**PHA6131 Introduction to Physiologically-Based Modeling**
**Spring 2022**
**3 Credit Hours – A-E Grading**

**Course Description**
Introduction to Physiologically-Based Modeling is a 3-credit course that provides students and trainees with the theoretical concepts as well as hands-on applications in physiologically-based modeling and its use in drug development and regulatory evaluation with focus on physiologically-based pharmacokinetic (PBPK) modeling. Upon completion of this course, students will have gained a basic understanding of PBPK model components and parameters, key PBPK model building and verification steps, and the data needed to inform these models. They will also have completed hands-on training in different PBPK software platforms.

**Course Coordinators**
Stephan Schmidt, PhD (sschmidt@cop.ufl.edu); Rodrigo Cristofoletti, PhD (RCristofoletti@cop.ufl.edu)

**Teaching Assistant**
Nasser Nassiri Koopaei, PhD (koopaei@ufl.edu)

**Course Faculty**
Lectures will be provided by a team of in-house house faculty and internationally-renown experts in the PBPK arena. Details and biographical sketches of the faculty can be found on the Canvas course site.

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

1. Understand the role of physiologically-based models at different stages of drug development and regulatory evaluation with focus on physiologically-based pharmacokinetic (PBPK) models.
2. Identify key PBPK model components and parameters
3. Understand and apply PBPK model building and verification processes
4. Identify the data needed to inform PBPK models
5. Parametrize clearance, volume of distribution, and absorption processes using different *in vitro* and *in vivo* data sources
6. Identify factors impacting clearance, volume of distribution, and oral drug absorption
7. Understand the role of transporters and parametrize them in PBPK models
8. Develop and verify models for major PBPK applications (i.e., absorption, drug-drug interactions, and special patients populations) in different software platforms
9. Have a basic understanding of additional major PBPK applications (e.g., virtual bioequivalence and non-oral routes of absorption)
10. Understand the setup of PBPK models for large molecules and how they differ from small molecules

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

**Course Outline**
Every week, two lectures will be assigned and made available online. In addition, reading assignment will be provided related to the recorded lectures. These lectures can be watched by the students at any time. Please routinely check your campus calendar and the Canvas course site for any messages about changes in the schedule and deadlines.

The following topics will be covered:

| Week/Date | Module | Instructor | Topics |
|---|---|---|---|
| **Week 1** | **1** | StephanSchmidt | **Introduction**<br>✓ Course overview & Setup<br>✓ Introduction to physiologically-basedmodeling |
| **Week 2** | **2** | StephanSchmidt | **Physiologically-Based Modeling Approaches inDrug Development and Regulatory Evaluation** |
| **Week 3** | **3** | StephanSchmidt | **PBPK Model Development and Verification**<br>✓ PBPK model components<br>✓ Development and verification workflow<br>✓ Variability |
| **Week 4** | **4** | Rodrigo Cristofoletti | **Clearance**<br>✓ In vitro-in vivo extrapolation (IVIVE)<br>✓ Factors affecting drug metabolism<br>✓ *In vitro* models for hepatic clearance<br>✓ Transporters in clearance<br>✓ Renal clearance |
| **Week 5** | **5** | Rodrigo Cristofoletti | **Volume of Distribution**<br>✓ Factors affecting tissue distribution<br>✓ *In silico* models for tissue partitioncoefficients<br>✓ Perfusion & permeability limiteddistribution |
| **Week 6** | **6** | Rodrigo Cristofoletti | **Physiological Models for Oral Absorption**<br>✓ Factors affecting drug absorption and gutbioavailability<br>✓ *In vitro* models for drug release<br>✓ Permeability, solubility, luminal stability<br>✓ Transporter mediated kinetics |
| **Midterm exam** | | | |
| **Week 7**<br>**Week 8** | **7** | All teaching partners | **Software Application 1: Absorption**<br>✓ Guided hands-on tutorial<br>✓ Software assignment 1 |
| **Week 9**<br>**Week 10** | **8** | All teaching partners | **Software Application 2: DDI**<br>✓ Guided hands-on tutorial<br>✓ Software assignment 2 |
| **Week 11**<br>**Week 12** | **9** | All teaching partners | **Software Application 3: Special Populations**<br>✓ Guided hands-on tutorial<br>✓ Software assignment 3 |
| **Week 13**<br>**Week 14** | **10** | All teaching partners | **Additional Major PBPK Applications**<br>✓ Metabolites<br>✓ PBPK/PD<br>✓ Virtual Bioequivalence<br>✓ Additional dosage routes<br>✓ Machine learning + PBPK in discovery |
| **Week 15** | **11** | All teaching partners | **Large Molecules** |
| **Final Exam** | | | |

**Recommended Textbooks**

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

Title: Physiologically-Based Pharmacokinetic (PBPK) Modeling and Simulation: Principles, Methods, and Applications in the Pharmaceutical Industry.
Author: S.A. Peters
John Wiley & Sons, Inc.
2012
ISBN number: 978-0-470-48406-7

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

**Problem Sets and Exams**

All problem sets and exams have a one-week window for completion.

**Materials & Supplies Fees**

None

**Student Evaluation & Grading**

Evaluation Methods and How Grades are calculated.

| Assessment Item | Grade Percentage |
|---|---|
| Exams 1 | 20% |
| Exam 2 | 20% |
| Take home assignments (3x20%) | 60% |
| Total | 100% |

| 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 |

**Additional Policy Specific to This Course: Problem Set and Exam Policy**
Students must finish the problem sets and exams within the one-week window indicated in the syllabus. Students who missed the quiz window will get a zero for that quiz without an excused reason. Students need to contact the course coordinator through email for any emergency situation that prevents the student from taking the problem set and explain the situation immediately when the situation resolved. The student will either take a make-up problem set or choose other options determined by the coordinator.

**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."