DMPK: Experimentation & Data Interpretation

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Prerequisite: Entry-level scientists with hands on experience in LC/MS as well as advanced students who wish to learn more about mass spectrometry applications in drug metabolism, pharmacokinetics (DMPK) and bioanalysis. The course is a unique opportunity for scientists already in the pharma, biotech, and other industries to broaden or enhance their expertise and knowledge. Due to the highly interactive format, managers and project leaders also may benefit from discussions on decision making, analytical technology, and emerging applications in DMPK and related topics.

Course materials: Electronic copies of PowerPoint presentations and a reference book (M. Lee and M. Zhu. Mass Spectrometry in Basic Short course: DMPK: Experimentation & Data Interpretation Drug Metabolism and Disposition: Principles and Applications. John Wiley & Sons) will be provided.

ASMS American Society for Mass Spectrometry

Course Overview

Mass spectrometry has become the dominant analytical tool throughout the DMPK and bioanalytical research areas in drug discovery and development continuum. This short course will provide thesis on mass spectrometry in DMPK and bioanalysis in support of R&D and the registration process. The course will use case studies to focus on the "why" and "how" knowledge base with regard to the use of mass spectrometry to measure small molecule drugs, biologics, and their conjugates in the discovery and development phases. Contents will include an introduction to the concepts / principles of DMPK, an overview of drug discovery / development processes, and common practices in DMPK studies. Current mass spectrometry technologies applied in ADME screening in lead optimization, drug quantification in PK studies, drug metabolite identification in animals and humans, as well as GLP bioanalysis quantification in clinical and toxicology studies will be discussed along with updated industry practices for experimental design, data interpretation, and data reporting. Case studies to solve common DMPK and bioanalytical issues will be given to reinforce concepts and analysis techniques learned in class.

MAJOR TOPICS COVERED IN THIS COURSE

• **Basic DMPK concepts applied in pharmaceutical research**: This portion will include basic principles of drug metabolism and pharmacokinetics, introduction of PK concepts and parameters as well as common metabolic reactions, metabolizing enzymes and metabolism research models.

• **Role of DMPK in drug discovery and development**: This portion will provide an overview of various types of drug metabolism and bioanalytical studies throughout the life time of a drug candidate.

• **Drug metabolite profiling and identification in drug discovery and development**: This portion
will cover basic concepts of drug metabolite identification (Met ID) including LC/MS workflow and mass spectral interpretation. Typical Met ID experiments will be discussed in detailed such as metabolic soft-spot identification and reactive metabolite screening in drug discovery, and metabolite identification in humans in drug development. Focus will be given on applications of a variety of LC-HRMS based data acquisition and data mining techniques to metabolite
detection and characterization.

MAJOR TOPICS COVERED IN THIS COURSE

• **Quantitative analysis of drug candidates and their metabolites in vitro and in vivo by LC/MS:** This portion will cover science, technique, regulation and compliance of bioanalysis, sample preparation, and LC/MS/MS technologies for quantification in preclinical and clinical studies. Quantification of protein and conjugate drugs by LC/MS also will be discussed. Focus will be placed on LC and MS technology and technique.

• **Application of LC/MS technologies in conducting special drug metabolism and ADME studies.** This position will cover evaluating in vitro drug interaction potentials and radiolabeled ADME studies in support drug development, including concept, assay, analytical method and case studies. In addition, strategy and method for studying release and metabolism of payload-containing components from non-cleavable ADCs will be discussed.

• **Applications of LC/MS in analysis of biologics and biomarkers**: This portion will cover recent applications of LC/MS in quantification of protein therapeutics and biomarkers as well as study of biotransformation / disposition of antibody-drug conjugates for characterization of ADME / PK of biologics and PK/PD of small molecule drugs.

Preliminary course schedule

Day One (9:00 – 4:30 with lunch 12:00 to 1:00 and coffee breaks 10:15 to 10:45 and 2:30 to 3:00)

1 - Introduction (20 min)
1.1. Introduction to the short course (10 min)
1.2. Discussion: what you want? (10 min)

2 - DMPK in drug discovery/development (1 hr 20 min)
2.1 Drug metabolism in drug discovery and development (20 min) (MZ)
2.2 Bioanalysis/PK in drug discovery and development (15 min) (NW)
2.3 Basic pharmacokinetics and applications (20 min) (NW)
2.4 Basics of drug metabolism and experimental models (20 min) (MZ)

3 - Fundamentals of the use of LC/MS technology for DMPK (1 hr 55 min)
3.1 Common LC/MS techniques for bioanalysis (45 min) (NW)
3.2 Common LC/MS techniques for drug metabolite identification (1 hr) (MZ)

4 – Workflows / problem solving in DMPK to move drug candidates forward (2 hr 20 min)
4.1 Use of LC/MS in addressing metabolite-related issues in drug discovery and development (70 min) (MZ)
4.2 Fit for purpose LC/MS bioanalysis strategy (40 min) (NW)
4.3 Measurement of free drug concentrations by LC/MS (30 min) (NW)

Preliminary course schedule

Day two (9:00 – 4:30 with lunch 12:00 to 1:00 and coffee breaks 10:15 to 10:45 and 2:30 to 3:00)

4 – Workflows / problem solving in DMPK to move drug candidates forward (2 hr 40 min)
4.4 Evaluating in vitro drug interaction issues: concept, assay, and analytical method (60 min) (MZ)
4.5 Biologics (and conjugates) quantification (40 min) (NW)
4.6 Radiolabeled ADME study in animals and human: concept, method and case study (60 min) (MZ)

5 - New Applications in PK, PD, and metabolism (2 hr)
5.1 LC/MS in biomarker analysis (30 min) (NW)
5.2 Strategy and method for studying release and metabolism of payload-containing components from non-cleavable ADCs (40 min) (MZ)
5.3 Regulation of bioanalysis in toxicology and clinical studies (40 min) (NW)

6- Concluding remarks, last questions, and feedback (10 min)
The time devoted to each of the course topics will be customized to meet the stated needs of the students enrolled. A preliminary course schedule is given above.

7- Back up content
7.1 HRMS-based non-targeted analysis of xenobiotics (40 min) (MZ)