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A Quantitative MS-based Multi-attribute Method (MAM) Approach for New Biological Entities and Biosimilar Candidates Presented by a Full Method Qualification for an IgG1 Market Product

Anke Schnabel, Gerhard Körting, Julia Brückner, Yvonne Jasper, Heiner Falkenberg, Roland Moussa

Protagen Protein Services GmbH, Dortmund, Germany

Detailed characterization including assessment of critical quality attributes of biopharmaceuticals is essential across process development, manufacturing and release. The multi-attribute method (MAM) Peptide Mapping with quantitative LC-ESI-MS rovides detailed and site-specific information on product quality attributes (PQAs), like amino acid sequence, terminal processing, truncation, deamidation, oxidation or glycosylation. The MAM approach has been proven to be a powerful tool during development and production of new biological entities and biosimilar candidates and has the potential to replace conventional protein analytical methods for characterization and quantification of PQAs. Thereby, the MAM approach has to meet various demands in the different development phases regarding sample throughput, standardization, and quality level with the ultimate discipline GMP-release testing. In originator monitoring and subsequent biosimilarity exercise the MAM needs to be qualified according to current guidelines with special regards to the comparability assessment and robustness.

We present the application of MAM in IgG1 biosimilar development using Thermo Scientific Q Exactive instrumentation and the software solution (Protein Metrics Inc.) for fast processing of post translational modification (PTM) levels, terminal variants and N-glycosylation profile. Based on a case study the principle of a molecule-specific method qualification of a MAM peptide mapping MS approach will be introduced including the evaluation of the quality parameters: analyte autosampler stability, repeatability, intermediated precision, linearity and specificity of the method using appropriate stress samples.

The MAM approach offers the technical potential for validation and usage as GMP release testing for biopharmaceuticals. However, multiple challenges need to be solved to use MS in fully compliant routine analyses, such as the variability for low-level impurities, and GMP-compliant software for data acquisition and automated data processing.

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