

## Biologics Stakeholder Forum

### Executive Summary

### August 10 & 12, 2021

Biologics are complex products that need extensive knowledge of the manufacturing process for their consistent production. The acquisition, analysis, and cross-checks of this information are laborious and time-consuming, creating high costs for the manufacturer and acting as a barrier to entry for some manufacturers. In response to this challenge, manufacturers are developing innovative technologies to increase the speed of data collection and analysis needed to monitor biologics production and move towards rapid decision making. In-line monitoring (ILM), real-time release testing (RTRT), and *in silico* models all have the potential to reduce costs significantly. *In silico* models can also reduce development and tech transfer time and improve process understanding. However, for these technologies to gain widespread adoption, they need to be supported by standards and appropriate control strategies to ensure the quality of the final products.

To help advance these technologies, the United States Pharmacopeia (USP) convened the second Biologics Stakeholder Forum (SF) on August 10 & 12, 2021. The SF brought manufacturers, regulators, and suppliers together to discuss challenges and possible solutions for these cutting-edge analytical and digital technologies. Each day began with talks from industry and regulatory leaders implementing novel technologies for this purpose and was then followed by moderated breakouts to discuss the real-world issues and opportunities to advance the work.

#### Challenges and solutions

The SF speakers and participants discussed several essential issues, including:

Regulatory risk – Manufacturers prefer technologies where they believe they can better predict regulatory expectations. In response, regulatory participants recommended that developers of novel technologies engage their agencies early and often educate reviewers and set those expectations.

Business case – New technologies require investment; therefore, they need a strong business rationale to justify their adoption. A better business case should also consider leveraging the knowledge gained from these technologies for an entire pipeline and not just a single product.

Comparability – Manufacturers want to limit the need for extensive bridging studies. The industry should therefore create guidance or standards on how to demonstrate comparability when implementing new manufacturing technologies. For example, Raman spectrometry is one of the more common types of analytical methods being evaluated for at- or in-line use. USP chapters <858> *Raman Spectroscopy*, <1858> *Raman Spectroscopy- Theory and Practice*, and <1039> *Chemometrics* provide best practices for the use of these technologies but do not directly address challenges related to their use for ILM and RTRT of biologics.

Common languages – There is a desire for open-source platforms that can take data from multiple instruments and integrate and supply consistent results shared between multiple companies or facilities within one company. This requires a common nomenclature. Instrument and software vendors typically use proprietary software that can be difficult to integrate within a company, while open-source providers are often not sufficiently funded to properly maintain and secure their platform for manufacturing purposes. Something as seemingly straightforward as electronic laboratory notebook adoption can be quite difficult for groups employing many technologies.

Existing efforts – In addition to USP, several groups are actively working in this area, including BioPhorum Operations Group (BPOG) and the National Institute for Innovation and Manufacturing Biopharmaceuticals (NIIMBL). Publication of standards, white papers, and peer-reviewed articles by these groups and individual manufacturers leading this work will spur adoption by the broader industry.

### **Role of USP and Next Steps**

USP is uniquely positioned to convene all types of stakeholders to investigate challenging topics and, where suitable, move important initiatives into its robust, transparent, standard-setting process. These public standards help educate manufacturers, regulators, and other decision-makers about these technologies. Developing physical or performance standards for these technologies will require time; however, USP is actively working on guidance and documentary standards to assist the industry, and several General Chapters are already available in the *USP-NF*.



Related to this Stakeholder Forum discussion, USP recently published for comment proposed chapter <1220> *Analytical Procedure Life Cycle* in the *Pharmacopeial Forum*, PF46(5). The chapter demonstrates the suitability of an analytical method over a product's entire life cycle, including development, validation, and continuous verification, and may be useful for the adoption of new technologies. Besides standards, there is also a need for educational material for regulatory and industry stakeholders to understand the benefits of these technologies and how to best implement and review their performance. USP may be able to help create these educational materials.

Finally, USP has consistently shown its capacity to break silos and link industry participants through its outreach efforts. It will continue to organize events to bring stakeholders together. Based on the findings from this SF, a roundtable will be organized in the near future to bring together subject matter experts working on these complex problems to more clearly define the scope of a potential informational general chapter that was requested by the SF participants. If you have any questions or want to participate in this roundtable, please contact Dr. Maura Kibbey, Principal Scientific Fellow, External Scientific Collaboration, Science-Global Biologics, at [mck@usp.org](mailto:mck@usp.org).

