RoundTable Session 2 – Table 7 – Analytical Platform Transfer: When and How Should it be Done?

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Abstract:

Question 1: Consideration for transfer a platform method. What steps should be taken to ensure a successful transfer?

Question 2: What representative materials should be used to support transfer?

Question 3: How to share historical platform knowledge during a transfer of a specific product?

Question 4: When should a platform method be transferred to a product specific method?

Discussion Questions and Notes:

1. Consideration for transfer a platform method. What steps should be taken to ensure successful transfer?
    a. Establishing universal parameters of the method (ie. qualification parameters) using similar products
    b. Use method templates, protocol templates, validation templates, robustness templates
        i. Good to use for plug and play, but there are challenges if it is not up to date. This leads to problems with knowledge sharing and how to overcome that
    c. Need to consider what is fit for purpose and each of different labs capabilities at different phases of the project
    d. Establishing good training practices and ensuring knowledge sharing/transfer
    e. Companies may host practice/training sessions at the early stages at one location to ensure quality of the reagents and the training provided for analysts.
        i. This would assist in the use of platform transfer if this familiarity is established earlier on before the transfer
2. What representative materials should be used to support transfer?
3. How to share historical platform knowledge during a transfer of a specific product?
    a. Leveraging from the validation and qualification of the platform methods
    b. Used a platform verification of the validated methods to save time
        i. Use knowledge transfer from those who had experience from prior transfers

        ii. If doing verification then you may not need to perform full qualification parameters.
        iii. LOQ/LOD, repeatability and autosampler stability seem to be typically performed even with verification
    c. Lifecycle management: will have method development report to capture knowledge of the reagents/methods (which also captures change control)
        i. Don't use electronic notebooks to reference to as the reports are typical what is used
        ii. Method development reports are easier to audit and keep track of and can be made readily available for regulatory agencies
            1. Challenges with keeping it up to date
        iii. Suggestion to keep broken CE capillaries to test molecules on to show what bad profiles look like so that analysts have visual representative of "good" vs "bad"
            1. This is a solution to ensure knowledge sharing during different lifecycle of the method
4. When should a platform method be transferred to a product specific method?
    a. If molecule is similar and there is familiarity then go forward with platform
    b. If platform method evaluation showed profiles that are reproducible and peaks are well resolved enough then use the platform

Other notes:

CE-SDS

- Target 80/85-20 for typical mAbs
- Platform CE-SDS (Various platform methods across the community)
    - Some based on the Sciex IGG purity kit method completely
    - Most are using Sciex PA800+ or Agilent
    - UV detection is commonly used
    - Some use In-house sample buffers in place of the kit buffer
    - Most use Sciex Kit gel buffer
    - Sciex sample buffer have had method induced changes on certain molecules which leads to stability issues and fragmentation
        - Consider this during development
- Best practice is to ensure the sample is fully denatured and linearized in order to have a good platform method which is why people may use their own buffers
- For process development/early-screening/early stage projects: Leveraging Labchip and Maurice methods before using the PA800 could save time
- Consensus on only using PA800 for Stability/release
- Labchip is also used as a platform for early phase through late phase

Charge variant: icIEF/IEX

- Maurice: characterization work was done with IEX fractionation then submitted for mass spec analysis and potency etc. and then retest onto your cIEF method to confirm the peak. Characterization work supports the use of platform methods
- Consider the use of pH vs salt gradients when developing IEX

Challenges:

- Issues with accessibility of the material in each of the countries could cause you not to be able to use platform transfer (ie. Sciex kit reagents, certain tube types, pharmalytes, etc.)
- High turnover rates at different sites/labs make platform transfer more difficult
    1. This increases the chance for bad practices as there could be improper training or lack of proper lifecycle management knowledge sharing
- Failure rates of the pharmalyte lots and lot to lot differences are a big challenge
    1. Vendor have certain unknown standard and have qualified lots of pharmalytes to try to mitigate issue. Close connection with vendor is a benefit so you know what lots may be better
        1. No description on how pharmalyte qualification is conducted
    2. Investigate the use of blending the pharmalyte lots since issues appear to be batch dependent
- Proprietary information from the reagents can propose a challenge as they are unknown
    1. Don't know the affect on the molecule/modality
    2. Could impact method development
    3. Suggestion to mitigate this with by using known NIST mAbs or other molecules that have lots of historical data
- Suggestion to challenges with the knowledge is to have vendors publish more on their findings so that it is available for us to reference (ie. application notes, technical notes, whitepaper)
    1. This would help knowledge sharing and training easier when dealing with contract testing labs
    2. This would assist in the platform transfer as it is more public
- Transferring to external CROs is different than transferring internally
    1. Internal can be smoother and easier to control as there is already knowledge sharing and familiarity