ASMS Biotherapeutics Interest Group Workshop

72nd ASMS Conference on Mass Spectrometry and Allied Topics, June 2 -7, 2024, Anaheim, CA

Presiding: Andrew D. Mahan, J&J; Sarah Rogstad, CDER, FDA

The Biotherapeutics Interest Group workshop, entitled "Multi-Attribute Method (MAM): Discussion of Best Practices and Diverse Implementations", was held from 5:45 PM to 7:00 PM on Monday, June 3, 2024. The primary goal of the workshop was to seed discussions and promote continuous learning in the MS community on the latest development and applications of Multi-Attribute Method (MAM) in the biopharmaceutical industry.

The workshop started with a welcome note from the co-chairs, and then a general introduction of co-chairs and six selected panelists including Da Ren from Biotherapeutics Solutions, Li Jing from US Pharmacopeia (USP), Andrew Dawdy from Pfizer, Diego Bertaccini from EMD Serono, Sara Carillo from The National Institute for Bioprocessing Research and Training (NIBRT) in Ireland, and Mark Hilliard from Pfizer MSAT Ireland.

After the panel introduction, the discussion group focus definition of What is MAM? the Multi attribute method, MAM as a single LC/MS Assay with potential to supplement and replace traditional chromatographic, electrophoretic, and binding assays for monitoring both product and process quality attributes. A MS based approach to simultaneously monitor several product quality attributes.

Discussion also covered how MAM is based on QbD strategy, a proper MAM method requires deep understanding at the molecular level of the attributes that are crucial for safety and efficacy and for ensuring that the desired quality of the purified protein drug product is met at the end of the manufacturing process (R. Rogers, MAbs. 2015 Sep-Oct; 7(5): 881–890).

A good portion of the meeting focused on introducing the USP General Chapter <1060> Mass Spectrometry-Based Multi-Attribute Method (MAM) for Therapeutic Proteins. Published Sep 1, 2023 with Comments Closed Nov 30, 2023. Status: Comments have been addressed and updated draft is under review by USP. Lin Jing from USP, one of the panelists was able to answer questions related to the USP MAM chapter and also provide a short description of key points include the LC-MS peptide mapping method with proper controls, and MAM has two stages: Characterization stage and Monitoring (QC) stage. Similar to previous years, the consensus from the audience is that the major hurdle encountered during implementation of MAM is not the technical aspect, but rather overcoming the barriers to change from the use of conventional assays and Sarah from FDA answered questions on regulatory

filings using MAM. In general, Sarah encouraged the sponsors to contact the FDA Emerging Technology Team (ETT) before submitting the regulatory filings, and it's a case-by-case decision depending on the nature of the use of MAM in the filings. Andrew from Pfizer, Sara Carillo from NIBRT, and Diego Bertacinni provided some examples and comments on MAM implementation from an industry perspective.

The workshop was adjourned around 7pm. Andrew Mahan will be rotating off as the workshop co-chair after this year. Sarah Rogstad from FDA (Sarah.Rogstad@fda.hhs.gov) will take the lead as coordinator and will add co-chair Sara Carillo (NIBRT) in the 2025 workshop.