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American Pharmaceutical Review

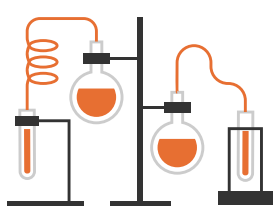
Using Microfluidic Modulation Spectroscopy for Quality Assurance of Biologic Drugs:

Five Applications to Remove Risk and Enable Better, Faster Decision-making.

The complex higher order structure (HOS) of biologic drug products influences their safety and efficacy.

Maintaining and measuring these structures throughout development, formulation and manufacturing is imperative to the commercial and clinical success of biologic drugs.

Biological Quality Assurance



Development → **Formulation** → **Manufacturing**

To date, the application of HOS analysis to biologic quality assurance has been curtailed by the limitations of traditional spectroscopic techniques — namely, low sensitivity, poor reproducibility, lack of automation and a limited dynamic range.

Microfluidic Modulation Spectroscopy (MMS) is a new technology that is purpose-built for biologic quality assurance. MMS offers direct, label-free, and highly reproducible analysis of protein HOS over a wider concentration range and with greater sensitivity than conventional spectroscopic methods. These benefits contribute to the essential utility of incorporating MMS into biopharmaceutical development as a quality assurance tool.

Traditional spectroscopic techniques	Microfluidic Modulation Spectroscopy
low sensitivity	greater sensitivity
poor reproducibility	reproducibility >98%
lack of automation	automated protocols and referencing
limited dynamic range	wider concentration range

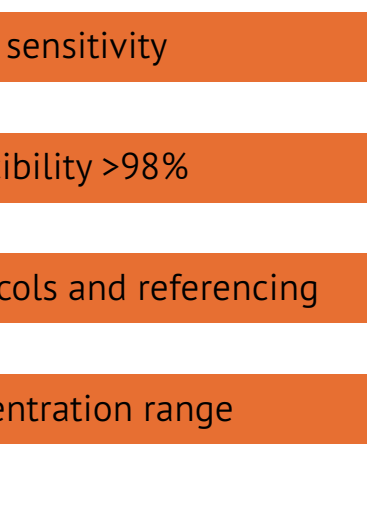
MMS Applications in Biologic Quality Assurance

1 Stability

Stability is a critical quality attribute of all biologics. In the presence of manufacturing and formulation stressors, biologics can experience diminished potency, off-target protein-protein interactions, and degradation. The high sensitivity and wide dynamic range of MMS allow the stability of a biologic to be tracked and maintained throughout its life cycle.

Aggregation 2

Biologics can aggregate when they unfold due to strong intermolecular interactions from solvent-exposed hydrophobic pockets that can be caused by vibrational, thermal, or oxidative stress. An increase in anti-parallel beta-sheet structures is a known indicator of aggregation. Among spectroscopic techniques, MMS is the best suited to detect the subtle changes in beta-sheet content that can alert to the onset of aggregation.

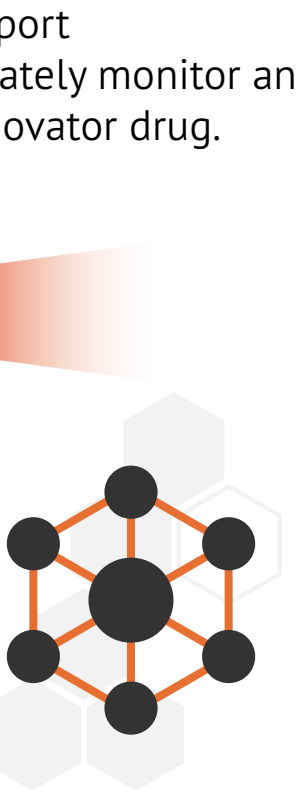


3 Biosimilarity

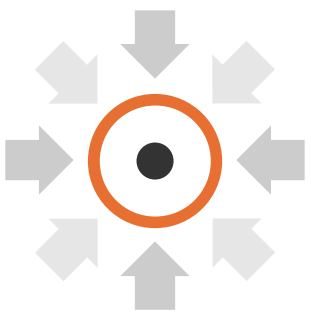
Biosimilars are important as cost-effective options for many biologic drug products and they are required to be as safe and effective as the molecules they resemble. MMS can be used to structurally characterize biologics and can support bioequivalence claims with the ability to accurately monitor and measure the similarity of a biosimilar to an innovator drug.

Structure 4

The secondary structure of a biologic is characterized by the folding patterns that repeat to form alpha-helices, beta-sheets, unordered, and turn structures. These higher order structures (HOS) are like fingerprints to a biologic drug product and monitoring the changes in them provides insight into the stability. MMS offers the ability to track a single wavenumber or structure in order to guarantee that the protein does not unknowingly change during development and manufacturing.



5 Concentration



A significant limitation of UV/Vis spectroscopy is the inability to measure the concentration of biologics that lack aromatic residues. MMS automatically calculates the concentration of all protein and peptide samples during routine spectral analysis and is effective for protein concentrations ranging from 0.1 to > 200 mg/mL.