ADMET, PK/TK, and Drug Metabolism

Course Scope and Description

This course is specifically designed for personnel in the pharmaceutical and biotechnology industries and contract research organizations (CROs), who need to understand the requirements for ADMET (absorption, distribution, metabolism, elimination, toxicity), pharmacokinetics/toxicokinetics (PK/TK) and drug metabolism (DM) experiments during the drug discovery and development processes.

It would be favorable for participants to have some knowledge of these processes and the desire to learn more about how ADMET, PK/TK, and DM studies are designed, conducted, and interpreted in order to characterize the fate of a drug candidate and select the candidate for preclinical development that meet the set criteria.

Nonclinical and clinical scientists, managers, and project team leaders at pharmaceutical companies and related industries will gain a detailed understanding of the state-of-the-art *in vitro* and *in vivo* ADMET assays, and how PK/TK, and DM research studies are conducted to select the candidates for preclinical development and to support submissions to regulatory authorities. *In vitro/in vivo* correlations, how to design and use in vitro ADMET studies to get maximum value out of *in vivo* studies will be addressed. Appropriate use of validated PBPK modeling during discovery and development of drug candidates will be discussed.

The content of this course will assist pharmaceutical, biotechnology, and CRO researchers and managers in understanding the requirements for a well-designed and successful ADMET, PK/TK, and DM program that is conducted within a drug development logic plan and in compliance ICH guidelines. The various types of ADME, PK/TK, and DM studies, which include *in vitro* metabolism and delivery, appropriate use of *in vitro* and *in vivo* mechanistic toxicity assays and their relationship with regulatory toxicology, animal and human pharmacokinetics, protein binding, mass balance, tissue distribution, metabolite isolation and identification, and toxicokinetic support, will be discussed. Case studies of well and poorly designed programs, study designs and potential results, with possible interpretations, from each of the study types will be presented. The generation of study reports and summaries, both of which are to be included in submissions to regulatory authorities, for completed research experiments will be delineated.

COURSE PROGRAM – DAY ONE

08:30 – 10:00 Introduction and Overview

Purpose and Goals
Drug Discovery and Development Logic Plan
Types of Drug Metabolism and ADMET Studies
GLP Regulations Overview

10:30 – 12:00 Developability Assessment Experiments

In Vitro Delivery and Example Profiles
In Vitro Metabolism
In Vitro Toxicity
Early Drug-drug Interactions Investigations
Preliminary Protein Binding
Bioanalytical Chemistry Method Definition
Preliminary Pharmacokinetics and Example Profiles
Bioavailability and Example Profile
Do I have a proper drug candidate or an early hit? - Case studies and group discussion.

13:00 – 14:30 Preclinical Drug Development Experiments

Bioanalytical Chemistry Method Validation
Pharmacokinetic Assessments in Toxicology and Pharmacology Animal Species
Absolute Bioavailability and Dose Proportionality Examples
Case study and group discussion

15:00 – 16:30 Preclinical Drug Development Experiments

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

COURSE PROGRAM – DAY TWO

08:30 – 10:00 Clinical Drug Development Experiments

Types of Human ADME and Drug Metabolism Experiments
Human Pharmacokinetic Evaluation Examples
Drug-drug and Drug-Food Interactions
Stereochemistry Issues
Bioavailability and Bioequivalence Evaluations
Renal and Hepatic Impairment Studies
Age Effects

10:30 – 12:00 Nonclinical Drug Development Experiments

Toxicokinetic Support
Feto-placenta Transfer and Lacteal Secretion Toxicokinetic Studies
Tissue Distribution (Single– and Repeat–Dose) and Whole Body Audioradiography
Studies Design and Sampling Requirements
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

13:00 – 14:30 Clinical Drug Metabolism and ADME

Study Protocols
Technical/Study Reports
Test Assay Methods
Standard Operating Procedures
Summaries for Submission to Regulatory Authorities

15:00 – 16:30 Documentation

Summary and Conclusions
Group discussion: Design and Discuss ADME and Drug Metabolism Studies Needed to Support the Discovery and Development of Various Drug Candidate Types – Discovery Lead Selection and Optimization.

For more information contact:

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