

Roundtable Session 1 – Table 9 - Managing Critical Reagents for Capillary Electrophoresis Methods

Facilitator: Richard Rustandi, *Merck & Co.*

Scribe: Huiyuan Li, *BMS*

Abstract:

Critical Reagents are part of very important component of each analytical assay including CE. Consistent supply with good quality critical reagents is the most desirable. Most common CE assays for example CE-SDS and cIEF are employing two critical reagents, separation gel buffer and ampholytes, respectively. These two critical reagents are single source so far, Sciex and ProteinSimple. In this roundtable we discuss how we control and manage these critical reagents and how to avoid single vendor suppliers.

Notes:

1. What are other lists of common and important critical reagents for CE in your companies

- Separation gel buffer from Sciex
- Ampholytes from Protein Simple (sourced from GE)
- EACA – CZE (Charge variant)
- Methyl cellulose (cIEF)
- Ion analysis kit
- Fluorescence PI marker

2. What is your mitigating strategy if vendor cannot provide good reagents or discontinue kits (single vendor issue)

- clinical environment -- diagnosis reagent batch reserve. Plan ahead for the project. In critical stage, plan at least a year ahead.
- gel buffer (SCIEX)
 - In case of backorder, contact the vendor to inquire about availability and request regular status updates.
 - Ask the vendor whether a certain level of lot-to-lot variation is acceptable for your application.
 - Note: Users may have the option to prepare the buffer in-house when gel buffer (SCIEX) composition patent expires. May need find a way to manage quality and consistency internally.
- Ampholytes
 - Pharmalyte (Cytiva) is currently the primary supplier. However, recent issues include frequent backorders, and lot-to-lot consistency concerns.
 - Actions:
 - Contact the vendor to understand the reasons behind the backorders.

- Investigate lot-to-lot variation by requesting batch records from the vendor or checking Cytiva's website.
 - Alternative Options:
 - AES HR Series: Offers performance similar to Pharmalyte. Some molecules are product-specific and require evaluation.
 - Serva: high background noise. Fluorescence detection can be used to minimize background interference. Used for fusion protein applications.
 - Bio-Rad: Another potential supplier.
- Methyl cellulose (cIEF)
 - Source: ProteinSimple
 - Contamination was found in both 1% MC and 0.5% MC batches manufactured between January 2023 and July 2024.
 - Consider identifying a second vendor as an alternative.
 - Another option is to purchase polymer powder and prepare the solution in-house.
- FL PI marker
 - Source: ProteinSimple; also available from SCIEX.
 - Artifact peaks have been observed in the lyophilized product.
- CZE method reagents
 - one group prepares their own reagents in-house.
- Test kit
 - For test kits, if discontinued, it is important to understand the components included. This allows for the possibility of purchasing individual components separately or preparing in-house.

Summary: In case of discontinuation/backorder, assess the feasibility of sourcing from a second vendor or preparing in-house.

3. How do you maintain your critical reagents

Most members of the group agreed that expired critical reagents can still be used in a method development environment. In contrast, only non-expired reagents are permitted in the QC space. However, in certain cases—such as when reagents are backordered and no non-expired reagents are available—it may be acceptable to evaluate the expired reagents for comparability with historical data. If the results are comparable, an extension of the expiration date may be justified.