**How Can We Ensure Our CE Methods are QC Ready?**

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Abstract

You've been running your CE method for years in your development and clinical labs without issue but now it's time to transfer the method to a Quality Control (QC) lab for the testing of commercial products – are you sure it's as good of a method as you thought? What parameters should you be assessing ahead of this method transfer to confirm your CE method is suitable for its intended purpose? What does it even mean to be QC ready? At this roundtable we will discuss how you can keep your QC scientists happy and hand-off a method that is robust and ready for validation.

Discussion Questions

1. What are your organization's minimum requirements for a QC method (qualification, robustness, etc.)?
2. How does your definition of "QC readiness" change for a platform vs. non-platform method?
3. What are the biggest challenges in transferring a method from development to QC (timelines, training, equipment availability, etc.)?
4. What are the characteristics of methods that have been the most successful or unsuccessful in QC?
5. What aspects of your CE methods have made them more simple or more difficult to transfer to a QC lab compared to other method types?

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Participant question: How does your department interface with QC?

> Lab 1 example: process development labs will qualify methods for own use, and co-qualify for transfer to QC labs. QC co-validates methods with commercial organization during transfer.

For clinical sample testing at an external vendor, organizations must consider whether validation work performed externally can be leveraged internally and to what degree is appropriate.

Question of whether early phase work can be utilized in later stage robustness. Consensus was that it is likely improper, but it depends on the particular case.

When asking for clarity on rigor behind qualification vs validation, the group agreed that acceptance criteria are less stringent for qualification, or should be "fit for purpose."

Platform methods are becoming more common, but teams may find over time that they are not suitable. Some organizations perform verifications instead of qualifications for platform methods. Risk assessments should be done when considering platform method use.

Topic of ICH robustness – Can robustness data collected during development be used for final validation? Can we use robustness from other projects if platform method is used? This is potentially risky, and it is likely better to recollect data.

When testing in-process samples, platform methods may also be used. This likely will require qualification of the method for in-process testing to assess how robust a method is for this purpose.

N.B. CE methods are often challenging for in-process samples due to complex sample matrices.

Discussion regarding automatic and manual CE integration.
Data review should identify proper use of manual integration, and exception documents should also address when it is appropriate.
Typically, manual integrations are necessary in the context of stability/degraded samples. Drug substance electropherograms should not usually present significant challenges with automatic integration *via* processing methods.
Depending on whether a system suitability sample is different than the sample molecule can impact use of multiple or manual integration events.
Comment was made that integration "stop" functions may become less acceptable to regulatory authorities.

Discussion surrounding validation results where a statistician observed variability from two analysts. Results were acceptable, but the conclusion was that integration was performed differently by the two analysts. This brought up further examples detailing the importance of thorough method testing to mitigate analyst and instrument result dependence. Additionally, CROs may require extra guidance with electropherogram integration in transfer packages.

How does your definition of "QC readiness" change for a platform vs. non-platform method?

- What do you need for both?
    - Still need robustness evaluation, but the depth of robustness may change.
    - QC should get the same package whether platform methods are used or not.
- Critical information that may not be written into method must be included. e.g. A platform method may be performed differently by different groups, individuals (for example, vortex vs shake, inverting)
- If method is overly-complicated or not straightforward to execute, QC readiness may be more difficult to establish than otherwise.
- It was recommended to perform transferability reviews between teams, in addition to method feasibility prior to validation.
- Similarly, if method comes internally from a CRO, a transfer review should happen when being brought in-house.
- When considering transfer review due diligence, important to recognize that while molecules (i.e. mAbs) usually behave well, this may not always be true.
- Additionally, a separations method may be easier to transfer to QC than a bioassay, and so the scope of readiness can change.

What are the characteristics of methods that have been the most successful or unsuccessful in QC?

- One group had a platform mAb but recognized potential issues early in development. This was addressed by performing extensive method development work early-on with thorough documentation of examples and explicit reasons in SOP.
- Linking methods with impurity characterization can help clarify certain integrations for analysts and other teams.
- It is important to consider addressing method variability and performing additional robustness testing if a project is known to be challenging.

Topic of managing assay acceptance criteria and communication between transfer teams.

- Two possible options:
    1) Having high-level meetings to be on the same page, i.e. every two weeks among teams
    2) Using a dedicated transfer group tasked with aligning the two different organizations
- It is good practice to have a master document that outlines acceptance criteria for external groups