Table 10: How Does the Emergence of the Multi-Attribute Methods (MAM) Impact the Role of CE?

Session 1
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Session 2
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Scope:
Recently, mass spectrometry-based methods intended to simultaneously monitor product quality attributes have been introduced to more deliberately assess the quality all along biopharmaceuticals manufacturing processes. As such, these multi-attribute methods (MAM) could offer potential to replace several traditional chromatographic and electrophoretic assays, including CE-based methods, currently used for characterization and release of biopharmaceuticals. This roundtable aims to discuss both the potential scope of MAM methods and challenges for their implementation in manufacturing and QC environment.

Questions for Discussion:
1. What are the requirements for selection of multi-attribute methods intended for support of process development vs QC release?
2. What are some of examples of multi-attribute methods and whether they can/should replace CE based methods currently used as QC release assays?

Discussion Notes:
- Most of participants shared an assessment that Multi-Attribute Method (MAM) is intended to provide a single assay that could potentially replace multiple traditional assays for either release and/or characterizations purposes.
  - Even though peptide map is expected to be a primary type of MAM, some participants left possibility that some other non-mass spectrometry based assays could be also considered as MAM methods.
- The question of how to perform MAM assay qualification was raised since no a single participant has it fully implemented in its respective organizations.
  - It was also stressed out that criteria for MAM in QC environment are expected to be more stringent vs if MAM is used as characterization assay.
  - In addition, need for help from vendors regarding GMP based software and robust mass spectrometry instrumentation is required for more widely acceptance of MAM method.
- Some of the challenges in implementation of MAM attribute are:
  - direct correlation between traditional assays that monitor change on the entire molecule, such as CE-SDS, icIEF, IEC vs site-specific results obtained by peptide map,
• former issue could be molecule dependent since traditional assays and MAM may not always monitor same product quality(ies),
  o regulatory agency expectations with respect of MAM replacing traditional assays.

• In conclusions, it appeared to be consensus by participants that in foreseeable future it would be difficult to replace CE based methods with MAM in QC environment for reasons listed above.

• Some other points expressed by participants are as follows:
  o a holistic approach that traditional assays provide is hard to drop completely, especially as “unknown” attribute could be detected on stability, for example, thus traditional assays and MAM may complement each other for its faster identification.
  o how to link measured information on a single detected peptide for protein fragmentation, for example, to total purity obtained by CE-SDS and how to report it?
  o release glycan method (CE or UPLC) is only traditional assay that seems to show a good correlation with glycosylation data obtained from glycopeptides by MAM
  o full automation (sample prep, data analysis) is likely to be used as part of MAM methods