

Key Takeaways from USP's qNMR and Digital Data Applications Virtual Workshop and Roundtable

Nearly 200 individuals from industry, government and academia in more than 25 countries registered for USP's virtual Emerging Technologies Workshop and Roundtable on quantitative NMR (qNMR) and Digital Data Applications held on November 17–19, 2020. The following are key take-home messages from the three-day event:

Validation — Addressing Challenges is Critical for Compendial Adoption

- qNMR enables the analysis of complex matrices (e.g., foods, dietary supplements) and can be used to assess bulk samples and the label purity of reference standards. Therefore, qNMR should be considered for further development as a compendial method.
- qNMR validation of high-field and low-field benchtop instruments is urgently needed to usher in wide adoption of qNMR for compendial and pharmaceutical industry applications, including quality control-related activities.
- qNMR validation is not straightforward. New models and concepts will be needed for the common terms and mechanisms used in performing the validation.
- USP is laying the framework for the development and validation of qNMR procedures by adopting analytical lifecycle management principles. The approach provides some of the building blocks and concepts for qNMR validation. Real-time verification using technologically appropriate standards could provide guidance for concurrent validation.
- A USP Expert Panel is currently revising *USP General Chapters <761> Nuclear Magnetic Resonance Spectroscopy* and *<1761> Applications of Nuclear Magnetic Resonance Spectroscopy* to introduce the concepts of Analytical Target Profile and Target Measurement Uncertainty, which are the principal benchmarks for validation of analytical procedures based on qNMR.
- The U.S. Food and Drug Administration is exploring qNMR capabilities in drug product evaluation and related research.
- Roundtable discussions indicated interest in expanding the qNMR global community, including major pharmacopoeias, to help move the technology forward.

qNMR Data — All-in-One Experiment for Identity, Strength and Purity

- qNMR provides absolute mass information. The combination of qNMR and chromatography can directly determine relative molar sensitivity values (also known as relative response factor).
- qNMR data represent direct interpretations of the sample molecule and therefore directly correlate with the structure without sample manipulation.
- The data collected from NMR instruments can be directly compared to data within qualified databases and through computer-aided methodologies.
- Use of a curated database has supported data integrity and management of qNMR methods.

Benchtop qNMR — Reliable and Practical for Quality Control

- qNMR applications are increasing for both high-field and benchtop instruments, driven by the use of qNMR data in formats ranging from artificial intelligence and big data to quantum mechanics and complete reduction to amplitude frequency table (CRAFT).
- Benchtop qNMR is a reliable, practical analytical methodology/instrumentation for use in manufacturing applications and has shown notable advantages and potential as a quality control method. In the near future, computer-aided methodologies and qualified databases will be valuable in helping to overcome some of benchtop qNMR's dominant disadvantages.
- High quality qNMR data can be acquired by users without specialized expertise.

Keep the conversation going by sending your comments and questions to [Yang Liu](#), qNMR Subject Matter Expert, Digital & Innovation Division, USP.