Roundtable Session 1 – Table 2 – Communicating Issues with Capillary Electrophoresis methods to Management, QA, and Regulatory

Facilitator: Kathir Muthusamy, *Regeneron Pharmaceuticals*

Scribe: Fang Wang, *SCIEX*

Abstract:

Capillary electrophoresis (CE) is a powerful analytical technique widely used in pharmaceutical and biotech industries due to its high resolution, speed, and efficiency. However, communicating issues related to CE methods to management, QA, and regulatory teams can be challenging. These issues may occur from method validation, instrument performance, or compliance with regulatory requirements. This round table discussion explores strategies to address CE-related issues, emphasizing the importance of tailoring communication to the non-expertise stake holders, and ensuring alignment with organizational goals and regulatory requirements. By fostering collaboration and transparency, organizations can mitigate risks and ensure the reliability and compliance of CE methods.

Discussion Questions:

1. What are the most common issues encountered with Capillary Electrophoresis methods in the industry?
2. How can technical challenges in CE methods be effectively communicated to non-technical stakeholders such as management, QA and Regulatory?
3. What strategies can be employed to ensure CE methods comply with regulatory requirements?
4. How can QA teams contribute to resolving issues related to method validation and instrument performance in CE?
5. What strategies can be employed for communicating old technology sustaining and phasing out issues in CE?

Notes:

1. What are the most common issues encountered with Capillary Electrophoresis methods in the industry?

   Technical Challenges

   -Migration Time Variability: Often caused by temperature fluctuations or buffer inconsistencies; mitigated using internal standards and marker calibration.

   - Peak Integration Difficulties: Analysts struggle to distinguish real peaks from spikes or artifacts, especially in noisy baselines.

Bubble Formation: Leads to false peaks; typically resolved through centrifugation and careful sample prep.

Consumables Variability: Chips and cartridges show batch-to-batch inconsistency, affecting reproducibility. When the cartridge is good, even over 200 injections can be achieved per cartridge.

Baseline

Method Development Hurdles

- New modality method development is not as simple as the traditional mAbs.
- Duplicate injections and internal standards are used to improve reliability.
- Troubleshooting often requires reproducing analyst errors (e.g., skipping centrifugation).

2. How can technical challenges in CE methods be effectively communicated to non-technical stakeholders such as management, QA and Regulatory?

   Communication Strategies

   - Face-to-Face Meetings Preferred: More effective than email for resolving complex issues with QA and management.
   - Contextual Framing: Providing background and rationale helps stakeholders understand the significance of anomalies.
   - Visual Aids: Annotated electropherograms and side-by-side comparisons of good vs. bad profiles are powerful tools.
   - Leverage vendor-provided, or publicly available materials to explain method limitations and performance.

   Training & Documentation

   - Interns used to test SOP clarity and identify gaps.
   - Use of video tutorials (internal and public platforms) to explain CE concepts.
   - Legacy troubleshooting guides and visual documentation support analyst training.

3. What strategies can be employed to ensure CE methods comply with regulatory requirements?

   - Platform Consistency: Standardizing CE methods across portfolios ensures uniformity and simplifies regulatory submissions.
   - Bridging Studies: Strategy varies by company; some move away from legacy specs to reduce unnecessary investigations.
   - Documentation Rigor: Clear SOPs and method validation reports are essential for audit readiness.

4. How can QA teams contribute to resolving issues related to method validation and instrument performance in CE?

   - Early Involvement: QA teams engaged during method development to anticipate validation hurdles.

- Technical Dialogue: Encouraged to understand nuances of CE data and avoid misinterpretation.
- Retesting Advocacy: Internal experts often push for retesting when external labs report questionable results.
- Training Support: QA helps reinforce critical SOP steps (e.g., proper tube selection, glove use) to avoid contamination and variability.

5. What strategies can be employed for communicating old technology, sustaining, and phasing out issues in CE?

   Didn’t get time to discuss this question. But generally, bridge study needs to be considered and designed based on the project.