Table 16: Intra-Site and Inter-Site Transfer of Analytical Methods for the Biopharmaceutical Products - Approach and Namely Regulatory Experiences.

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Scope:

The transfer of analytical procedure or method, is the documented process that qualifies a laboratory (the receiving unit) to use an analytical test procedure that originated in another laboratory (the transferring unit), thus ensuring that the receiving unit has the procedural knowledge and ability to perform the transferred analytical procedure as intended (USP <1224>). Transfer can be performed between laboratories at the same site, between sites at the same company, or between companies during the clinical, scale-up, or commercialization phases of product development.

This roundtable will facilitate the discussions about the various modes of analytical method transfers that are executed between both intra-sites and inter-sites through different product lifecycle stages. We will also discuss about the experimental design/strategy, approach used for setting transfer acceptance criteria and the regulatory experiences. We will also touch base on the impact of pandemic on method transfer approaches, challenges faced by your company and the lessons learned.

Questions for Discussion:

1. Across different product lifecycle (clinical and commercial), how does your company select the appropriate mode of method transfer (comparability, co-validation, and waiver)? Any regulatory input received when "waiver by scientific rationale" transfer approach is used?
2. For the intra-site (between laboratories at same site) and inter-site (between laboratories at different sites) method transfers –
    a. What kind of strategy/experimental design (analysts, days, instruments, replicates etc) is used for testing between the transferring and receiving labs?
    b. Does the historical performance of the method (i.e qualification, validation) is used to establish the transfer acceptance criteria?
    c. What kind of statistical calculation method is used for setting transfer acceptance criteria?
3. For co-validations of assay and quantitative purity/impurity methods - What kind of ICH characteristics or parameters were evaluated between the transferring and receiving labs? Is it only "Precision-reproducibility" or both "Precision-reproducibility and accuracy" were evaluated?
4. What is the impact of COVID-19 pandemic timeline on your company's current method transfer approach (mode of transfer, design of experiments and acceptance criteria etc)? What are the changes made, challenges faced, and lessons learned? What is the feedback

received from regulatory agencies? How is your company adopting these new changes for the future?

Discussion Notes:

Pre-defined questions are numbered
Ad-hoc questions are italicized

1. Across different product lifecycle (clinical and commercial), how does your company select the appropriate mode of method transfer (comparability, co-validation, and waiver)? Any regulatory input received when "waiver by scientific rationale" transfer approach is used?
    - <1224> Compendial Waiver: requested waiver for transfer between 2 different sites for commercial product: (same analysts, instruments) moved to new building. Waiver was not granted based on feedback that <1224> didn't apply → resulted in need to conduct full transfer.

    - Ways to maintain instrument's compliance status:
        - Need to conduct full qualification of instrument upon move
        - Reconnect to previous network system

    - Analytical Development transferred into Technical Operations into commercial QC: co-validation conducted between TechOps & QC. Once method is validated, can transfer to other sites.
        - Generate sending lab data set to enable transfer to multiple receiving labs
        - Use EAC based on sending lab data and compare receiving lab to sending lab data.
        - In case of differences in equipment, conduct re-validation at receiving site
            - Does the "differences in equipment" introduce method changes? Not necessarily, but may be different on phase of development
            - Other experience including "this instrument" or equivalent during qualification
            - Build flexibility in during method development

    - *How do you approach your transfer criteria based on phase of development?*
        - Pre Ph3 transfer needs to be somewhat rigorous to allow for leveraging of supporting data in BLA
        - Transfer from analytical development to QC will likely show an increased variability in QC
        - Avoided equivalence between sites by transferring from previous QC into development, then to next site's QC – does this allow drift?

2. For the intra-site (between laboratories at same site) and inter-site (between laboratories at different sites) method transfers

a. What kind of strategy/experimental design (analysts, days, instruments, replicates etc.) is used for testing between the transferring and receiving labs?
   - Transferring to multiple sites: each had different instrumentation (developmental stage) → validation at each site. Can start at one site & provide template validation to next site. One site had a different software package, resulting in slight differences in how calculations were performed. Had to make decision on single platform when going into QC.
   - *How many analysts, etc. do you use for a transfer?*
     - 3 days/analyst, 2 analysts (each site)
     - 2 analysts each do 4 runs; no criteria each run is on a different day (sometimes by default)
     - Same [single] batch? Yes: use reference standard; cell therapies may be asked to use multiple lots
     - Multiple samples: Create 50 – 150% of an impurity or 80 – 120% of a bioassay → Assume a stressed sample is used during the method transfer (tested at both sites simultaneously)

b. Does the historical performance of the method (i.e qualification, validation) is used to establish the transfer acceptance criteria?
   - Use reference standard data
   - Can use method validation intermediate precision data
   - IP from validation may under-represent variation in method – can use product-specific reference standard data from method trending over time

c. What kind of statistical calculation method is used for setting transfer acceptance criteria?
   - EAC on difference in means
   - Ratio of variances

3. For co-validations of assay and quantitative purity/impurity methods - What kind of ICH characteristics or parameters were evaluated between the transferring and receiving labs? Is it only "Precision-reproducibility" or both "Precision-reproducibility and accuracy" were evaluated?

- Lab has to demonstrate reproducibility of assay & accuracy of measurement (wrt residual DNA)
- For HPLC, etc: conduct IP during qualification

4. What is the impact of COVID-19 pandemic timeline on your company's current method transfer approach (mode of transfer, design of experiments and acceptance criteria etc)? What are the changes made, challenges faced, and lessons learned? What is the feedback received from regulatory agencies? How is your company adopting these new changes for the future?

- [Not discussed]