Roundtable Session 2 – Table 1 – Method Comparability Considerations

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Abstract:

During development, for licensure and during the lifecycle of biological products it may be necessary to replace existing methods by alternative / new / modified methods. What are the (technical) requirements to allow claiming that two different methods yield comparable results of the same sample?

Notes:

What is a standard approach?

- Labs have guidance documents in place prior to execution, setting acceptance parameters.
- Show equivalency between:
    - Range of assay (for example: 50-150%)
        - Make large set of samples. Use same samples in both method validations
            - Some do validation of second method at same time as bridging study.
    - Lot Release samples
        - Test retains in new methods and compare to initial results
            - Overall %difference in results rather than sample to sample comparison
    - Stability Indicating samples
        - Not set criteria except that both methods need to show downward trend overtime in conditions.

Why are people changing methods?

- Current method worked for early phase, but not scalable
- Cell line IP issues; ok for small scale, but not for commercial
- Change in instrumentation/laboratory
- Change in replicate strategies (save $$); regulators won't accept cost savings as practical reason.
- Continuous cell line switch to Assay Ready Cell Banks (ARCB)
    - Overcome or skirt around bridging by including both in initial validation.

How do you deal with Bridging to New Method, better than existing

- OK to fail equivalency tests so long as explanation as to why exists.
- New method might better reflect MOA; can keep first assay running for characterization to continue to collect data, but new assay used for release.

Example Scenario

10 DP and 10 DS both tested in both methods. The new method is superior. Actually shows more sensitivity and specificity, indicating the DP/DS that was released into the clinic actually had more contaminating HCP that initially measured in first assay.

- What is the risk that new data is being presented for an already released lot?
    - There should be low risk. The assumption is that there were no adverse reaction in the clinic, so while the contaminant level was under reported before, the now elevated level by measurement in new assay can be considered safe.

What Guidelines do Company's provide labs?

- Most have SOPs for typical bridging studies; however very vague
    - Not a lot of guidance on sample size, statistical approach
        - Some give better guidance based on assay type
            - If FC receptor CBA, do "X"
            - If LBA, do "Y"
    - Sample size depends on assay variability
        - Can use retains, but also stability samples, or mixture of the two to create new samples to avoid repeat testing.

Regulatory Filings

- How much data should be included?
    - Report all data and justification of any specification changes
    - Include graphs of stability sample downward trend
    - What if you know (scientifically) why there are differences between the methods, should you point that out?
        - Don't really need to, but good to have in back-pocket if questions arise.
- Can be expensive. Most wait for other changes and group together.