

Executive Summary of USP mRNA Virtual Summit 2025

The USP mRNA Virtual Summit was held on March 11-12, 2025, and brought together leading experts and industry professionals to explore advancements and address critical challenges in the field of mRNA therapeutics. This two-day event was a platform to share innovative analytical techniques and cutting-edge methodologies that are driving the development of high-quality mRNA-based vaccines and therapeutics.

Day 1- Focused heavily on analytical approaches, beginning with the reliable assessment of mRNA vaccine integrity through techniques like Capillary Electrophoresis (CE) coupled to Laser Induced Fluorescence (LIF) detection and Ion pair reversed-phase LC. Sessions showcased advancements in double-stranded RNA quantification using novel luminescent assays and strategies for dsRNA impurity detection in IVT mRNA. Practical case studies demonstrated the application of CE in vaccine and therapeutic analyses, while insights from NMR spectroscopy revealed its role in understanding mRNA structure, optimizing processes, and maintaining quality control. The day also featured discussions on comprehensive characterization of multivalent mRNA vaccines, poly(A) tail analysis using complementary techniques, and the critical importance of cell-based assays for lifecycle quality control. Advanced technologies like infrared-based microfluidic modulation spectroscopy provided new perspectives on RNA base pairing and ligand interactions, while interactive Q&A sessions facilitated engaging dialogue among participants.

Day 2 - Shifted focus to the challenges and future opportunities in mRNA therapeutic development. The summit examined real-world experience with analytical hurdles and outlined solutions for mRNA vaccine production. Several talks addressed the validation of platform methods for quality control, exploring whether these approaches remain viable for future advancements. Novel tools for long-read sequencing and enhanced CE techniques were showcased as transformative solutions for evaluating critical quality attributes and supporting the RNA vaccine revolution. Mass spectrometry (MS) enables direct sequence mapping and detailed characterization of mRNA, while innovative approaches like LC-MS/MS with novel RNases provide in-depth analysis of 5' cap impurities and poly(A) tails during oligonucleotide mapping. The summit wrapped up with a collaborative panel Q&A session, highlighting key

takeaways, next steps, and fostering a sense of community among attendees.

Overall, the summit underscored the pivotal role of robust analytical strategies, innovative technologies, and interdisciplinary collaboration in advancing the field of mRNA analysis. It provided invaluable insights into overcoming current challenges and ensuring the production of safe, effective, and high-quality mRNA therapeutics and vaccines for future applications.