Roundtable Session 1 – Table 3 - Learnings from Bioassay Transfer

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Abstract

Despite decades of experience in bioassay development, method transfer continues to be a source of significant delays, resource consumption, and technical challenges across the biopharmaceutical industry. Common issues include:

Technical Variability: Differences in instrumentation, reagent lots, environmental conditions, and analyst experience can lead to method performance discrepancies.

Knowledge Transfer Gaps: Incomplete documentation and loss of tacit knowledge during handoffs between teams, sites, or CROs can create transfer risk.

Regulatory Uncertainty: Evolving expectations for comparability studies, validation requirements, transfer protocols, and change control documentation can complicate transfer strategy.

Resource Allocation: Organizations must balance speed-to-market pressures with sufficient method qualification, robustness evaluation, and risk mitigation.

Cross-Functional Alignment: Successful transfers require coordination across analytical development, manufacturing, quality assurance, quality control, regulatory affairs, and external partners.

Discussion Topics

1. Pre-Transfer Planning & Risk Assessment

Focus areas:

- Effective method characterization before transfer initiation
- Early identification and mitigation of critical transfer risks
- Establishing realistic acceptance criteria and success metrics

Instrumentation and Equipment Differences

A major discussion point was how to manage differences in equipment or instrumentation between the sending and receiving laboratories.

Examples discussed included changes from the **Vi-CELL XR** to the **Vi-CELL BLU** and how these changes can affect cell count and viability results. Some participants observed viability differences between the XR and BLU platforms, and discussions included correction factors used with the Vi-CELL BLU. These differences may need to be evaluated through robustness or bridging studies.

A proposed strategy was to perform a **three-way comparison study**:

- Manual cell count
- Vi-CELL XR
- Vi-CELL BLU

Participants also discussed differences in timing across CROs, particularly around when new instruments are installed, qualified, and supported by completed documentation. These timing gaps can create transfer delays or force teams to proceed with incomplete information.

Plate Readers and Endpoint Readouts

Endpoint readouts were another area of concern, especially when different plate readers are used between method development and receiving laboratories.

Key points:

- Confirm exactly which instrument the receiving lab has.
- Do not assume equivalence between plate readers.
- During method development, test different readers where possible.
- Understand reader-specific performance before initiating transfer.
- Low sample sizes can make it difficult to separate sources of failure, such as plate reader effects versus analyst execution.

There was also discussion that receiving labs can sometimes be changed late in the process, making it difficult to fully evaluate equipment gaps and transfer risks ahead of time.

Gap Assessments and Risk Mapping

Participants emphasized the value of performing structured **gap assessments** before transfer. These assessments should map out key risks, including:

- Instrumentation differences
- Reagent and material differences
- Analyst experience
- Site-specific practices

- Documentation gaps
- Critical method parameters
- Environmental or timing constraints

Gap assessments can help identify where additional controls, bridging studies, training, or documentation updates are needed before transfer execution.

Pre-Qualification and Transfer Planning Tools

Several practical tools were discussed:

- Pre-qualification slide decks
- Structured transfer-readiness meetings
- SOP templates to ensure consistency
- Standardized documentation of volumes, mixing steps, incubation times, and reagent preparation
- Early alignment on assay-critical steps and acceptance criteria

Using standard SOP templates can improve consistency and reduce ambiguity, especially when multiple sites or CROs are involved.

2. Technical Troubleshooting & Knowledge Transfer

Focus areas:

- Common root causes of transfer failures and diagnostic approaches
- Strategies for capturing and transferring tribal knowledge
- Collaborative problem-solving between sending and receiving laboratories

Tribal Knowledge Transfer

A key theme was how to effectively transfer “tribal knowledge” that may not be fully captured in SOPs.

Recommended approaches included:

- Structured pre-transfer meetings
- Detailed walkthroughs of critical steps
- In-person training where possible

- Hands-on demonstration of assay execution
- Clear discussion of instrumentation-specific details
- Open dialogue between method developers and receiving lab analysts

In-person training was viewed as highly valuable because it allows analysts to clarify ambiguous steps in real time. However, this can be challenging when labs are geographically distant.

SOP Clarity and Interpretation

Participants noted that SOPs can often be unclear or interpreted differently by different analysts or sites.

One example discussed was the sensitivity of **LNPs to vortexing or mixing**, where seemingly minor differences in technique can have a meaningful impact on assay performance.

A recurring challenge is finding the right balance between:

- Being descriptive enough to prevent misinterpretation
- Avoiding excessive detail that unnecessarily locks QC analysts into overly rigid execution
- Keeping procedures clear, concise, and practical

Suggested improvements included:

- Adding specific examples for formula use
- Providing clearer reagent preparation instructions
- Having someone unfamiliar with the method review the SOP with fresh eyes
- Identifying steps where analysts may make assumptions based on prior experience

Documentation Completeness

One CRO example highlighted the importance of requesting the full data package and supporting documentation.

In that case, the SoftMax Pro data looked acceptable based on what was initially sent. However, a full review showed that the cell line viability was borderline failing.

The lesson was clear: **ask for all documentation**, not just processed output or summary data.

Relevant documentation may include:

- Raw instrument files
- Cell count and viability data
- Plate maps
- Analyst notes
- Reagent preparation records
- Deviations or invalid assay records
- Environmental or timing records
- Full data review packages

Troubleshooting Transfer Failures

Participants emphasized that good communication is critical to identifying true root causes of invalid or failed assays.

Common diagnostic challenges include:

- Separating analyst effects from instrument effects
- Determining whether failures are due to procedure, materials, equipment, or training
- Interpreting small datasets where conclusions may be uncertain
- Understanding whether the receiving lab executed the method exactly as intended

Collaborative troubleshooting between method developers, SMEs, and receiving labs was viewed as essential.

Training Alternatives

When in-person training is not possible, some groups have used training videos.

Best practices discussed included:

- Breaking videos into smaller, discrete steps
- Avoiding one long end-to-end recording
- Highlighting critical manipulations
- Showing examples of acceptable and unacceptable technique
- Using videos to supplement, not replace, live discussion

Participants noted that receiving labs may sometimes be reluctant to follow method developer or SME guidance if it does not come from higher-level management. This reinforces the importance of cross-functional alignment and clear governance during transfer.

3. Regulatory Strategy & Operational Excellence

Focus areas:

- Navigating regulatory expectations for method transfer documentation
- Balancing compliance requirements with operational efficiency
- Metrics for measuring transfer success and continuous improvement

Transfer Strategy and Protocol Visibility

Participants discussed the importance of clear visibility to the technical transfer protocol and overall transfer strategy.

There was discussion around different approaches to transfer study design, including:

- Equivalence testing
- More traditional qualification or validation-style approaches
- Use of five levels of simulated potency samples

Some companies use formal equivalence testing, while others rely on a more traditional qualification or validation setup. The preferred approach may depend on method maturity, product phase, regulatory expectations, assay variability, and intended use.

Balancing Speed and Robustness

Resource allocation was identified as a major challenge. Teams often need to move quickly while still ensuring the assay is sufficiently robust for transfer.

Strategies discussed included:

- Standardizing methods as much as possible
- Using platform approaches where appropriate
- Building robustness into assay development before transfer
- Avoiding unnecessary customization by site
- Identifying high-risk parameters early

- Using pre-transfer assessments to reduce late-stage surprises

Standardization and platforming were viewed as key ways to improve efficiency while maintaining technical rigor.

4. Open Discussion & Peer Learning

Focus areas:

- Real-world case studies and lessons learned from participants
- Emerging challenges and innovative solutions
- Networking and knowledge sharing

Method Developer Perspective

From the method developer perspective, participants wanted to see more specific and practical detail in SOPs, especially around:

- Formula handling
- Reagent preparation
- Critical timing steps
- Mixing or vortexing instructions
- Instrument-specific execution details
- Examples of common mistakes or ambiguity points

A suggested best practice was to have someone unfamiliar with the method review the SOP before transfer. This can help identify areas where the method developer may have built-in assumptions that are not obvious to a new user.

Use of AI in Transfer and Troubleshooting

Participants discussed whether AI has been helpful in method transfer and assay troubleshooting.

Feedback was mixed.

AI was viewed as less mature for:

- Writing SOPs from scratch
- Editing SOPs in a fully reliable, inspection-ready way

- Predicting future assay problems without sufficient data

AI was viewed as more useful for:

- Data trending
- Data tracking
- Visualization
- Reviewing existing data
- Thinking through potential root causes
- Helping design experiments to rule causes in or out

One positive example involved using AI to troubleshoot an assay across three sites where a parameter was trending low. AI helped organize possible root causes, rule some out, and support experimental planning to test others.

The key takeaway was that AI can be useful when applied to the right problem, especially where existing data are available. However, it is not yet ready to replace human technical judgment or SME review.

Cluster Map: High-level, and easy to read at a glance of the major topics discussed during round table discussion.