USC Mann
Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences

PSCI 662 - Advanced Pharmacokinetics/Pharmacodynamics
2 Units
Fall 2024 Monday 10:00 AM - 12:00 PM
Location: PSC B13

Course Coordinator(s):

John Andrew MacKay: jamackay@usc.edu
Office: PSC 306A Phone: (323) 442-4118

Office Hours:

MacKay: Tuesdays at 2

Office hours will be held on Zoom.

Instructors:

John Andrew MacKay: jamackay@usc.edu
Paul Beringer: beringer@usc.edu
Michael Bolger: bolger@usc.edu
David D'Argenio: dargenio@usc.edu

Communication:

IT Help:

Brightspace is the Learning Management System (LMS) used at the USC Mann School of Pharmacy and Pharmaceutical Sciences. For 24/7 help with Brightspace

- Call (213) 740-5555 and select Option 1.
- Send an e-mail to brightspace@usc.edu.
- Visit USC's Brightspace Online Help site for how-to videos and guides: https://www.brightspacehelp.usc.edu/
- **Zoom and Panopto may be used for lecture capture and delivery, Zoom and Poll Everywhere may be used as an audience response system, and Brightspace and ExamSoft may be used to administer quizzes and examinations.**
- For help with Zoom, visit https://itservices.usc.edu/zoom/.
- For help with Panopto, call the 24/7 Panopto support team at (855) 765-2341 or e-mail support@panopto.com
- For help with ExamSoft, call the 24/7 ExamSoft support team at (866) 429-8889, e-mail support@examsoft.com , or visit https://help.examsoft.com/.
- You may also visit our Technical Support Specialists in PSC 302B, M- F from 8:00 AM-5:00 PM, call (323) 442-0002, or e-mail mannit@usc.edu
- **For all other technology-related questions, call USC Information Technology Services at (213) 740-5555**

Course Description

Advanced Pharmacokinetics/Pharmacodynamics (PSCI 662) will present concepts, standard terminology, and mathematical models of drug disposition. Students will focus on understanding and/or practicing common methods for the collection, analysis, interpretation, and comparison of pharmacokinetic data. In addition to derivation of analytical solutions for common pharmacokinetic profiles, students will be introduced to several software packages capable of solving and fitting more complex models. The course also introduces students to parameter estimation methods, including allometric scaling, Bayesian Statistics and Physiologically-Based Pharmacokinetic (PBPK) modeling. By providing a hands on experience using traditional PK analysis, this course prepares learners for a subsequent course on PBPK modeling (PSCI 518).

Course Learning Objectives

By the end of this course on Pharmacokinetics, learners will master:

- OBJECTIVE 1: Model Derivation. Use mass balances to derive analytical solutions for common PK profiles following a single dose. These include one and two compartment models of an intravenous bolus, during and after short and long intravenous infusions, and absorption of an extravascular/oral dose. Differentiate between compartmental and model-independent PK.
- OBJECTIVE 2: Understanding Parameters. Describe, calculate, and interpret common parameters and outputs involved with PK, which include volume of distribution, clearance, half-life, area under the curve, bioavailability, protein-binding, loading dose, and maintenance dose.
- Objective 3: Analyze, compare, write, and communicate regarding experimental PK data using available data and tools.

Course Notes

Brightspace: This is utilized as the learning management system for this course. Lecture slides, lecture videos, assignments, solutions, and grades will be posted on Brightspace. Assignments will be submitted for grading through Brightspace. Instructions related to examinations and discussion activities will be provided through Brightspace.

ZOOM: Accessed via Brightspace, Zoom may be used on computers for office hours and possibly other content as needed. In general, zoom office hours will not be recorded for this course.

SAAM2: A software program (Simulation, Analysis, and Modeling 2, SAAM2) may be used to fit and model pharmacokinetic data. Instructions for accessing this software and using it to solve HW and cases for your term paper will be made throughout the course.

Required Readings and Supplementary Materials

- Rowland and Tozer's Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications, 5e Hartmut Derendorf, Stephan Schmidt (2020), https://premiumpharmacy-lwwhealthlibrary-com.libproxy1.usc.edu/book.aspx?bookid=2695 (https://tinyurl.com/mddrxbxf)

Description and Assessment of Assignments

Homework will be assigned via Brightspace. Completed assignments should be uploaded into Brightspace before the posted deadline. Assignment solutions will be posted within one week of the due date. There will be between 5 and 11 homework scores; however, the two lowest scores will be automatically dropped from the calculation of your grade. You do not need to email to request this.

Assessment methods used in this course:
Multiple guess questions
Fill-in-the-blank/Short answer questions

Hand-written essay questions
Homework assignments
Written Term project with Oral presentation

Methods

Teaching Methods

Before Event

- Online lecture
- Assigned reading/writing (texts)
- Online activity

During Event

- Classroom lecture
- Small group discussion
- Student presentation
- Team based learning
- Polling questions

Assessment Methods

Examination

- Multiple choice
- Short answer

In Class

- Oral presentation
- Attendance and Participation

Longer Term

- Term paper

Grading Breakdown

Assignment	Percent
Homework	25
Midterm	25
Term Project	25
Final Exam	25

Grading Scale

A 95-100.00
A- 90-94.99
B+ 87-89.99
B 83-86.99
B- 80-82.99
C+ 77-79.99
C 73-76.99
C- 70-72.99
D+ 67-69.99
D 63-66.99
D- 60-62.99
F 59.99 and below

Additional USC Mann School Policies

Policy on Learning & Assessment Feedback (LAF)

Feedback on examinations/assessments will be provided using the following methods.

- Complete examination will be returned and a key will be made available

Policy Regarding Assignments and Examinations

The following actions are all violations of academic integrity and subject to disciplinary action:

a. Any use or attempted use of external assistance in the completion of an academic assignment and/or during an examination, or any behavior that defeats the intent of an examination or other classwork or assignment, unless expressly permitted by the instructor.
b. The following are examples of unacceptable behaviors: communicating with fellow students during an exam, copying or attempting to copy material from another student's exam; allowing another student to copy from an exam or assignment; possession or use of unauthorized notes, calculator, or other materials during exams and/or unauthorized removal of exam materials.
c. Other examples of academic misconduct have been and will be considered.

Policy Regarding Missed Examinations

The policy for this course will follow the policy contained within the Academic Policies and Procedures section of the Student Handbook located on the USC Mann School of Pharmacy and Pharmaceutical Sciences Intranet. Students who miss an examination are referred to this policy.

Policy on Absences

University policy grants students excused absences from class for observance of religious holy days. Faculty are asked to be responsive to requests when students contact them IN ADVANCE to request such an excused absence. The student should be given an opportunity to make up missed work because of religious observance. Students are advised to scan their syllabi at the beginning of each course to detect potential conflicts with their religious observances. Please note that this applies only to the sort of holy day that necessitates absence from class and/or whose religious requirements clearly conflict with aspects of academic performance. For additional program specific absence policies, please refer to the Student Handbook on the USC Mann School of Pharmacy and Pharmaceutical Sciences Intranet.

Policy for Written Assignments Regarding Citation Style

All written assignments in the course should use the uniform style of the USC Mann School of Pharmacy and Pharmaceutical Sciences for formatting in-text citations and reference lists. This style corresponds to the AMA (American Medical Association) format and can be found through this following guide https://libguides.usc.edu/ama11 and handout https://libguides.usc.edu/ld.php?content_id=54130825. The complete AMA Manual of Style is also available as an e-book at tinyurl.com/bdh8amka .

Technological Requirements and Software Updates

Students may be required to bring an internet-enabled device with browser capabilities, such as a cell phone, tablet, or laptop to class. During class time, it is expected that students will use their devices only to participate in activities guided by the instructor. Use of devices for other purposes is not permitted during class time.

The USC Mann School of Pharmacy and Pharmaceutical Sciences recommends that students purchase a computer that meets, at minimum, the "medium" level hardware requirements that are also recommended for faculty and staff: https://itservices.usc.edu/recommendations/

Students who use Zoom should be running the latest version of Zoom available at https://zoom.us/download.

Students who use ExamSoft will also be required to have the latest version of Examplify installed on their laptops at all times compatible with their operating system. Occasional updates to the software may be asked of you throughout the year. It is your responsibility to read your USC e-mails regarding Examplify and follow the instructions as listed.

Learning Experience Evaluation Notes:

Extra credit may be provided for completion of the online course evaluation during the last week of classes.

Statement on Academic Conduct and Support Systems

Academic Integrity:

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university. All incidences of academic misconduct will be reported to the Office of Academic Integrity and could result in outcomes such as failure on the assignment, failure in the course, suspension, or even expulsion from the university.

For more information about academic integrity see the student handbook or the Office of Academic Integrity's website, and university policies on Research and Scholarship Misconduct.

Please ask your instructor if you are unsure what constitutes unauthorized assistance on an exam or assignment, or what information requires citation and/or attribution.

Course Content Distribution and Synchronous Session Recordings Policies

All class recordings (Zoom, Panopto, etc.) are accessible only to students currently enrolled in the class, instructors, and TAs. These recordings may not be shared or used for purposes outside of this course. Students are also not permitted to record or distribute any course materials or activities on their own without the instructor's permission.

About Your Instructor(s)

J. Andrew MacKay, Ph.D.
Office: 306A
Contact Info: jamackay@usc.edu

Attempts will be made to respond to emails within one week; however, students are urged to make use of scheduled office hours, recorded lectures, solutions to assignments, and in-class discussion sessions.

Summary of Course Schedule

Date	Lecturer	Event
Monday 08/26/24 10:00 AM - 12:00 PM	John MacKay	Module 1: Course Overview, Topics in PK, ADME, graphing
Tuesday 09/03/24 1:00 PM - 3:00 PM	John MacKay	Module 2: rate constants, compartmental models, Clearance, Volume of Distribution, Half-life
Monday 09/09/24 10:00 AM - 12:00 PM	John MacKay	Module 3: AUC, Bioavailability, IV Infusion Model, IV Short Infusion vs. Bolus model, Protein Binding
Monday 09/16/24 10:00 AM - 12:00 PM	John MacKay	Module 4: Extravascular (Oral) Model, Time Maximum Concentration, Method of Residuals
Monday 09/23/24 10:00 AM - 12:00 PM	John MacKay	Module 5: Two-compartment IV Bolus Model, Macroconstants, Microconstants, Volume at Steady State
Monday 09/30/24 10:00 AM - 12:00 PM	John MacKay	Module 6: Hepatic Physiological Clearance Equation, Intrinsic Clearance
Monday 10/07/24 9:00 AM - 12:00 PM	John MacKay	Exam 1
Monday 10/14/24 10:00 AM - 12:00 PM	Paul Beringer	Module 7: Renal Clearance, Assessment of Renal and Hepatic Function, Drug Dosing in Renal and Hepatic Disease

Monday 10/21/24 10:00 AM - 12:00 PM	Paul Beringer	Module 8: Multiple Dose: IV Bolus, IV Short Infusion, Oral Rapid and Controlled Release, Time to Steady-State, Loading Doses
Monday 10/28/24 10:00 AM - 12:00 PM	John MacKay	Module 9: Modeling Data in Term Paper using SAAM
Monday 11/04/24 10:00 AM - 12:00 PM	Michael Bolger	Module 10: Allometric scaling, Physiologically-based Pharmacokinetic models (PBPK)
Tuesday 11/19/24 1:00 PM - 3:00 PM	David D'Argenio John MacKay	Module 11: Modeling Monoclonal Antibody PK, Bayesian Estimation
Monday 12/02/24 10:00 AM - 12:00 PM	John MacKay	Module 12: Term-paper presentations and due date
Monday 12/16/24 9:00 AM - 12:00 PM	John MacKay	Exam 2 (Date TBD)

Expanded Course Schedule

Date	Lecturer	Event
Monday 08/26/24 10:00 AM - 12:00 PM	John MacKay	Module 1: Course Overview, Topics in PK, ADME, graphing MODULE DESCRIPTION: In this module, you will be introduced to common pharmacokinetic parameters required to solve and interpret pharmacokinetics. LEARNING OBJECTIVES: - Compare and contrast pharmacokinetics and pharmacodynamics - List processes involved with ADME - Explain differences between blood, serum, plasma - List applications of PK from drug development to therapeutic dose monitoring - Use graphing paper to plot PK data TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read chapters 1,2 (Rowland & Tozer) - Prior to class review HW1 (need not complete) - During class be prepared to discuss asynchronous content, participate in small group discussions, solve problems. - HW1 will be due after Module 2.
Tuesday 09/03/24 1:00 PM - 3:00 PM	John MacKay	Module 2: rate constants, compartmental models, Clearance, Volume of Distribution, Half-life MODULE DESCRIPTION: In this module, you will be introduced to additional pharmacokinetic parameters, as well as methods to use graphing to quantify pharmacokinetics. LEARNING OBJECTIVES:

		- Explain variables important to the solution of PK models - Use mass balances to setup equations for compartmental models - Describe how changes in clearance and volume of distribution influence the observed half-life of the drug TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read Chapter 3 (Rowland & Tozer) - Prior to class complete homework (HW1) - During class be prepared to discuss homework - After class HW is due by 11:59pm
Monday 09/09/24 10:00 AM - 12:00 PM	John MacKay	Module 3: AUC, Bioavailability, IV Infusion Model, IV Short Infusion vs. Bolus model, Protein Binding MODULE DESCRIPTION: In this module, you will learn how to solve and calculate drug concentration after IV administration. LEARNING OBJECTIVES: - Calculate AUC after a single IV bolus dose using the trapezoid method - Calculate bioavailability following single dose IV and PO - Solve the plasma concentration-time profile after a single bolus iv - Identify factors that affect the plasma concentration-time profile after a single bolus iv administration - Use IV infusion model to solve for the concentration after: -a long infusion, which reached steady state -a short infusion, which did not reach steady state - Calculate loading doses by infusion using -bolus model -short infusion model TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read chapters 5,10, Appendix A,C,D (Rowland & Tozer) - Prior to class complete homework (HW2) - After class HW is due by 11:59pm
Monday 09/16/24 10:00 AM - 12:00 PM	John MacKay	Module 4: Extravascular (Oral) Model, Time Maximum Concentration, Method of Residuals MODULE DESCRIPTION: In this module, you will be introduced to additional pharmacokinetic parameters, as well as methods to use graphing and model independent methods to quantify pharmacokinetics. LEARNING OBJECTIVES: - Use mass balance to model concentration after absorption of an extravascular dose - Explain and calculate parameters related to absorption - Explain and use method of residuals - Explain how bioavailability affects the estimation of

		clearance and volume of distribution TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read Chapter 6,7 Appendix F (Rowland & Tozer) - Prior to class complete homework (HW3) - During class be prepared to discuss homework - After class HW is due by 11:59pm
Monday 09/23/24 10:00 AM - 12:00 PM	John MacKay	Module 5: Two-compartment IV Bolus Model, Macroconstants, Microconstants, Volume at Steady State MODULE DESCRIPTION: In this module, you will learn how to solve and interpret data for drugs that follow a 'two-compartment' model after IV administration. LEARNING OBJECTIVES: - Compare and contrast the 1-and 2-compartment PK models - Use method of residuals to determine distinct exponential terms relevant to PO, IV-infusion, 2-compartment drugs - Calculate the plasma concentration following a iv bolus that follows 2-compartment PK model - Explain/estimate the the difference between microconstants and macroconstants in the 2 compartment model - Describe volume of distribution and clearance as it relates to 2 compartment drugs - Analyze the effect of changing pk parameters on the plasma concentration-time profile after iv bolus of drugs that follow 2-compartment pk model TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read Chapter 19, Appendix E (Rowland & Tozer) - Prior to class complete homework (HW4) - During class be prepared to discuss homework - After class HW is due by 11:59pm
Monday 09/30/24 10:00 AM - 12:00 PM	John MacKay	Module 6: Hepatic Physiological Clearance Equation, Intrinsic Clearance MODULE DESCRIPTION: In this module, you will learn how to apply models of physiological clearance in the context of the liver and their implications in drug interactions. LEARNING OBJECTIVES: - Describe the physiological meaning of total body clearance in terms of organ blood flow, intrinsic clearance, fraction of unbound drug, and extraction ratio - Describe the effect of changing the hepatic intrinsic clearance and blood flow on the hepatic extraction ratio - Analyze the effect of changing either intrinsic clearance or liver blood flow on the plasma concentration-time

		profile after IV and oral administration - Describe the relationship between hepatic clearance and liver blood flow, enzyme activity and protein binding - Discuss biliary excretion and enterohepatic recycling TASKS: - Prior to class review asynchronous lectures and slides (1 hr)Â - During class participate in small group discussions - During class be prepared to discuss homework
Monday 10/07/24 9:00 AM - 12:00 PM	John MacKay	Exam 1 This exam tests the content covered on Modules 1 through 6.
Monday 10/14/24 10:00 AM - 12:00 PM	Paul Beringer	Module 7: Renal Clearance, Assessment of Renal and Hepatic Function, Drug Dosing in Renal and Hepatic Disease MODULE DESCRIPTION: In this module, you will learn how to apply models of physiological clearance in the context of the kidneys and their implications in dose adjustment and drug interaction. LEARNING OBJECTIVES: - Identify some causes of variability in drug pharmacokinetics in different individuals. - Determine the factors that affect the change in drug pharmacokinetics in patients with kidney dysfunction during multiple drug administration. - Analyze the effect of changing the kidney function and the fraction of dose excreted unchanged in urine on drug pharmacokinetics. - Recommend an appropriate dosing regimen in patients with kidney failure. - Evaluate the appropriateness of dosing regimens in patients with kidney dysfunction. TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read Chapter 3 (Beringer & Winter) - Prior to class complete homework - After class HW is due by 11:59pm
Monday 10/21/24 10:00 AM - 12:00 PM	Paul Beringer	Module 8: Multiple Dose: IV Bolus, IV Short Infusion, Oral Rapid and Controlled Release, Time to Steady-State, Loading Doses MODULE DESCRIPTION: In this module, you will learn how to apply multiple dosing models to estimate plasma concentrations after doses when a patient has been taking a regimen for some duration. LEARNING OBJECTIVES: - Define steady state during multiple dose administration. - Determine whether a loading dose is needed given a

		multiple dose regimen and pharmacokinetic parameters. - Calculate an appropriate loading dose to rapidly achieve target concentrations. - Choose the appropriate dosing model to predict steady-state concentrations following multiple dose administration. - Determine the steady state drug concentrations and patient pk parameters during multiple dose administration. - Analyze the effect of changing one or more of the pk parameters on the steady state plasma concentration during multiple dose administration. - Recommend a maintenance dosing regimen to achieve specific plasma concentrations in patients. TASKS: - Prior to class review asynchronous lectures and slides - Prior to class read Chapter 2 (Beringer & Winter) - Prior to class complete homework - During class be prepared to discuss homework - After class HW is due by 11:59pm
Monday 10/28/24 10:00 AM - 12:00 PM	John MacKay	Module 9: Modeling Data in Term Paper using SAAM MODULE DESCRIPTION: In this module, you will learn to use SAAM to model your PK data for your term paper. LEARNING OBJECTIVES: - Identify a compartmental model that can be used to characterize your data. - Determine if there is a testable hypothesis that you can answer using available data and models - Tabulate fit parameters - Create prediction curves for a regimen - Hands on help using SAAM software TASKS: - Prior to class review asynchronous lectures and slides - Prior to class complete homework - During class be prepared to work on your data fitting - After class HW is due by 11:59pm
Monday 11/04/24 10:00 AM - 12:00 PM	Michael Bolger	Module 10: Allometric scaling, Physiologically-based Pharmacokinetic models (PBPK) MODULE DESCRIPTION: In this module, you will be introduced to PBPK modeling and allometric scaling, two methods useful for predicting PK in humans. LEARNING OBJECTIVES: - Review examples of how PK parameters can be estimated across species. - Understand what parameters can be used in PBPK models - Explain and understand relative strengths of PBPK vs compartmental modeling. - Introduction to Simulations Plus PBPK software

		TASKS: - Prior to class review asynchronous lectures and slides - Prior to class complete homework - During class be prepared to discuss HW - After class HW is due by 11:59pm
Tuesday 11/19/24 1:00 PM - 3:00 PM	David D'Argenio John MacKay	Module 11: Modeling Monoclonal Antibody PK, Bayesian Estimation MODULE DESCRIPTION: In this module, you will be introduced to population pharmacokinetic modeling, using examples of monoclonal antibody therapies. LEARNING OBJECTIVES: - Introduce concept of Bayesian Parameter Estimation - Connect this with the concept of using population PK parameter fits to make estimates of individual PK parameters using sparse data - Be able to describe examples of monoclonal antibody therapeutics. TASKS: - Prior to class review asynchronous lectures and slides - Prior to class complete homework - During class be prepared to discuss HW - After class HW is due by 11:59pm
Monday 12/02/24 10:00 AM - 12:00 PM	John MacKay	Module 12: Term-paper presentations and due date MODULE DESCRIPTION: In this session, we will hear from each group a short presentation on their term paper. LEARNING OBJECTIVES: - Demonstrate competence discussing PK data and parameters - Identify strengths and weaknesses of your own PK data - Identify possible connections between PK parameter issues and evidence for toxicity/efficacy TASKS: - Prior to class review powerpoint slides of entire class - During class be prepared to present your topic and provide comments - Take time to complete Learning Experience Evaluation - NOTE: The HW for this week is the term project and powerpoint presentation, Due Dec 6th , 11:59 pm
Monday 12/16/24 9:00 AM - 12:00 PM	John MacKay	Exam 2 (Date TBD) This exam tests the content covered on Modules 7 through 11.