Session 4 Small Working Group Session

Theme 1: Measurement

Question 1: **How does defining the measurement purpose influence method selection, sample preparation, and data interpretation?**

a) Differences in needs across product development, quality control, and bioequivalence studies.
b) Ties between measurement purpose and specification setting (e.g., NMT vs. ±%).
c) When particle size acts as a proxy for product performance (e.g., dissolution, processing).
d) Barriers to method selection (e.g., unclear requirements, vendor communication gaps).
e) Avoiding "garbage in = garbage out" through early alignment of goals and methods.

Question 2: **What factors determine whether a particle size method is robust, transferable, and validated?**

a) Criteria for robustness in light scattering or laser diffraction techniques.
b) Managing cross-instrument or cross-technique variability—how much difference is acceptable?
c) Challenges in method transfer (e.g., lab-to-lab, CRO to sponsor, development to QC).
d) Method change: when is revalidation required, and to what extent (partial vs. full)?
e) Extent of permissible parameter adjustments during method transfer and their impact on comparability and robustness.

Question 3: **What materials and standards support method development, and where are the current gaps?**

a) Choosing between real product, surrogate materials, or reference standards.
b) Limitations and variabilities in sourcing materials (e.g., RLD, ANDA product, or NIST-traceable).
c) Wishlist for ideal materials, and how these affect precision or bias.
d) What's missing in current technology, and how can emerging tools fill the gap?

Question 4: **What future directions should measurement methodologies take to meet evolving needs?**

a) Technological limitations of current platforms (e.g., resolution, sample prep complexity, algorithm dependence).
b) Ideas for next-generation technologies and methods?
c) Translating novel methods to routine QC—barriers and enablers.
d) Research needed to close measurement gaps or enable new applications.
e) Challenges in regulatory acceptance of novel techniques.

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Theme 2: Data Analysis, Comparison, and Reporting

Question 1: **What's the most meaningful way to compare particle size results across batches or labs?**

a) Limitations and uses of PBE, EMD, and other statistical approaches.
b) Deciding on number-, volume-, or intensity-based reporting for different settings.
c) Managing variation: what counts as "same enough" in different contexts?
d) QC vs. BE studies—do different use cases require different acceptance criteria?
e) What is the relative importance of each "accuracy" and "precision" when the true size distribution is unknown
f) Complementary vs Orthogonal? What is the importance of a complementary method? What is the importance of an orthogonal method?

Question 2: **How should uncertainty and limitations be communicated in regulatory or technical documents?**

a) Strategies for reporting limitations transparently without affecting approvals.
b) Explaining analytical uncertainty and assumptions to reviewers.
c) Role of common terminology and formats in improving mutual understanding.
d) Examples of effective vs. problematic communication in past filings.

Question 3: **How can we improve collaboration and communication across stakeholders (industry, vendors, regulators)?**

a) Identifying systemic barriers to open dialogue and knowledge sharing.
b) Opportunities for precompetitive collaboration or forums (e.g., working groups).
c) How shared terminology, visual tools, or reporting templates can bridge gaps.
d) Role of vendors in method development, validation support, and post-approval changes.

Question 4: **What would harmonized expectations for particle size methods look like—and how do we get there?**

a) Existing standards (e.g., ISO, ASTM)—how helpful are they? Where do they fall short?
b) Adequacy of current FDA PSG guidances—where is more clarity needed?
c) Global harmonization vs. regional differences—what's realistic?
d) What role can academic-industry-regulator partnerships play in setting norms?

Session 9 Small Working Group Session

Each table will be assigned one sample (some samples may be assigned to multiple tables), and follow the steps below sequentially (the prompts below will be both displayed on screen as well as handouts for each table):

Step 1: Observation
What did we observe from the measurement results for this sample?

- Were results generally consistent or inconsistent across vendors?
- Were any results unexpected or surprising based on sample type?
- How did different instrument types or methods affect the measurement results?

👉 Encourage participants to reflect on data shared earlier in the workshop or through pre-workshop materials.

Step 2: Root Cause Exploration
What might explain the results we observed?

- Could differences be due to sample-specific factors (e.g., viscosity, heterogeneity, aggregation)?
- Could measurement differences arise from how the sample was prepared (e.g., dilution, sonication, filtration)?
- Could variations in instrument configuration or settings have played a role?
- Were there any known challenges with the sample (e.g., stability, light scattering behavior)?

👉 This step draws on workshop learnings from DLS/LD theory, vendor demos, and case studies.

Step 3: Best Practice & Recommendation
What would you recommend as a best practice for measuring this sample?

- How would you improve method development for this sample?
- What preparation steps or measurement conditions should be standardized?
- What would you recommend for future studies or regulatory submissions?
- Are there specific validations or controls that should be put in place?

👉 Encourage participants to propose practical, sample-specific recommendations based on their discussion.