

Higher-Order Structure Assessment

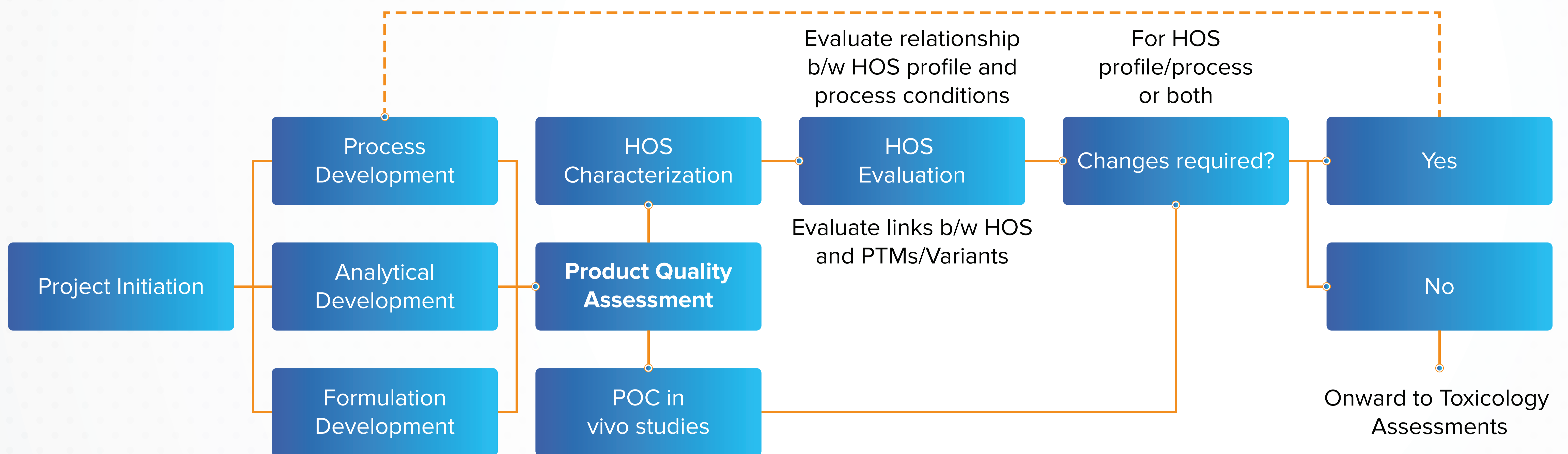
A Critical Step in Biosimilar
Development



Importance of HOS in Biosimilars

This scientific briefing delves into the intricate relationship between Higher-Order Structure (HOS), conformation, and their status as Critical Quality Attributes (CQAs) in biosimilar development. The paramount importance of understanding the correct structure is underscored, influencing crucial aspects such as batch-to-batch consistency, stability, and the prevalence of variants/aggregates. The accuracy of HOS and conformation, considered Critical Quality Attributes (CQAs), is crucial for the effectiveness of biosimilars. Going beyond just looking similar, the precise alignment of these attributes significantly influences how the product behaves in the body (pharmacokinetics) and its therapeutic effects (pharmacodynamics). This precision instills confidence not only in regulatory bodies but also in healthcare practitioners, emphasizing the importance of these characteristics in ensuring the success of biosimilars.

Typical development path in Biosimilars for HOS Monitoring



HOS: Governing Factors

Conformational Stability

Importance

Conformational stability ensures the integrity of the desired three-dimensional arrangement of biomolecules.

Factors

pH, temperature and ionic strength's impact on conformation.
The role of stabilizing agents and excipients in preserving native conformation.
Effect of post-translational modifications, in specific, glycosylation.

Functional Stability

Importance

Ensuring the cohesion of functional attributes is paramount for biosimilar efficacy.

Factors

The impact of environmental factors (process and product related) on the functional aspects of HOS.

Evaluation of stability concerning biological activity and therapeutic efficacy.

Thermal Stability

Importance

Thermal stability addresses the biosimilar's ability to withstand temperature variations without compromising its correct structure.

Factors

Examination of protein unfolding kinetics under different temperature conditions.

Strategies to mitigate heat-induced alterations in HOS.

Aggregation

Importance

Aggregation poses challenges to maintaining structural integrity, impacting the safety and efficacy of biosimilars.

Factors

Identification and characterization of conditions promoting protein aggregation.

Solubility

● Importance

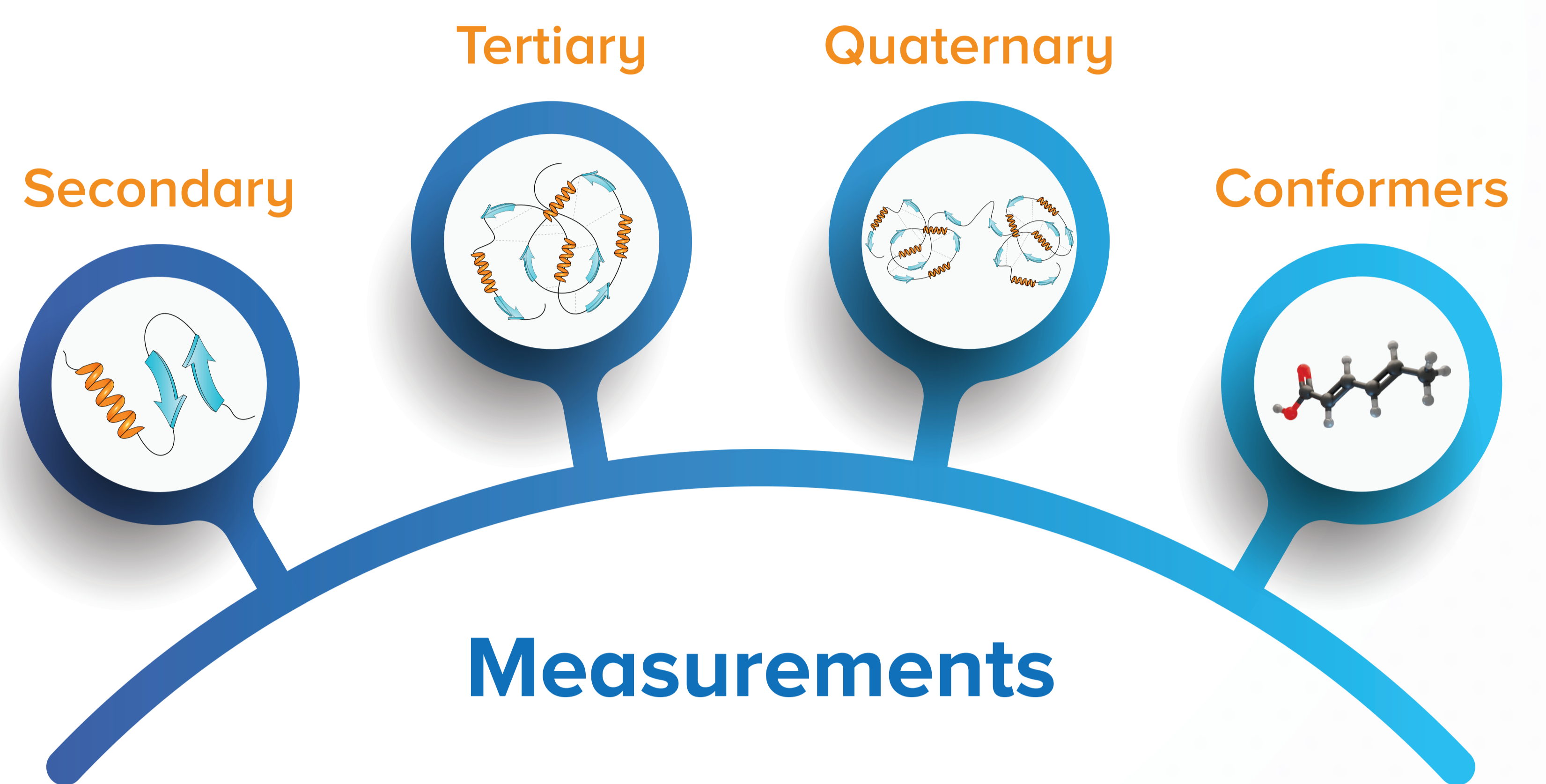
Solubility is integral to biosimilar functionality, influencing administration and bioavailability.

● Factors

Exploration of factors affecting protein solubility, including pH, ionic strength, isoelectric points and molecular size.

Correlating the change in formulations to enhance solubility while preserving conformations.

Methodologies



Method Development Approach & Veeda Biopharma HOS Capabilities

Veeda Biopharma's comprehensive capabilities in exploring secondary and tertiary protein structures, protein conformers, protein stability, and protein dynamics highlight its commitment to advancing the understanding of complex biological systems, ultimately contributing to the development of novel therapeutic interventions and biopharmaceutical solutions with enhanced efficacy and safety profiles.

● Secondary Structure

● Protein Stability

● Tertiary Structure

● Protein Dynamics

● Protein Conformers

Early Screening

Full Characterization

Routine Monitoring

Technology	OEM	Compliance
Circular Dichroism Spectroscopy (CD)	Applied Photophysics Chirascan V100	Good laboratory practices Good documentation practices User license based Audit trail enabled 21 CFR Part 11
Fourier-Transform Infrared Spectroscopy (FTIR)	Bruker Confocheck system	
Size Exclusion Chromatography/Field-Flow Fractionation – Multi-Angle Light Scattering (SEC/FFF-MALS)	Postnova AF2000 MultiFlow FFF Series	
Differential Scanning Calorimetry (DSC)	TA nanoDSC	
Dynamic Light Scattering (DLS)	Anton Paar Litesizer 500	



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