including new general chapters on plasmid starting material, AAV-based gene therapies, and lentivirus-based products and reference standards and materials to support common test methods.
- USP will continue to advance work on standards for protein biomarkers used in drug development to support consistent measurement of biomarkers across different immunoassay platforms and kits, with a particular focus on biomarkers used in cell therapy and oncology.
- USP will investigate opportunities to develop microbiology testing reference materials for in-process and release testing of pharmaceuticals in support of existing USP documentary standards. The objective is to facilitate implementation of rapid microbiology testing methods that support industry efforts to make more affordable high-quality drugs for larger patient populations through innovative technologies.

Contact

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