Challenges in Product Specifications with Asian Regulatory Authorities: A Case Study

In the pharmaceutical industry, navigating regulatory requirements across different regions can be particularly challenging. This presentation focuses through a case study on the difficulties encountered with certain Asian authorities, specifically in South Korea and China, regarding the specifications of our products.

Traditionally, Size Exclusion High-Performance Liquid Chromatography (SE-HPLC) has been used for the testing of the high molecular weight species (HMWS), monomer (purity) and low molecular weight species (LMWS) for monoclonal antibodies. However, our data indicates that Non-Reducing Capillary Gel Electrophoresis (NR-CGE) provides a more accurate representation of purity for our products. SE-HPLC fails to achieve baseline resolution between monomer and LMWS due to the close mass of heavy chain-light chain (HHL) species to the monomer. This leads to underestimation of LMWS and overestimation of monomer.

The literature confirms also that NR-CGE is becoming the method of choice over SE-HPLC across the industry. NR-CGE offers optimal separation between monomer and LMWS, ensuring accurate purity assessment and maintaining product quality. Despite presenting historical data and external evidence supporting the transition from SE-HPLC to NR-CGE, the reviewers remain unconvinced. They argue that impurities and monomer should be tested in a single method, achieving a total of 100% when combined. Their expectation persists regardless of product specificities and method performances.

In conclusion, although 16 countries had already accepted the strategy to test and report the monomer and LMWS by NR-CGE, we had to implement additional specifications for the monomer by SE-HPLC to avoid delaying patient access in these Asian countries. By sharing this case study, we hope to highlight the importance for the authorities to revise their standard approaches and expectations. Harmonizing specifications across regions will not only improve product quality but also expedite patient access to essential medications.