SSCI™
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Analytical Support for Protein Formulation Development Fact Sheet

Overcoming physical and chemical instabilities is the most challenging task in the development of protein therapeutics. The molecular structure of all proteins is delicate in nature compared to small molecule drugs and is highly sensitive to environmental changes and stresses. Ensuring native-like higher order structure in a biologic drug is essential because the overall conformation not only defines the stability and biological activity, but also the efficacy and safety.

SSCI offers analytical services in support of protein drug development at different stages and provides data to meet the expectations outlined in the ICH Q6B Specifications: *Test Procedures and Acceptance Criteria for Biotechnological/ Biological Products*.

Pre-formulation screen

SSCI evaluates the impact of various formulation excipients such as ionic strength, buffers, pH, surfactants, sugars, salts, antioxidants, and amino acids on the physicochemical properties of the protein.

- **Size exclusion chromatography (SEC) coupled with a static-light-scattering (SLS) detector** is a routine method for detecting and quantifying protein aggregation.
- **Nano-DSC** is a powerful analytical technique that is used to monitor conformational stability of biologics in their formulations. Structural alterations (unfolding/aggregation) in a biologic can be detected in the form of a Tm (denaturation temperature) shift or a change in the shape of the endothermic peak (ΔH and ΔHv for domain and subunit organization)
- **Dynamic light scattering (DLS) or quasi elastic light scattering (QELS)** is used to evaluate the aggregation state. DLS is a non-destructive technique for the determination of size distribution of particles in the diameter range of 1 nm to 2 µm.

Lyophilization process development and optimization

SSCI offers small scale lyophilization services to screen common excipients for protein stability. Testing is tailored to each client's individual requirements.

- **Formulate the protein in compatible excipients** based on the physicochemical properties of the protein during preformulation screen.
- **Determine the glass transition temperature of the formulation in the frozen state (Tg')** by modulated differential scanning calorimetry (MDSC) and the collapse temperature by freeze-drying microscopy.
- **Determine the optimal shelf temperatures and chamber pressures for primary and secondary drying.**
- **Characterize the finished lyophilized product** using analytical techniques such as X-ray powder diffraction (XRPD) and polarized light microscopy (PLM) to assess crystallinity, thermogravimetry (TG) and DSC for thermal properties, scanning electron microscopy (SEM) for particle morphology, Karl Fischer titration for water content, dynamic vapor sorption/desorption for hygroscopicity testing; solid state NMR, FT-IR, and Raman spectroscopy for chemical and physical finger printing.
- **Evaluate physical stability (unfolding/aggregation) of protein upon lyophilization** by SEC, nano-DSC, and DLS.

Real time and accelerated stability studies

- **Physical stability assessment**: aggregation state evaluation by SEC and DLS, conformational change by nano-DSC, and solid state characterization by various analytical techniques including but not limited to XRPD, TG, DSC, SEM, SSNMR, FT-IR, and Raman.

- **Chemical stability assessment**: with the ultra-high resolution Bruker maXis-Plus Q-TOF mass spectrometer and Agilent DD2-400 solids/liquids NMR spectrometer in conjunction with other techniques such as peptide mapping, MALDI-TOF MS, amino acid analysis, and Edman N-terminal sequencing. SSCI is capable of providing accurate mass and primary sequence of proteins and peptides, to ensure structural integrity and physicochemical identity.

About SSCI

SSCI, a Division of Albany Molecular Research Inc., provides industry leading contract solid-state and analytical testing services and exists to help companies in the pharmaceutical, food, agrochemical, and other chemical industries develop better products and get them to market more quickly. Over the past quarter century, SSCI has provided comprehensive cGMP research and analytical services in the characterization and chemistry of solid materials, with particular expertise in small and large molecules being investigated for pharmaceutical use. As the AMRI's Center of Excellence for Solid State Chemistry, its offerings include early candidate support services (in vitro analysis, stability, solubility, dissolution, excipient compatibility), solid form screening and polymorph, salt and cocrystal screening, form selection, particle engineering (process development, particle size method development), property improvement, crystallization of difficult materials, process control, biochemical analysis, full analytical chemistry support including method development and validation, intellectual property consulting and litigation support, and related research activities.

For information about SSCI's services, please contact 1-800-375-2179 | www.ssci-inc.com.

About AMRI

Albany Molecular Research Inc. (AMRI) is a global contract research and manufacturing organization that has been working with the life sciences industry to improve patient outcomes and quality of life for more than two decades. With locations in North America, Europe and Asia, our key business segments include Discovery and Development Services (DDS), Active Pharmaceutical Ingredients (API), and Drug Product Manufacturing (DPM). Our DDS segment provides comprehensive services from hit identification to IND, including expertise with diverse chemistry, library design and synthesis, in vitro biology and pharmacology, drug metabolism and pharmacokinetics, as well as natural products. API supports the chemical development and cGMP manufacture of complex API, including potent and cytotoxic compounds, controlled substances, steroids, peptides, hormones, and sterile API. DPM supports development through commercial scale production of complex liquid-filled and lyophilized parenterals, sterile suspensions and ophthalmic formulations.

For more information about AMRI, please visit our website at www.amriglobal.com or follow us on Twitter (@amriglobal).