Platform Size Exclusion Chromatography (SEC) Method Development for a Broad Range of Monoclonal Antibodies

Yasa,Isil; Chandrasekar, Vandana; Adamo, Michael; Katiyar, Amit; Das, Tapan; Knihtila, Ryan

Analytical Method Development, Bristol-Myers Squibb, Hopewell, New Jersey

Understanding of size heterogeneity in biotherapeutic proteins is essential since it is one of the Critical Quality Attributes (CQA) due to its impact on safety and efficacy. The size heterogeneity covers the product related species/impurities that includes fragments, monomers, and aggregates. Size exclusion chromatography (SEC) has been widely used to separate aggregates, monomer, and fragments of monoclonal antibodies (mAbs) that might form during manufacturing, storage and shipping. The progress in biologics pipeline and the urgency to reach first-in-human (FIH) has provided an opportunity to develop a generic method that can serve as a platform method for monoclonal antibodies. This study describes platform SEC method development for monoclonal antibodies using commercially available high-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC) SEC columns. For this purpose, several antibodies covering a broad range of isoelectric points (pI) and hydrophobicity were analyzed. Initial comparison was performed using six different mAbs to understand the impact of mobile phase and organics on separation of aggregates and fragments.