

FACT SHEET 4

ANALYTICAL AND FORMULATION CAPABILITIES

CMC Biologics offers an extensive range of analytical services to evaluate the integrity, purity, structure, and function of complex biologicals. The breadth of our in-house capability means that we can provide almost all the analytical testing required for cGMP production, thus ensuring complete control over the project schedule.

Our analytical team has broad capabilities in developing techniques and executing analyses throughout the development and production process. Our core competencies include assay and formulation development, analytical characterization, in-process monitoring, cGMP drug substance and drug product release testing, cGMP stability studies, and extensive experience executing comparability studies using a wide range of analytical techniques.

ANALYTICAL METHOD DEVELOPMENT AND PROTEIN CHARACTERIZATION

Methods are available to support the following analyses and determinations during development:

- Identity/structure
 - N-terminal sequence, peptide mapping, LC/MS/MS
- Conformation
 - Circular dichroism, fluorescence, and Fourier transform infrared spectroscopy
- Aggregate analysis
 - Size exclusion chromatography with multi-angle laser light scattering
- Mass spectrometry
 - MALDI, ion trap, and quadruple-mass spectrometry
- Protein modifications
 - Post-translational, inadvertent, and stress induced
 - Glycosylation
 - Glycosidase digestions, glycan profiling, and sialic acid quantitation
- Protein chromatography
 - HPLC: reversed-phase, ion exchange, size exclusion, and hydrophobic interaction chromatography
- Activity assays
 - ELISA, cell-based assays, and specialty assays such as one-stage clotting assay
- Binding constants
 - Surface plasmon resonance and isothermal titration calorimetry
- Standard HPLC-based methods for purity, heterogeneity, aggregate, and titer analysis. Detection capabilities extend to refractive index, fluorescence, and ELSD
- Quantitation of host cell impurities and process residuals, DNA by dye binding and qPCR, HCP ELISA, chromogenic LAL, detergent residue analysis



FORMULATION DEVELOPMENT

Customizable program to develop liquid and frozen drug substance formulations

- Preformulation studies
 - Stress and accelerated degradation to characterize product sensitivity to stress conditions, and identify a set of stability indicating assays and select candidate formulations
- Formulation selection study
 - Real-time and accelerated conditions, typically for three months
 - Freeze-thaw and shaking
- Testing may include visual appearance, sub-visual particle count, potency assay, OD 280 nm, turbidity, IEX-HPLC or IEF, SE-HPLC, RP-HPLC, reduced/non-reduced SDS-PAGE, and bioactivity

Custom Formulation Studies

- Lyophilized drug product formulation development
 - Cycle development and pilot run on a VirTis Genesis Model EL pilot unit
 - Formulation and reconstitution diluent development
 - Real-time and accelerated stability of lyophilized and reconstituted product
 - Physical analysis including visual appearance (cake and reconstituted product), cake structure, residual moisture, and reconstitution time
- Compatibility and in-use stability studies
 - Toxicology support
 - Clinical handling support (e.g., IV bags, syringes, and filters)
 - Product fill volume optimization based on clinical needs
- Formulation optimization, photostability, shipping studies, characterization of degradation pathways, and spectroscopic assessment of product conformational stability

QUALITY CONTROL ANALYTICAL CAPABILITIES

- Formal cGMP stability program:
 - Design and execution in compliance with ICH guidelines
- Drug substance and drug product release testing
- QP release in the EU
- Clinical kit ID testing
- Special request cGMP testing



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