Table 9: Technical Transfer of Analytical Procedures - Best Practices, Pitfalls and Regulatory Considerations

Facilitators –

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Scope:

Analytical method transfers are defined in USP <1224> as "the documented process that qualifies a laboratory (the receiving unit) to use an analytical test procedure that originated in another laboratory (the transferring unit)". The major objective of method transfers is to ensure that the receiving laboratory obtains the adequate knowledge to execute testing as intended and demonstrated through method validation or qualification. While USP <1224> does not include transfer of microbiological or biological procedures in its scope, it provides a comprehensive approach to method transfers for most method types and potential scenarios for receiving and transferring units. The decision of any given method transfer approach should rely on devising a solid plan including elements such as:

- Risk assessments by method type.
- Selection of appropriate data analysis tools to assess whether the method transfer was successful.
- Outlining a regulatory strategy to appropriately report changes to testing site, once the method transfer is complete.

Questions for Discussion:

1. What are major challenges encountered while transferring analytical procedures?

2. Has the COVID pandemic affected or changed routine strategies for method transfers?

3. Describe best practices used within your organization for selection of method transfer approach by method type or other considerations (eg. phase-appropriate method transfers).

4. Discuss successes and roadblocks to selected regulatory paths for reporting testing laboratory changes post-transfer.

Discussion Notes:

January 25 –

1. Challenges
    a. COVID has put additional hurdles for method transfers
        i. Cannot send an SME to work on knowledge transfer.
        ii. Time zone differences
        iii. Creative Solutions
            1. Use of virtual reality (glasses) - prove cumbersome at times for on the fly interactions
            2. Use video recordings - more detailed and can be planned; but do not address questions on the fly
        iv. Timely shipment of critical reagents
2. Best Practices
    a. Examples of reference data sets to evaluate transfer criteria - use the same material as used in method validation or use control chart data
    b. EMA transfers example - use equivalence testing approach; compare the output of both laboratories; select suitable data between labs that takes into consideration statistical and analytical significance
    c. Control chart data tends to be limited earlier in development (eg. when transferring from R&D lab to QC lab); may require reliance on side-by-side testing between transferring and receiving laboratories.
3. Regulatory successes and roadblocks
    a. What to include in dossier updates? (Module 2 and 3 updates)
        i. Sponsors typically submit method transfer reports in Regional sections and Manufacturer section update.
        ii. May have to submit summary of test method numbers if multiple labs using different method number identifiers.
    b. Use of PACMPs to shorten/facilitate regulatory path for method transfers
        i. Idea: Establish a method transfer policy to classify methods and use to work a PACMP.

c. Some Sponsors relay having a quality document outlining general approaches for method transfers based on method types or intended purposes, following USP<1224> guidance.

4. Any questions/inquiries to add for further discussion in other sessions?

    a. Method transfer failure due to robustness issues - How do you approach transfer knowing that the method is not entirely robust?

        i. Do you transfer the method, note failures and work on addressing issues after the fact?

        ii. Maybe assess system suit criteria along with results reported with representative material?

        iii. May be able to justify transfer success, but addressing robustness separately and re-transferring select parameters after understanding root cause of lack of robustness.

January 27 –

What are major challenges encountered in Tech Transfer for analytical procedures?

How to use statistical tool to come up with acceptance criteria (confidence interval). What is this group's experience? Statisticians in-house required greater n

See Guidance in USP 1010 and USP 1224

Need to take into account the type of method that is being transferred (quantitative vs. qualitative)

In early phases, statistical analysis may be difficult

Different ways to resolve: Take into consideration accuracy, precision of the method

If it's an in-process control method, compare to output of the process

In later phases, after clinical data is available, stats analysis guidance can be more easily applied.

Tracy Dauber (AZ): It's been a challenge to implement internal company stats tools; setting acceptance criteria such that they are justifiable to the agency. Input data from TT sending unit and TT receiving unit and tool generates an output. T-test in the background (perhaps)

In certain cases, T-test shows trend, but actual data doesn't seem all that different; perhaps too stringent parameters in the tool.

Based on assay qualifications, set the N, then work with the stats to set and justify the spec

Should this be used the same as a stats tool used in process comparability

Christopher Yu (Genentech) – are we including in scope the post-approval tech transfers? (Yes)

Internal as well as external transfers are both in scope as well.

Is it assumed we have done method validation before transfer? Or if we are transferring from dev lab to commercial lab (Method transfer can be a form of method validation in this case)

USP allows for transfer waivers that can be applied to compendial methods, also applicable to internal transfer from dev to commercial. More difficult to transfer-waiver a complex method like potency method.

Example if receiving lab just needs to qualify themselves with small number of confirmatory testing

ICH Q12 has a section for post-approval protocols that can be leveraged for method transfer (layout the plan in the first filing); can mention your waiver plan in the protocol (PACMP)

Genentech ex: For non-compendial methods FDA want sponsor to be careful about using transfer waivers; they want to see evidence that the new test site has experience with the method and experience testing the product in the method. If you can satisfy these two requirements, then FDA may accept the waiver

Other risks to assess: equivalence of the equipment (needs to be proven/justified); expertise: process knowledge and what we know about the parameters we're trying to assess.

If the method is claimed to be stability-indicating, do we need to include a stressed sample in the TT?

Stress condition must be suitable for the CQA you are measuring and be representative of the known degradation pathway of the material. Not all stress conditions will induce degradation.

If your molecule is extremely stable, you can use spike samples.

Sufficient to demonstrate only intermediate precision at early stages, as you know more assess precision and accuracy across the range

How are companies approaching the method transfer at different phases? How would method transfer differ?

One approach:

- Do method phase appropriate method validation at dev site, then transfer to commercial site prior to PPQ (called a co-validation)
- For platform methods like size exclusion, et al. do one validation exercise for phase 1 and 2 (specificity and repeatability), a little more for phase 3. Meet all ICHQ2 by BLA stage.
- For more specialized methods, do more validation exercises

Other:

- Meet all ICHQ2 but fewer n in early stages
- Larger n in later stages

Early phase is pre-CQA; after you know more about how process behaves, set CQA to influence the validation design.

Genentech: The platform validation is summarized for linearity, accuracy, intermediate precision for multiple other products, and is included in the IND of a new product to demo that new product fits into the platform. The platform method becomes almost like a compendial method.

Has the COVID pandemic affected or changed routine strategies for method transfers?

Getting materials from partners

Communication (same challenge even without COVID)

Social distancing requirements slow down lab work (data generation)

Inability to meet face-to-face (manageable)

Availability of online training modules was important to successful analyst training

Delays in shipping material (need to plan ahead a little more)

The general timeline for tech transfer is a challenge. It seems never to be enough time – any mitigations to keep the transfer on fast track?

Good communications between the two labs. Lots of pre-planning far in advance (4 mo before target completion date)

Having templated documents

Having a library of samples from throughout the development /lifetime of the product

- Pull samples after significant process changes

Discuss successes and roadblocks to selected regulatory paths for reporting testing laboratory changes post-transfer.

PACMP approach for method transfer has been very successful and useful

Japan regulatory environment is challenging due to multiple regulatory agencies

Brazil/ANVISA – resolution RDC#166 in July 2017; very specific guidance on method validation requirements.

February 2 and 4 –

1. What are major challenges encountered while transferring analytical procedures?

-transfer requires multiple analysts and failures can be analyst specific. Poor training can impact timelines.

- External transfers are obviously most challenging. Transfer which includes multiple sites may require procedures to minimize drift. One solution is to include materials that are utilized at all sending and receiving labs for the testing and comparison.

- having quality and regulatory systems that facilitate easier transfer is advantage of bigger organizations. Other companies may need to generate documents from scratch.

-Transfer of platform methods may be helpful just because some elements within a method such as columns may be considered platform. Platform methods help but can still end up being NOT an exact fit and require additional optimization. Control charts or other performance controls can help.

-Transfer which goes through a development group can facilitate a SME review prior to utilization in QC.

- Question was asked if anyone had experience transferring methods which include "automation" but no one at the table had any.

2. Has the COVID pandemic affected or changed routine strategies for method transfers?

- One example was given which the sending lab did not want the receiving lab to re-validate the method as it would impact the original validation and make the timeline for a Covid project challenging to meet.

3. Describe best practices used within your organization for selection of method transfer

approach by method type or other considerations (eg. phase-appropriate method transfers).

-Comparative testing to demonstrate similarity was most common approach.

-Co-validation was favored by some but was admitted as requiring more time. However, the extra time was considered to be worth it.

- A wider range of samples including stability samples should be included.

- The LOD/range of the method should be included as part of the transfer to demonstrate adequate performance

- The robustness of method should be established or expect additional work in the future. The transfer should be carried out with the thought about how it will perform in QC in the future. Some times the focus is too much on the transfer only.

4. Discuss successes and roadblocks to selected regulatory paths for reporting testing

   laboratory changes post-transfer

   - Some transfers within a “campus” can still require appropriate regulatory filing including PAS and CBE30.

   - was described that feedback received can be inconsistent between different regulatory bodies. Specific approaches for transfer are not well understood.