PHA6418 Introduction to Model-Informed Drug Development (MIDD)
Fall 2022
3 Credit Hours – A-E Grading

Course Description
Introduction to Model-Informed Drug Development (MIDD) is a 3-credit course that serves as a broad overview of applying modeling and simulation strategies to improve drug development decision-making and trial designs. Examples of applications include translational approaches from preclinical to clinical research, translation from biomarker to clinical endpoint, dose finding during Phase 1 and 2, clinical confirmation during Phase 3, avoiding the need for certain clinical trials, characterizing sources of variability in drug response, regulatory interactions and post-marketing assessment. Upon completion of the course, students will have a basic understanding of how model-based drug development can be applied to help bring new drugs to market more efficiently.

Course Coordinator
Thomas Schmittgen, PhD (tschmittgen@cop.ufl.edu)

Participating Faculty
Guenther Hochhaus, PhD, co-Course Coordinator
Francine Azeredo, PhD
Stephan Schmidt, PhD
Brian Cicali, PhD
Richard Lalonde, PharmD
Mark Rogge, PhD

Assistant Course Coordinator
Nasser Nassiri Koopaei, PhD (koopaei@ufl.edu)

Course Faculty
Lectures will be provided by numerous, adjunct faculty members from the pharmaceutical industry with vast experience in model-based drug development. Details and biographical sketches of the faculty can be found on the Canvas course site.

Course-Level Objectives
Upon completion of this course, the student will be able to:

1. Discuss and appreciate the role of model-informed drug development during the following stages: discovery, preclinical, clinical, regulatory review and post-approval.
2. Identify specific drug development questions or issues that can be addressed using MIDD.
3. Select and apply pharmacometric method(s) used in MIDD: population PK or PK-PD, clinical trial simulation, meta-analysis, systems pharmacology, PBPK, etc.
4. Contrast MIDD applications to support regulatory agency decisions versus drug development decisions within pharmaceutical industry.
5. Understand the development strategies for various therapeutic areas and identify the question that needed to be answered using MIDD
6. Describe MIDD approaches used to answer the above question: e.g. modeling, simulation, results, key assumptions and uncertainties.
7. Explain the impact of MIDD on specific drug development examples and regulatory decisions or interactions.
8. Apply MIDD concepts to all Phase(s) of drug development: preclinical, Phase 1, 2, 3, regulatory agency interactions, and post-regulatory approval.

9. Explain the critical aspects of conducting clinical trials including human subject protections, Phase 1, 2, and 3 trials, regulatory requirements, and clinical data management.
10. Answer specific drug development questions or issues that can be addressed by MIDD: dose selection, trial design for Phase 1, 2, or 3, go/no go, labeling, development strategy, avoiding the need to conduct a clinical trial, selecting between compounds in development, etc.
11. Apply MIDD to various therapeutic areas: cardiovascular, neuroscience, metabolic diseases, oncology, rare diseases, etc.

Course Pre-Requisites: none
Course Co-Requisites: none
Course Contact Hours: 45

Course Outline
Please routinely check your campus calendar and the Canvas course site for any messages about changes in the schedule and deadlines.

Every week, two lectures will be assigned and made available online. In addition, reading assignments will be provided related to the recorded lectures. These lectures can be watched by the students at any time. Furthermore, an active learning session (ALS) will be held that will allow interactive participation by the students. The time of the ALS will be **12:00-1:00 EST on Thursdays**. Please see the comment below on ALS attendance.

Week	Lecture available	ALS	Topic	Lecturer	ALS coordinator
1	Aug 24th	Aug 25th	Overview of Model-Informed Drug Development; Course overview	Lalonde	Lalonde, Schmittgen
2	Aug 29th	Sept 8th	Fundamental Concepts and Basic Pharmacokinetic and Pharmacodynamic Parameters; Introduction to PKPD	Hochhaus	Hochhaus
3	Sept 5th	Sept 15th	Introduction to Population PK/PD; Introduction to PBPK	Azeredo, Cicali	Azeredo, Cicali
4	Sept 12th	Sept 22nd	Drug-Drug Interactions; Preclinical to Clinical Scaling of PK and PD	Schmidt, Sinha	Azeredo, Cicali
5	Sept 19th	Sept 29th	Model-Based Meta-Analysis (MBMA) to Support Phase 3 Dose selection of Apixaban; Mechanism-based models for cross-species translation of efficacy & safety to inform early development	Byon, Mettetal	Hochhaus
6	Sept 26th	Oct 6th	PBPK of Perampanel (Role in Approval); PBPK of Perampanel (Support of Monotherapy)	Schuck	Cicali
7	Oct 3rd	Oct 13th	MIDD Dose Optimization Oncology; MI Dosing Recommendation using PBPK and Translation to Prescribing Information	Gupta	Lalonde
Midterm	Week of Oct 3rd				
8	Oct 10th	Oct 20th	MIDD Development of Nivolumab; Pharmacometric Approaches for change in Dosing Regimen for Anti-PD-1 monoclonal Antibodies	Bello, Davis	TBN
9	Oct 17th	Oct 27th	MIDD in Oncology: Rational Dose Selection; Model-Based Meta-Analysis to Replace a Head-to-Head Clinical Trial in Type 2 Diabetes	Venkatakrishnan, Weber	TBN
10	Oct 24th	Nov 3rd	MIDD in Phase 2 Development; MIDD Strategies and Antibacterial Drug Development	Krishnswami, Schuck	Azeredo
11	Oct 31st	Nov 10th	Quantitative DDI Analysis for Regulatory Interactions: Case Examples; Model-Informed Drug Development for Dose Selection and DDI	Reddy, Masson	Azeredo

12	Nov 7th	Nov 17th	Streamlining approval for generic inhalation drugs	Hochhaus	Hochhaus
13	Nov 14th	Dec. 1st	Practical Decision Analysis Tools to Enable Key Drug Development Decisions; Application of MIDD to RNAi Therapeutics	Krishna, Robbie	Schmittgen, Hochhaus
14	Nov 21st		No classes - Thanksgiving Break		
15	Nov 28th	Dec 1st	Pediatric Drug Development; Using Nonclinical Data and PBPK Modelling to Inform on Risk of Victim DDI in Discovery	Sinha, Gibson	Cicali
16	Dec. 5th	Dec 8th	Role of Biomarkers in Developing CNS Drugs; MIDD applications when organ impairment is a determinant of dose	Conrado, Rogge	Rogge
Final	Week of Dec 12th				

Lecture videos will be released on the Monday of each week.
An active leaning session (ALS) will be held on each Thursday at 12:00-1:00 PM EST via Zoom which will be accessible through the course calendar on Canvas. The meeting will cover both lectures from the previous week with lecturers joining the call to answer students' questions.

Recommended Textbooks

- Title: Applied Pharmacometrics
- Authors: S. Schmidt, H. Derendorf
- AAPS Press/Springer
- 2014
- ISBN number: 978-1493913039

- Title: Rowland and Tozer's Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications
- Authors:. H. Derendorf, S. Schmidt
- Wolters & Kluwer
- 2020
- ISBN number: 978-1496385048

Additional reading assignments will be made available on the Canvas course site.

Quizzes

There will be a 10-question multiple choice quiz following most weeks.

Discussion Boards
See affiliated course materials for instructions.

Materials & Supplies Fees
None

Student Evaluation & Grading
Evaluation Methods and How Grades are calculated.

Assessment Item	Grade Percentage
Class participation	5%
Quizzes (10X5%)	50%
Midterm exam	22.5%
Final exam	22.5%

Percentage Range	Letter Grade
92.50-100%	A
89.50-92.49%	A-
86.50-89.49%	B+
82.50-86.49%	B
79.50-82.49%	B-
76.50-79.49%	C+
72.50-76.49%	C
69.50-72.49%	C-
66.50-69.49%	D+
62.50-66.49%	D
59.50-62.49%	D-
< 59.50%	E

Class Attendance Policy
Pease refer to UF attendance policy: https://catalog.ufl.edu/UGRD/academic-regulations/attendance-policies/

Students are required to watch lectures within the period that is indicated in the syllabus. Conflict with work schedules is not an excused absence for not watching the lectures.

Class attendance is mandatory for all active learning sessions (ALS). Student attendance may be excused by Dr. Schmittgen in the following situations: documented illness, family emergencies, religious holidays, and other reasons of serious nature. Conflict with work schedules is an unexcused absence.

Requests for excused absences MUST be made by an email prior to the scheduled session.
The student is responsible for follow up. Failing to follow this policy will render the absence not excusable. A request for an "excused absence" does not guarantee acceptance. No precedence can be drawn from any courses in the College of Pharmacy or any other college within University of Florida.

Makeup exam or quiz(s) will be made for any excused absence(s) and must be submitted ***within one-week of the missed session(s)***. If the situation leads to missing multiple class sessions and makeup becomes difficult, the student and course coordinator will discuss with the administration to explore options such as a remediation plan or course withdrawal. There will be a one-point deduction for missing any ALSs up to 5% of the final grade.

Academic Integrity Policy
Students are expected to act in accordance with the University of Florida policy on academic integrity (http://www.dso.ufl.edu/sccr/honorcodes/honorcode.php). This Honor Code specifies a number of behaviors that are in violation of this code and the possible sanctions. Furthermore, you are obliged to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult the course's Teaching Partnership Leader. Students are also expected to abide by the UF Honor Code.

The following is the UF Honor Pledge: We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity by abiding by the Honor Code.
On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: "On my honor, I have neither given nor received unauthorized aid in doing this assignment.