## Accelerating Scientific Discovery 5<sup>th</sup> World Congress on **Bioavailability and Bioequivalence** Pharmaceutical R&D Summit

September 29-October 01, 2014 DoubleTree by Hilton Baltimore-BWI Airport, USA

## High-resolution NMR as a higher order structure assessment tool for protein therapeutics

John P Marino

National Institute of Standards and Technology, USA

In contrast to small molecule therapeutics whose conformations can be absolutely defined by constitution and stereochemistry, biopharmaceuticals are distinguished by the requirement for folding into higher order structures (secondary, tertiary, and quaternary) for therapeutic function. While proper folding of a protein biologic is critical for drug efficacy, misfolding may impact drug safety by eliciting unwanted immune or other off-target patient responses. High-resolution Nuclear Magnetic Resonance (NMR) provides a robust spectroscopic approach for obtaining higher-order structural 'fingerprints' of the conformation(s) of protein therapeutics at atomic resolution in solution. Such spectral 'fingerprints' of the structure(s) of protein therapeutics can be used as a tool for establishing consistency in drug manufacturing, for detecting drug product variations resulting from modifications in the manufacturing process, and for comparing a biosimilar to an innovator reference product. In this presentation, the author will describe the application of NMR spectral 'fingerprinting' to assess different source granulocyte colony stimulating factor (G-CSF, a.k.a. Filgrastim) drug products, carried out through a benchmark interlaboratory comparability study, involving groups from the FDA, NIST, Health Canada and MPA-Sweden. Results from the study demonstrate the precision with which NMR spectral 'fingerprints' can be used as a higher order structure assessment and comparability tool for protein therapeutics.

## **Biography**

John P Marino received an AB from Princeton in 1989 and a PhD from Yale in 1995. He then held a Humboldt Fellowship for two years at Goethe-Universität. He joined NIST in 1997 and is currently the leader of the NIST Biomolecular Structure & Function Group, Adjunct Professorship at the University of Maryland, and Associate Director of the Institute for Bioscience and Biotechnology Research (IBBR), a joint research institute of the University of Maryland and NIST, in Rockville, Maryland. His research focuses on developing NMR and other biophysical methods to advance precision measurement of biomolecular structure and dynamics.

john.marino@nist.gov