

USP India Biologics Roundtable on Biological Standards
February 4, 2019
Hyderabad, India – The Westin Hotel & Resort

Executive Summary: The USP moderated a roundtable discussion between the U.S. Food & Drug Administration (FDA), the Medicines and Healthcare Products Regulatory Agency (MHRA), the World Health Organization (WHO) and biologics manufacturers from India and South Korea. The participants came together to focus on challenges facing the industry, including the urgent need for new standards for validating the suitability of analytical methods for monitoring critical quality attributes (CQAs) during the production of biologic therapies. A consensus was reached on a set of potential reference standards and methods that would address several significant problems. The proposed list of standards was further refined based on impact and the feasibility of development by USP. The finalized list of recommended standards reflects a comprehensive overview of industry needs and regulatory expertise.

Main bullet points from the discussion:

- Advanced analytical tools can highlight differences between products, and discretion is required to judge their clinical relevance.
- The industry has yet to come up with agreed-upon methods for detecting and measuring many in-process impurities.
- Participants prioritized several standards based on unmet needs, high demand, and broad applicability across industry and products in conjunction with the feasibility of development by USP.
- The final list includes standards for detecting and quantifying;
 - Protein A leaching off of chromatographic media during the purification of therapeutic monoclonal antibodies
 - Host Cell proteins (HCPs) and Host cell DNA (HCD)
 - mAb charge heterogeneity as a result of post-translational modifications such as deamidation, C-terminal lysine, glycosylation, lysine glycation, and N-terminal pyroglutamate
 - Isoelectric point (pI) and charge variants for mAb analysis by Capillary Electrophoresis (cIEF)
 - Product-related fragmented species of mAbs by Capillary Electrophoresis (CE-SDS).
- Participants also agreed that there is a lack of standard statistical approaches among the various software packages offered by multiple vendors. Different software packages produce different results, and there is a need for harmonized algorithms for data analysis and interpretation for Mass spectrometry, Bioassay and Higher-Order Structures (HOS) using FTIR, CD, FLR when analyzing therapeutic proteins and mAbs.

Path forward:

The roundtable focused attention on current needs for reference standards and procedures for monitoring biologic manufacturing. Industry representatives stressed their desire for standards that work with multiple analytical techniques so that they can be adopted easily. Regulators were also interested in giving manufacturers more flexibility in choosing methods that fit their purpose. The needs expressed by stakeholders align with USP's goal of developing performance standards that enable their use throughout the product development cycle, which likely includes changes in scale, site, and analytical methods.

Please direct all questions or comments to Mitali Samaddar, Director of Biologics, Hyderabad, India at MVS@usp.org.