Workshop Report

ASMS 73rd Annual Conference – Baltimore, MD
Monday, June 2, 2025
Biotherapeutics Interest Group Workshop: Mass Spectrometry in Quality Control for Complex Biotherapeutic Modalities

Introduction

The Biotherapeutics Interest Group hosted a workshop on "Mass Spectrometry in Quality Control for Complex Biotherapeutic Modalities" during the 73rd ASMS Annual Conference in Baltimore. The session, held on June 2, 2025, attracted a diverse audience from academia, industry, and regulatory agencies. The workshop focused on the evolving role of mass spectrometry (MS) in the quality control (QC) of advanced therapeutic formats—including antibody-drug conjugates (ADCs), bispecific antibodies (bsAbs), and fusion proteins.

These modalities represent some of the most promising drug classes, especially in oncology, but their structural complexity poses unique challenges for development, characterization, and regulatory approval. The workshop explored how MS can address these challenges, its current level of regulatory acceptance, and the path toward broader implementation in QC laboratories.

Coordinators and Presiders

The session was presided over by Dr. Sara Carillo (NIBRT) and Dr. Andrew Mahan (Janssen) serving as workshop coordinator. Together, they framed the session by emphasizing the potential of MS as a Quality by Design (QbD) tool and highlighted both opportunities and limitations for implementation in QC settings.

Panelists

- Adam Evans (Janssen) – LC-MS/MAM expert in analytical development and QC implementation
- Tom Slaney (Bristol Myers Squibb) – Specialist in biotherapeutics characterization and high-throughput assays
- Xiaoxi Zhang (Thermo Fisher Scientific) – Application manager with regulatory and industry collaborations in China
- Jaqueline Picache (AstraZeneca) – Researcher in biotherapeutics and metabolomics mass spectrometry
- Tim Guo (United States Pharmacopeia) – Expert in biologics standards, PTM analysis, and host cell protein quantification

Topics and Discussion Points

1. Current Role of Mass Spectrometry in QC

• Overview of cases where MS has been referenced in BLAs and post-approval supplements.
• Examples of MS used for identity, PTM quantification (oxidation, deamidation, glycosylation), host cell protein analysis, and polydispersity.
• Comparison with traditional orthogonal QC methods such as HPLC-UV.

2. Regulatory Acceptance and Compliance

• How open are agencies to MS as a primary QC method?
• Data integrity, system suitability controls, and integration with existing QC systems.
• Feedback from QC labs and regulators on the feasibility of MS in release testing.

3. Technical and Practical Challenges

• Method transferability from R&D to QC labs: robustness, reproducibility, and training.
• Barriers to adoption: mindset, instrumentation cost, and expertise gaps.
• Bridging feedback loops between QC investigations and R&D method development.

4. Applications in Complex Modalities

• ADCs: Determining drug-to-antibody ratio (DAR), monitoring payload heterogeneity, linker stability, and detection of low-abundant impurities.
• Bispecific antibodies: Resolving chain-pairing issues, validating methods for heterodimeric species, and ensuring structural fidelity.
• Fusion proteins: Strategies for assessing PTMs, addressing size/heterogeneity, and validating MS for complex constructs.

5. Future Outlook

• Potential for MS to replace certain orthogonal methods in QC within the next decade.
• Role of automation and AI/ML in streamlining MS data analysis for QC.
• Real-time release testing (RTRT) and process analytical technology (PAT) approaches for biologics using MS.
• Recent instrument advancements and their promise for regulatory acceptance.

Conclusion

The workshop highlighted that while mass spectrometry is already proving its value in advanced biotherapeutic characterization, its adoption in routine QC remains limited and remains mainly limited to multi-attribute method for standard IgGs products. Consensus emerged around the need for:
1. Regulatory alignment on acceptance criteria.

2. Standardization of methods across organizations.
3. Training and infrastructure to support MS in QC labs.

The panel agreed that MS will play an increasingly central role in ensuring product quality for ADCs, bispecifics, and fusion proteins, but its widespread implementation will require overcoming both cultural and technical barriers.