ADME, PK/TK, AND DRUG METABOLISM IN DRUG DISCOVERY AND DEVELOPMENT

The content of this overview course will assist pharmaceutical, biotechnology, and CRO researchers and managers in understanding the requirements for a well-designed and successful ADME, PK/TK, and DM program conducted within a drug development logic plan and in compliance with ICH guidelines. The various types of ADME, PK/TK, and DM studies, which include in vitro metabolism and delivery, animal and human pharmacokinetics, protein binding, mass balance, tissue distribution, metabolite isolation and identification, and toxicokinetic support, will be discussed.

Study designs and potential results along with possible interpretations from each of the study types will be presented. The generation study reports and summaries, both of which are to be included in submissions to regulatory authorities for completed research experiments, will also be discussed.
INSTRUCTOR CREDENTIALS
Duane B. Lakings, Ph.D., is the Principal and President of Drug Safety Evaluation Consulting, Inc. DSE Consulting assists pharmaceutical and biotechnology companies in designing, conducting, and interpreting results from experiments for characterizing and developing drug candidates into therapeutic products. Dr. Lakings has over 25 years of experience in drug discovery and developability assessment, preclinical and nonclinical development, and clinical development and has designed and conducted animal and human research studies on both small organic molecules and macromolecules.

His primary areas of expertise include pharmacokinetics and toxicokinetics, drug metabolism and ADME, drug delivery, and bioanalytical chemistry and he has excellent knowledge of the pharmacology, toxicology, and clinical requirement for successful drug development. During his career, he has been involved in characterizing drug candidates for a number of therapeutic diseases and disorders, including CNS, cardiovascular, metabolic diseases, oncology, infectious diseases (bacterial and viral), and dermatology. Since opening DSE Consulting, he has used his knowledge to assist clients with defining drug development logic plans, selecting and managing CROs, and preparing study reports for completed nonclinical and clinical research studies.

LEARNING OBJECTIVES
Upon completing this course, participants will have a basic knowledge of the research studies conducted to characterize the likelihood of success for a drug candidate (either a small organic molecule (NCE) or macromolecule) after administration to animal models and humans.

Participants will learn about and understand the requirements for ADME, PK/TK, and DM studies conducted to select the optimal drug discovery lead (developability assessment), to support first-in-human clinical trials (preclinical studies) and to compare and extrapolate metabolism profiles from animal models to humans (nonclinical and clinical evaluations).

FIRST DAY

 Session 1: Introduction and Overview (9:00 – 10:15 AM)
• Purpose and Goals
• Drug Discovery and Development Logic Plan
• Types of Drug Metabolism and ADME Studies

 Session 2: Developability Assessment Experiments – Part 1 (10:30 AM to noon)
• Developability Assessment Overview
• In Vitro Delivery and Example Profiles
• Preliminary Protein Binding
• In Vitro Metabolism

 Session 3: Developability Assessment Experiments – Part 2 (1:00 PM to 2:30 PM)
• Bioanalytical Chemistry Method Definition
• Preliminary Pharmacokinetics and Example Profiles
• Bioavailability and Example Profiles
• GLP Regulations

 Session 4: Preclinical Drug Development Experiments – Part 1 (3:00 PM to 4:30 PM)
• Bioanalytical Chemistry Method Validation
• Pharmacokinetic Parameter Definitions
• Pharmacokinetic Assessments in Toxicology and Pharmacology Animal Species
• Absolute Bioavailability and Dose Proportionality Examples

SECOND DAY

 Session 5: Preclinical Drug Development Experiments – Part 2 (9:00 AM to 10:15 AM)
• Toxicokinetics
• Multiple Dose Evaluation Examples
• Gender Effect Examples
• Drug Candidate Radioisotopic Labeling
• Choice of Label and Labeling Site
• Radiochemical and Metabolic Stability Evaluations
• Mass Balance in Toxicology Species
• Metabolic Profiling Assay
• Study Design and Sampling Recommendations
• Extent of Metabolism
• Route(s) and Rate(s) of Elimination
• Definitive Protein Binding in Various Species

 Session 6: Clinical Drug Development Experiments (10:30 AM to noon)
• Types of Human ADME and Drug Metabolism Experiments
• Human Pharmacokinetic Evaluation Examples

 Session 7: Clinical Drug Development Experiments (1:00 PM to 2:30 PM)
• Drug-Drug and Drug-Food Interactions
• Stereochimistry Issues
• Bioavailability and Bioequivalence Evaluations
• Renal and Hepatic Impairment Studies
• Age Effects

 Session 8: Nonclinical Drug Development Experiments – Part 1 (3:00 PM to 4:30 PM)
• Toxicokinetic Support
• Feto-placenta Transfer and Lactal Secretion Toxicokinetic Studies
• Tissue Distribution (Single– and Repeat–Dose) and Whole Body Audioradiography
• Studies Design and Sampling Requirements

THIRD DAY

 Session 9: Nonclinical Drug Development Experiments – Part 2 (9:00 AM to 10:15 AM)
• Metabolite Isolation and Identification
• Development and Validation of Bioanalytical Method(s) for Metabolites
• Pharmacokinetic Evaluation of Metabolites
• Definition of Metabolism Pathway
• Induction and Inhibition of Drug Metabolizing Enzymes
• Animal Bridging Studies

 Session 10: Documentation (10:30 AM to noon)
• Study Protocols
• Technical/Study Reports
• Test Assay Methods
• Standard Operating Procedures
• Summaries for Submission to Regulatory Authorities

 Session 11: Workshop (1:00 PM to 3:00 PM)
• Summary and Conclusions
• Workshop to Design and Discuss ADME and Drug Metabolism Studies Needed to Support the Discovery and Development of Various Drug Candidate Types

HOTEL INFORMATION
The Hilton LAX, Los Angeles, CA (CfPIE room rate of $167/night if booked 3 weeks in advance of the course date)
The Desmond Hotel & Conference Center, Malvern, PA (CfPIE room rate of $141/night if booked 3 weeks in advance)
The Club Quarters Hotels, Boston, MA (CfPIE room rate of $255/night if booked 4 weeks in advance).
The DoubleTree by Hilton London - Victoria (CfPIE room rate of £199.00/night if booked 4 weeks in advance).