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National Institute for Bioprocessing Research and Training

Contract Research

CASE STUDY

Characterisation of a biotherapeutic in early-stage drug development

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Challenge

NIBRT Contract Research were approached by a client who requested in-depth characterisation of their novel biotherapeutic that was currently in the development stage of its lifecycle. ICH Q6B guidelines describe the characterisation requirements for new biotechnological/biological products in the development phase, using suitable techniques "necessary to allow relevant specifications to be established". These requirements include, protein and glycan structural characterisation, physicochemical characterisation, and measurement of product/process-related impurities. To fully meet the client's requirements for testing, a tailored characterisation service package was generated.

Solution

NIBRT Contract Research prepared a bespoke characterisation service package, implementing several different analytical techniques to yield the highest possible level of structural information.

For glycan structural characterisation, both *N*- and O- linked glycan characterisation were performed, with *N*-linked glycan characterisation covering both site-specific characterisation and glycan site occupancy analysis. These techniques enabled extensive characterisation of *N*-glycan heterogeneity present at both glycosylation sites, and further determined the occupancy of these sites for the first time on this novel biotherapeutic.

For protein structural characterisation, peptide mapping by mass spectrometry of the reduced and non-reduced trypsin digested sample, allowed for sequence and disulphide bond confirmation. To investigate the physicochemical properties of the protein, intact mass was performed on the native molecule and subunits, both before, and after de-glycosylation. To determine the presence of product-related impurities, analytical ultracentrifugation (AUC) analysis was performed. AUC analysis provided information on the presence of aggregates and degradation products in the sample, and has the advantage of analysing molecules in native conditions, thereby mitigating any matrix interference effects, which are a commonly encountered issue when using other similar platforms. AUC further provided relative quantitation of all molecular weight species present.

Outcome

Through working closely with the client, NIBRT Contract Research gained a comprehensive understanding of their testing requirements. A bespoke experimental plan was designed, featuring an array of techniques to extensively characterise their biological product. Data from this analysis enabled the client to progress their biotherapeutic forward to phase 1 clinical trials.

Project Process

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