Supporting the Success and Consistency of Analytical Methods in Multiple Laboratories

Case Study using Microfluidic Capillary Gel Electrophoresis

Mike Smith
GlaxoSmithKline
King of Prussia, PA
CASSS CE Pharm, September 2018
Presentation Agenda

– Analytical method consistency and performance: common challenges
– GSK approach to improving and sustaining method performance and consistency
– Case study of initiatives to improve microfluidic capillary gel electrophoresis (mCGE)
The Industry's Challenge with Analytical Method Performance in Commercial Testing Sites

- Contributing factors
  - Rapid pace of technology change
  - Lack/dilution of experience at the testing laboratory
  - Different ways of working between development lab and commercial testing lab
  - Distance
  - Project constraints (acceleration)

The process of transferring analytical methods from research labs to commercial labs is fraught with challenges...especially for overseas transfers

[A] “one-size fits all approach” will not work

Biotech Firms Struggle To Replicate Analytical Methods For Commercial Use

https://pink.pharmamedtechbi.com/PS120033/Biotech-Firms-Struggle-To-Replicate-Analytical-Methods-For-Commercial-Use
Undesired Effects of Inconsistent Method Performance

Invalid assays
- Testing delays
- Stability re-pulls
- Is the method under control?
  - Deviations

Resource Issues
- Stressed scientists
- Inefficient working practices

Supply chain risks
- Out of specification
  - Stockout risk
Achieving and Sustaining Consistent Method Performance

Before Transfer
- The right methods developed by the right SMEs
- Extensively test method robustness
- Diligently monitor method performance

During Transfer
- Involve the QC Lab in method qualification
- Carefully choose meaningful transfer criteria
- Training is critical and a "proficient" analyst is not automatically a SME

After Transfer
- Consistently partner with the QC Lab
- Understand and harmonize best working practices
- Document your institutional knowledge and make it easy to transmit from lab to lab
- Establish method performance expectations and transparently monitor performance
Levers for Improving Analytical Method Performance and Consistency at GSK

- Technical Workshops
- SME Forums
- Documentation of Institutional Knowledge

Improved method consistency
Case Study:
Microfluidic Capillary Gel Electrophoresis
Timeline of mCGE History in GSK

Platform Establishment
- 2009: mCGE platform selected

Industrialization
- 2010: First late-phase method transfer/validation
- 2013: Second late-phase method transfer/validation
- 2014: First commercial approval (Tanzeum)

Lifecycle Management
- 2013-present: refining tools and approaches
Invalid assay rates exceeding donor lab experience

Poor 2-way communication between Development and QC Labs

Frequent instrument malfunctions

Inexperienced users in QC Labs

Best practices not standardized in QC Lab

Frequent analyst turnover
We needed a new strategy…

Existing Strategy
- Reactive troubleshooting
- Inconsistent communication
- Method performance monitored by individual project teams
- Opaque performance metrics
- Institutional knowledge owned by individual SMEs
- Heirarchical support structure
- No formal context for ongoing SME development

New Strategy
- Proactive engagements with QC Labs
- Ongoing communications through formal and informal channels
- Centralized, cross-project method performance monitoring
- Transparent performance metrics
- Institutional knowledge formally documented and transmitted amongst laboratories
- Collaborative technical support
- Purposeful and ongoing SME development
Three-Lever Approach to mCGE Performance and Consistency Improvements

- Technical workshop hosted in QC Lab
- Creation of mCGE SME Forum
- Group authorship of mCGE Guidance Document

Improved method consistency
Lever 1: mCGE Workshop

**Objectives**
1. Baseline method performance in QC Lab
2. Identify alignment gaps and deviations from best practice
3. Identify most prevalent failure modes and develop action plans

**Inputs**
- Technical presentation
- Invalid assay rates and failure mode metrics for most active QC Labs
- Voice of customer feedback

**Process**
- Perform GEMBA
- Conduct brainstorming sessions
- Evaluate performance metrics and develop improvement targets
Key Findings

- QC Lab trains on SOPs, not techniques
- Quality of training is trainer-dependent
- User-to-user differences in technique
- Better root cause analysis tools are needed—many invalids are assigned “root cause unknown” in the log
- “Site-specific” failure modes can be different from lab to lab
Assessment of Method Performance Gaps

Identifying Failure Mode Misalignments Between Two QC Labs

![Bar chart comparing US QC Lab failure modes with UK QC Lab failure modes.](chart.png)
Key information was collected to baseline the current state of the method in the QC Lab

Identified failure mode misalignments between QC Labs

Most frequent failure modes were identified and discussed, and action plans were developed for each

Performance improvement (invalid rate reduction) targets were agreed with QC Lab
Lever 2: Monthly mCGE SME Forum

Purpose and Objectives

- Develop a network of SMEs
- Transfer Knowledge
  - Data discussions
  - Real-time collaborative troubleshooting
  - Technical presentations
- Standardize best practices
  - Educate new users on past learnings
  - Develop consistent training procedure
  - Document critical method parameters and steps
  - Harmonize assay workflow

Connect users from different labs
CGE SME Forum: 1-year accomplishments

- Successfully onboarded two new QC Labs
- Completed mCGE Guidance Document and received approval from all QC Labs
- Substantial progress in networking users from different labs
- Improved communications
- Reduction in instrument malfunctions and “event-driven” failure modes
- Improved the failure mode gap identified in mCGE Workshop
Lab-to-lab performance alignment substantially improved in 12 months
Lever 3: CGE Guidance Document

Contents

- Deep dive into the science behind the separation
- Optimized process flow
- Formal training procedure
- Detailed method walkthrough
- Suitability/acceptance criteria interpretation instructions
- Detailed data processing instructions
- Troubleshooting tips
- Data examples
– Document has been approved internally and accepted by the lab management of all QC Labs

– Next steps
  – Consistent usage and deployment in all labs
  – CRO-friendly version
  – Embed within QC Lab training procedures/programs
  – Continuous improvements—multimedia elements, external links to troubleshooting resources
GSK uses a multifaceted approach to drive method performance and consistency across multiple laboratories.

- The 3-Lever approach for mCGE has produced several tangible improvements:
  - Improved performance alignment between QC Labs and reduction in “event-driven” failures
  - Completion of Guidance Document

- Future work for mCGE Forum:
  - Continue to work to reduce invalid rates in all labs
  - Bring new labs online
  - Establish a plan for how to use the Guidance Document

- This Performance/Consistency approach is being expanded to additional technologies.
Conclusions

Business Value

Patient Value
Thanks…

- Jen Dally
- Vicki Smith
- Jen McGee
- Ryan Stewart
- Andy Jones
- Dwight Moore
- Jonathan Barnett
- Nigel Howes
- Elizabeth Schmidt
- Wayne Kelley
- Troy Adams
- Vinh Lam
- Michelle Ward
- Han-Wen Yang
- Tino Costaras
- Graham Taylor
- Paul Boyd