

Roundtable Session - Table 2 - Innovative Mass Spectrometry Approaches for Emerging Biotherapeutics

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Abstract

Next-generation modalities, from bi- and tri-specific antibodies and ADCs to oligonucleotides and AAVs, redefine the biopharmaceutical pipeline. Analytical characterization demands are reaching unprecedented complexity. Standard LC-MS workflows frequently hit performance ceilings when resolving extreme structural heterogeneity, charge variants, or trace impurities under tight timelines and changing environmental regulations (such as impending PFAS restrictions). This roundtable will explore cutting-edge MS innovations, including native MS, high-confidence structural characterization, multi-attribute methods (MAM), and sustainable mobile-phase strategies. Participants will discuss practical approaches to bridge the gap between high-end analytical capability, daily laboratory robustness, and regulatory acceptance in modern biopharmaceuticals.

Discussion Questions

1) Complex Modalities:

Which emerging biotherapeutic formats (e.g., LNPs, bispecifics, AAVs) currently present the biggest analytical headache in your lab, and where are conventional LC-MS methods failing you?

2) Native MS vs. denaturing LC-MS, qualitative vs. quantitative:

How close are we to seeing native MS or hybrid approaches transition from pure characterization tools into routine QC and release testing? What are the remaining technical bottlenecks and can AI help with data annotation?

3) Green Analytics & PFAS Pressure:

With growing regulatory and corporate pressure to phase out PFAS additives (like TFA) and toxic solvents, how are your teams adapting mobile phases without sacrificing chromatography performance or MS ion yield?

4) Data Bottlenecks & MAM:

As multi-attribute methods (MAM) generate massive datasets, is data processing and software validation now a bigger bottleneck than sample preparation or hardware capabilities? Can AI assist in integrating results from multiple experiments and orthogonal methods?

5) Regulatory Acceptance:

What specific validation data or benchmark studies are regulators (FDA/EMA) consistently asking for before accepting innovative, non-standard MS workflows for release or comparability studies?

Notes

The main takeaway is that advanced MS offers valuable characterization capabilities, but routine QC adoption depends on robust methods, trustworthy data interpretation, manageable costs, and consistent instrument performance.

The draft covers:

Structural heterogeneity and chain mispairing.

AI-assisted interpretation and confidence in results.

Native MS adoption in routine QC.

Data consistency and integration.

Operational and regulatory considerations.

Greener analytical workflows.