Table 5: Unaddressed Challenges & Technical Innovations

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Scope:

Numerous challenges still exist in analytical characterization of complex biopharmaceuticals. In some cases, simply looking at a challenge through a different lens helps create a solution. Often however, innovative approaches in methodology or instrumentation may be required in order to truly solve the problem. This roundtable aims to identify and discuss existing gaps and potential solutions to address these challenges.

Questions for Discussion:

1. What challenges currently exist for mAb-related therapeutics that could benefit from new development or enhancement of existing CE methodologies?
2. What challenges exist in analysis of new modalities (DNA/RNA, LNP, AAV, etc)? Can we apply existing CE solutions or is new development required?
3. What gaps exist around non-therapeutic material encountered during development (polysorbate, cyclodextrins, etc) Can we apply existing CE solutions or is new development required?
4. What does the development of new/future CE need to consider? Throughput vs. new capability?
5. What new CE-assay related technology is being developed?

Discussion Notes:

We have discussed the following four questions. The comments were summarized below:

1. What challenges currently exist for mAb-related therapeutics that could benefit from new development or enhancement of existing CE methodologies?
    - Chemistry does not catch up with molecule development. For icIEF, new reagents (e.g. new ampholytes) need to be developed for specific molecules studied in pharmaceutical companies.
    - CE-SDS does not work very well when the sample is very complex. The analysis of non-polar molecules is challenging. Noisy baseline is also an issue.
    - For CE-SDS, need to better resolve the mAb fragments with similar molecular weight/ glycosylated and non-glycosylated species. The separation is not just

based on the molecular weight, other factors such as molecule shape and charge could also influence the separation.
    - Shift of migration time from Lot to Lot. Need to improve the reproducibility and robustness of the CE system.
    - Need to have better quality control of the capillary detection window.
    - Need to improve the reproducibility of capillary coating.
2. What challenges exist in analysis of new modalities (DNA/RNA, LNP, AAV, etc)? Can we apply existing CE solutions or is new development required?
    - For the virus samples, need to figure out a way to better interpret data. (Understand what separation profile means; better software is also needed)
3. What gaps exist around non-therapeutic material encountered during development (polysorbate, cyclodextrins, etc) Can we apply existing CE solutions or is new development required?
    - Polysaccharide is a problem.
    - Histidine residue is an issue. Maybe we can run a blank and then subtract the signal.
    - For the new instrument, we need direct collaboration to test samples before deciding to buy the instrument.
4. What does the development of new/future CE need to consider? Throughput vs. new capability?
    - Throughput. Maybe apply multiple capillaries strategy and do the parallel separation.
    - Need to develop CE-MS methods.
    - CE-MS for QC: need to improve the reproducibility; provide better software for data analysis.