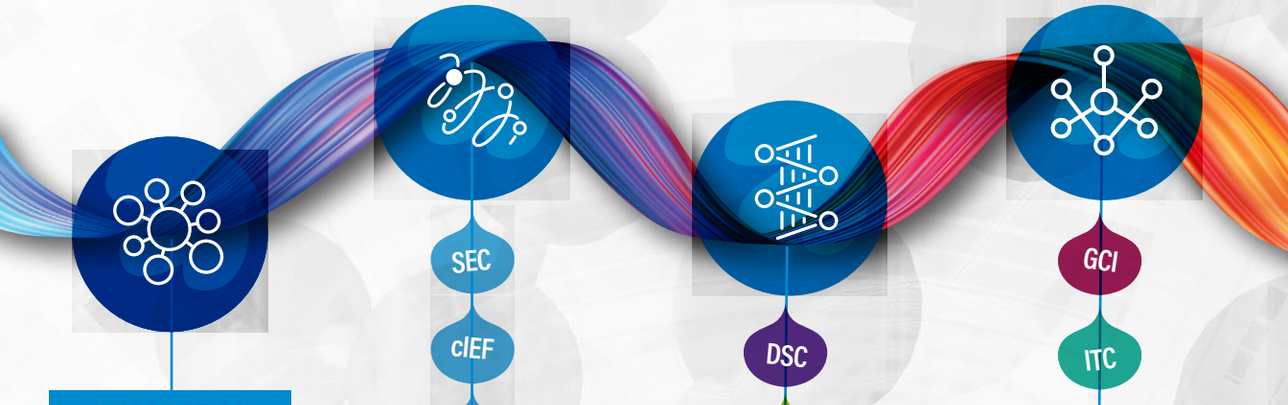
Stability Workflow in Biopharmaceuticals

Biologic drugs are susceptible to compromised structural and conformational stability and these changes can lead to loss of activity. Building from our **HDX LC-MS**, and through our TA Instruments™ business, these concerns are assessed by the **Nano DSC** for higher order structure and to address affinity and function, **ITC**. Through strategic partnerships, emerge another pair of tools: RedShiftBio™'s **MMS**, for secondary structure and Creoptix™'s **GCI** for affinity. These biophysical solutions are combined with biochemical data to provide invaluable information toward the "totality of evidence" of a biomolecule.



COLLOIDAL STABILITY

Measuring both hydrodynamic size (DLS) and scattering intensity (SLS) and the bulk effective charge (ELS) of a protein formulation at various concentrations allows better prediction of the destabilizing particle-particle interactions.

CHEMICAL STABILITY

Understanding the stability and integrity of a protein from its molecular weight profile (SEC) glycosylation variations (MS), and charge variants (cIEF).

CONFORMATIONAL STABILITY

Quantifying secondary structure in formulation conditions (MMS), as well as conformational dynamics (HDX) and thermodynamic stability (DSC) area critical to designing a stabile drug product.

ACTIVITY

Once formulated, ensuring the drug product is still active, ITC or GCI, provide label free technique for assessing ligand binding.

A Vibrant Palette of Tools for Biopharmaceutical Analysis

Hydrogen-Deuterium Exchange – LC-MS

Advanced mass spectrometry technique for examining protein structure, conformational dynamics, and ligand binding. Deuterium exchange of labile amide backbone protons is measured.

Microfluidic Modulation Spectroscopy

Provides a fingerprint of higher order structure as well as a deconvolution of secondary structural components in a protein using the Amide I region of the IR Spectrum.

Grating-Coupled Interferometry

Detects refractive index changes due to change in mass by complex formation of interacting molecules. It is used to determine kinetic rates, K_{on} and K_{off}, and affinity constants.

Isothermal Titration Calorimetry

A label-free, in-solution binding technique used to determine specificity (ΔH), affinity (K_d) and stoichiometry (n) of an interaction.

Differential Scanning Calorimetry

Measures the conformational stability of a protein and is sensitive to the domain transitions of complex biopharmaceuticals such as antibodies. Provides thermal fingerprint for similarity studies including T_{onset}, T_m, ΔH, and ΔC_p.