Roundtable Session - Table 8 - Mitigating lot-to-lot variability in critical CE reagents

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Abstract

Capillary Electrophoresis (CE) is a hallmark analytical technique used to monitor the critical quality attribute (CQA) of fragmentation across increasingly diverse protein modalities. Imaged Capillary Isoelectric Focusing (iCIEF) is used in the biopharmaceutical industry as both an identity method and technique for monitoring charge variants. Despite being two well-known applications, lot-to-lot variability and accessibility to available high quality critical reagents remains a challenge during analytical method validations, transfers, and workflows. In this roundtable, we will highlight known reagent performance concerns and potential opportunities to mitigate reliance on single vendors and reduce variability.

Discussion Questions:

1. What are some examples of analytical method challenges that you have experienced that were attributed to critical reagent variability?

2. Do you use digital monitorization tools to track the performance of your reagents in order to better identify when reagent issues occur and justify a potential root cause?

3. What is your strategy for bridging different reagent lots from the same vendor, and alternative solutions when those specific reagents become unavailable to the testing sites?

4. How do you overcome communication siloes that may arise from the product manufacturer and assess whether the lot variability is isolated or more global?

5. Reagents of the future - What is your wish list for future reagent capabilities not yet on the market?

Analytical challenges you attribute to reagents:

Pharmalytes – raised baseline causes integration issues.
pI – issues with proteins between 6.5 and 7.5

pI – switch to a different pharmalyte
Analysts should be 'aware' of the ranges on the lots. There is always a +/- range.
pI – switched to CZE for more consistency and easier to optimize.
Vendor point of view – adducts on modality and not sure why, but want to
Urea – stock supply and impurity issues and can show up
Vendor (AES) – adding more urea raises/lowers baseline late in pherogram; acts as a spacer. Treat urea with amphilyte to 'neutralize.' Drops current significantly.

No one used LabChips at table; lots of issues with reagents
No alternative if Revvity has no 'other' alternate if out.

Digitalization monitorization tools – do you track quality of reagents? What do you do if there is an issue? Merck is tracking this.
One participant uses bolt on dashboard for cold (sp?) charting

Another buys small volume of reagents
Can make your own reagents if easy to do so (SCIEX reagent was one)
Vendor (AES) perspective – depends on what aspect you want to monitor
Do you extend the shelf life of reagents? Last resort when a shortage; and yes for method development;
Merck – analyst are doing multiple separations now so hard to control

Bridging different lots?

AES – keep 5 year stock pile of raw materials; 3 suppliers of each raw material
Stock lots easy; retro lots to match performance are more involved
When developing methods, request from the vendors at least 2 different lots.
Method development kit – like a flight of beers!

How do you overcome communication slices that may arise from the manufacturer to access whether variability is isolated or globally?

SCIEX coolant was a hot mess
Some vendors do not communicate any info on shortages/variability. Very frustrating.
Vendors need a resource page on past issues or some sort of forum.
Vendors put burden on the customer to troubleshoot (look at # on bottom of vial, # on boxes, etc.

Reagents of the future?

Gel buffer that has more than just SDS plus STS, SHS, etc and add it to the sample buffer!
Rapid charge – need to target low pI range with analytes have RNA attached.
Protein Simple go to 8 sample cartridges; and don't give an injection limit
Biophase sample plate different and hard to put on heat block; need better transferability.