SSCI™

A Division of Albany Molecular Research Inc.

FACT SHEET

Biochemical Testing for Macromolecules and Biochemistry Services

Our biochemistry team provides cGMP support for all stages of biopharmaceutical development through manufacturing. We specialize in method development, validation, and transfer; cGMP batch release testing, impurity characterization and identification, drug substance and product stability and comparability studies, protein/peptide crystallization and solid state characterization, which is critical for lyophilized drug products.

As of October 2014, SSCI, a division of Albany Molecular Research, Inc. is providing ultra-high resolutionQ-TOF mass spectrometry services for large and small molecule analyses. The **Bruker maXis-Plus Q-TOF mass spectrometer** is a state of the art instrument that will significantly enhance our capabilities in analysis and data interpretation for small and large molecules, including biologic drugs, metabolites and polymers to meet the expectations outlined in the ICH Q6B Specifications: *Test Procedures and Acceptance Criteria for Biotechnological/Biological Products*. This sophisticated spectrometry technique will allow:

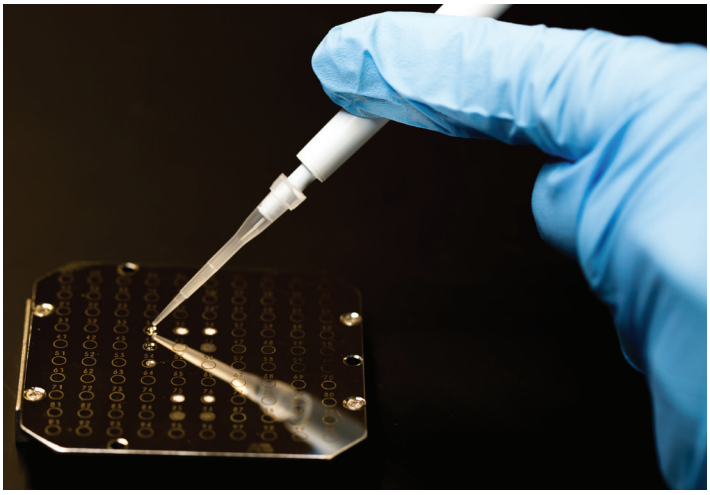
- **Unambiguous assignment of molecular formulae** for small molecules to larger molecules, including biologic drugs, metabolites, and polymers. This mass resolving power enables analyses in the presence of complex matrices (biological, petrochemical, etc.).

- **Identification of active and/or high-percentage metabolites** in drugs to meet the requirements of the United States Food and Drug Administration *Guidance for Metabolites in Safety Testing (MIST)* guidance. Q-TOF mass spectrometry is a fast and accurate analytical method for characterizing low levels of analytes. High resolution mass spectrometry can provide MIST information early in the development path.

- **Enhanced sensitivity** (versus previous-generation instruments): This is particularly important for impurity assays of drug substances and drug products. The limit of detection is in the pg/mL to fg/mL range.

- **Extreme mass range**: The Q-TOF MS has a range from 20 Da to 40,000 Da (assuming a singly-charged species; far larger masses can be analyzed if multiple charges are present). This enables analyses of small molecules, polymers, carbohydrates, oligonucleotides, and proteins such as antibodies.

- **UPLC compatibility for LC-MS**: UPLC chromatography is typically 5-10 times faster than HPLC with up to 2-3 times the chromatographic resolution. This means much faster sample analyse and generally easier method development. Higher through-put enables more rapid turnaround for large numbers of samples.



- **CAD detection for UPLC**: In addition to standard UV detection, state-of-the-art charged aerosol detection is available to enable analyses of materials without UV chromophores.

- **MS and MS/MS capability for a wide range of molecules** combined with detailed interpretation of the results for obtaining the most information from a limited amount of sample.

- **MS of biologic drugs** such as proteins, oligonucleotides, carbohydrates, and other polymers both biological and nonbiological. Sequencing of proteins from the N-terminus or C-terminus is also possible.

When this ultra-high resolution mass spectrometry service is coupled with SSCI's industry-leading expertise, the resulting data and expert scientific interpretation is unmatched in the contract preclinical research industry. In addition to this new capability, SSCI offers a wide range of analytical technologies to characterize biologics and biosimilars, such as: HPLC (RP, IEX, SEC, IC), gel electrophoresis (SDS-PAGE/Native PAGE; IEF) for separation and purity evaluation, N-Terminal Edman Sequencing and Amino Acid Analysis for protein identification, MALDI-TOF MS for molecular weight determination, Dynamic Light Scattering, SEC MALS, and SEM for aggregation state evaluation, and a variety of spectroscopic techniques (NMR, UV/VIS, IR and Raman) for fingerprinting of macromolecules. In addition, ligand binding and activity assays together with LAL endotoxin testing are provided to support batch release of biologicals and biosimilars.

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Biochemical Testing for Macromolecules and Biochemistry Services

Biochemical Testing Services for Macromolecules

SSCI offers the following analytical services relevant to ICH Q6B – Specifications: test procedures and acceptance criteria for biotechnological products in support of IND/NDA submission.

Characterization

- Purity/impurity:
  - HPLC: RP, IEX, SEC, chiral
  - Gel electrophoresis: Native, SDS-PAGE, IEF
- Physicochemical properties
  - Molecular weight: ESI/MS, MALDI-TOF MS, Q-TOF MS
  - Isoform pattern: IEF
  - Extinction coefficient
  - Electrophoretic patterns: Native, SDS-PAGE, Western blotting
  - Liquid chromatography: RP, SEC, IEX, IC, chiral
  - Spectroscopic profiles: UV-VIS, NMR (1D, 2D), IR, Raman
- Stability: nanoDSC
- Potency: Ligand binding assays, activity assays
- Safety: Endotoxin testing, host cell protein and DNA
- Structural elucidation:
  - N-terminal Edman sequencing, mass spectrometric protein sequencing, AAA, peptide mapping, disulfide bond mapping, conformational changes

Aggregation Characterization

SEC-MALS, DLS, SEM, Native-PAGE, SDS-PAGE, sulfhydryl group determination

Comparability and Stability Testing

Various analytical techniques for biophysical and biochemical characterization will be applied to comparability and stability testing. The services will be offered as a means of assessing whether process changes or storage conditions have had an effect on the properties of protein drug substances.

Method Development, Transfer, and Validation

Support all stages of pharmaceutical development through manufacturing

Solid State Biochemistry Services

SSCI offers the following services for biologics in the solid state.

Protein/Peptide Crystallization and Structural Analysis

- Crystallization screening
- XRPD pattern indexing
- Single crystal structure determination (peptides)

Protein/Peptide Formulation Development Support

- Lyophilization formulation and process development
- Screen common excipients for stabilizing of amorphous proteins
- Determine glass transition temperature of the formulation for lyophilization cycle development
- Spray-drying formulation development

Solid State Characterization of Drug Substance and Drug Product

- XRPD
- Spectroscopy – SSNMR, IR, NIR chemical imaging, Raman
- Light microscopy
- SEM
- Particle size distribution
- Surface area
- Thermal analysis: nanoDSC, DSC, mDSC, TG, Hot stage microscopy
- Hygroscopicity testing: DVS
- Accelerated stability testing
- Comparability testing

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 the 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. 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 Manufacturing supports the chemical development and cGMP manufacture of complex API, including potent, controlled substances, biologics, peptides, steroids, and cytotoxic compounds. Drug Product Manufacturing supports development through commercial scale production of complex liquid-filled and lyophilized parenteral formulations.

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