Clinical Pharmacology and Pharmacometrics for Statisticians and Clinical Trialists
(in collaboration with the American Society of Clinical Pharmacology and Therapeutics)

Pharmacometrics is a quantitative pharmacological science that involves the analysis and interpretation of data generated in pre-clinical and clinical drug trials. These data may be generated in cells, preclinical animal models, healthy human volunteers, individuals with disease and populations. Appropriate methods of analysis require an understanding of the underlying science including a knowledge of drug action and toxicity (pharmacodynamic information); a knowledge of the dynamic changes in drug concentrations in plasma and the relationships between dose and drug concentrations in biological fluids (pharmacokinetic information), biostatistics, computational methods, and pharmacokinetic/pharmacodynamic modeling. In this workshop, four fundamental areas will be covered.

**Fundamentals of Pharmacokinetics:** Pharmacokinetic parameters including half-life, clearance, drug exposure, and bioavailability will be introduced conceptually. Examples will be included to show how clinical trial design is impacted by the pharmacokinetics and how drug products fail because of pharmacokinetic problems. A description of how drug concentrations are related to drug response will be included.

**Drug-drug Interactions and Pharmacogenomics:** This will cover the assessment of sources of clinical pharmacokinetic variability in drug development, with a focus on mechanisms of drug-drug interactions and pharmacogenetic variation in drug exposure, and their evaluation in drug development, including impact on drug response and safety.

**Principles of Pharmacometrics:** Analysis of data from clinical trials including pharmacokinetic and response data using pharmacometric methods will be presented including the sources and correlates of variability in both the pharmacokinetics and response in clinical trials. An underlying disease progression model will be included, helping to identify drug efficacy over time as diseases invariably progress. A second presentation will focus on clinical
trial simulation. Dose-concentration effect relationships will be used to simulate clinical trials. How the simulated models inform the design and the questions to be addressed will be discussed. How simulation can be used to design effective clinical trials that minimize subject recruitment, time and expense, and maximize information will be emphasized.

**Target Audience**
Statisticians, clinical investigators and research methodologists.

**Goals**
To understand the common mechanisms of drug-drug interactions and pharmacogenetic variation in drug exposure and response, and approaches to their translational and clinical evaluation in drug development.

To elucidate the value of pharmacometric approaches in characterizing concentration-effect relationships utilizing examples of modeling and simulation applied to clinical data.

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