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National Institute for Bioprocessing Research and Training

Contract Research

CASE STUDY

Using Sedimentation-Velocity Analytical Ultracentrifugation (SV-AUC) to quantify and compare fragments and aggregation between different biotherapeutic formats

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Challenge

A client requested NIBRT Contract Research to perform SV-AUC analysis to compare the fragment and aggregation profile of reference material alongside a batch of half-life extended material (HLE). Biopharmaceutical manufacturers are under increasing pressure from regulators to ensure the safety and quality of their products. Aggregation of a protein therapeutic can have serious implications for patient safety, product stability, potency, biological activity, quality, and efficacy.

Solution

NIBRT performed SV-AUC analysis to determine the molecular weight and relative abundance of fragments and aggregates present in the samples. Analytical ultracentrifugation (AUC) employs a high-speed centrifuge equipped with absorbance and interference optics. When using AUC as an orthogonal method to SEC, the sedimentation velocity mode of operation is used (SV-AUC). Samples are spun at high rates of speed, with larger species sedimenting to a greater degree than the smaller ones. The velocity and shape of the moving boundary, detected by the AUC optics, is used to estimate the sedimentation coefficient, which can then be related to molecular weight once shape information is obtained or assumed. The resolution of oligomeric species such as dimers and trimers from the monomer by AUC is generally greater than it is for SEC. This can be a significant advantage of the SV-AUC technique. During data processing the frictional ratio was optimised for the HLE modified batch which due to its modification had an altered protein shape, thereby affecting the protein's hydrodynamic properties.

Outcome

A comprehensive report was provided to the client detailing SV-AUC profiles, calculated molecular weight of fragments and aggregates and their percentage abundance in the samples. The data allowed the client to assess any change in product related impurities in the HLE batch compared to the reference material.

Project Process

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