Table 1: How Can We Ensure Our CE Methods Are QC Ready?

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Scope:

The goal of biopharmaceutical analytical method development is to deliver robust methods for validation and transfer to a Quality Control (QC) group for routine control testing of licensed products. In the context of capillary electrophoresis, an analytical method development team needs to consider which method parameters to optimize and assess for Robustness. Parameters to be assessed could include sample preparation conditions, sample injection, electrophoresis conditions as well as peak integration and data analysis. Additional considerations to be considered are the availability of instrumentation in QC, the setup of system suitability criteria, the software used, the consistent supply of critical reagents, monitoring of method performance and training of QC analysts. In this workshop, we will discuss what should go into the preparation to ensure a successful hand-off of CE methods from an analytical development team to a QC group.

Questions for Discussion:

1. What does a QC-ready/friendly method require?
2. What are the key method parameters to assess for robustness?
3. What are the current challenges of implementing CE methods in QC environment?
4. What role does analyst training play in successful method transfer?
5. What are the strategies to manage vendor-driven changes and discontinuations of instruments/critical reagents?

Discussion Notes:

1. What does a QC-ready/friendly method require?
    - Easy to perform
    - Robustness
    - Easy to use instrument
    - Trainings to QC
    - Flexible and alternative suppliers for critical regents
    - Clearly written method: e.g. iCIEF method requires urea to be fully dissolved. The definition of "fully dissolved" needs to be clearly defined in the method.

2. What are the key method parameters to assess for Robustness?
    - Method parameters related to CQA and have impact on specifications

- Method robustness allows flexibilities on the methods but without compromising method/reportable values precision and accuracy
- Key method parameters to assess for robustness: sample/reagent concentration; sample mixing; sample onboard stability (allowing practical analysis time for QC lab); baseline (if not flat needs to define integration strategy and provide example in the method); instrument variation etc.
- Perform DOE and use aQbD approach for method robustness assessment
- Book recommended for CE method robustness assessment: "Chemometric Methods in Capillary Electrophoresis"

3. What are the current challenges of implementing CE methods in QC environment?
    - CE peaks are not like LC peaks which are better characterized and identified
    - How to build up long-term supply strategy with vendors
    - Reagent lot-to-lot variation such as ampholyte. Specs on reagents set by vendors could be too wide
    - Reagent instability, e.g., degradation of internal standard
    - IT challenge: need to make sure the right version of data analysis software is used and data is stored on the right drive
    - CE methods may need better general lab practice than LC methods, e.g., unlike LC columns, capillaries might be dust sensitive

4. What role does analyst training play in successful method transfer?
    - Really invest time to perform the trainings. Trainings could include multiple steps:
      - Step 1: background readings
      - Step 2: lab visit by receiving lab analyst to see the method run in person
      - Step 3: receiving lab analyst runs the assay with supervision
      - Step 4: recertification and retraining after a certain time
    - Peak integration strategy is an important part of training: method developers need to have a good understanding of QC standard practice and global SOP for integration if any
    - Trainings should be performed not only on things work, but also on things don't work by including troubleshooting instructions and degraded samples
    - Perform root cause analysis and document the problems occurred during method development, and share the experience/knowledge to QC lab during method transfer

5. What are the strategies to manage vendor-driven changes and discontinuations of instruments/critical reagents?
    - Perform comparison studies to show equivalency
    - Get better understanding of QC methods used by vendor

- Labs should be notified on changes related to critical reagents by vendor
- Suggestion to vendor: provide options of ordering individual reagents besides the whole kit, so more cost efficiently and environment friendly

6. How to set up specification?
    - Generate good amount of data for statistical evaluation and start data collection from method development stage
    - Perform data trending using the selected sample and on critical reagent lot
    - Based on clinical experience and manufacturing capability
    - Proper data recording to ensure the ease of pulling interested historical data together