

USC Mann

Alfred E. Mann School of Pharmacy
and Pharmaceutical Sciences

Spring 2024: RXRS 407: The Discovery, Development and Marketing of Modern Medicines

12.06.2023

Instructors: Daryl Davies, PhD
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HSC Office: PSC 528
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Office Hours by appointment

Course Weight: 4 Units (two 1.5-hour sessions; plus 1 hour outside activities)

Day/Time/Location: TTH 9:30-10:50 am, Vivian Hall (VHE) 217

Introduction

This course introduces the student to the biomedical community as it relates to current strategies undertaken to move research discoveries from the laboratory (bench) into clinical practice (bedside) to diagnose and treat patients. This concept is commonly referred to as Translational Science or Translational Medicine. The tenets of this course will be defined and explained in terms of promoting focused multidisciplinary interactions between science and medicine to enhance disease research and drug development. In addition, the wider inter-relationships with regulatory, ethical and societal sectors will be presented.

Objectives

This course is designed for undergraduates of both scientific and non-scientific majors with an interest in learning about principles and concepts underlying drug discovery and development of medicines. Chapters from the required textbook will be supplemented with a variety of source materials including articles from scientific journals and public websites. Selected cases studies will be critically reviewed and emerging “hot” topics discussed.

Upon successful completion of this course, the student should be able to:

- Describe the importance of a team effort in the drug discovery/drug development process as seen through the eyes of the pharmaceutical industry.
- Describe the many challenges faced by a start-up pharmaceutical company.

- Explain the importance of intellectual property (IP); critical IP issues and timing.
- Summarize the preclinical drug development process from therapeutic target to marketable drug.
- Become fluent with the basic terminology used in characterizing a new drug (e.g. potency, EC₅₀, IC₅₀, MTD, efficacy, selectivity, ADME, etc....).
- Explain the importance of a properly designing a scientific experiment (Scientific Method).
- Describe critical components of drug discovery as it relates to genotoxicity, carcinogenicity and reproductive/developmental toxicology issues during the course of a drug discovery campaign and how to test for them.
- Summarize the difference between a small molecule drug and a biopharmaceutical and describe the advantages and disadvantages of each therapy.
- Explain the importance of good laboratory practices (GLP), good manufacturing practices (GMP) and good clinical practices (GCP).
- Discuss the various facets and the role of clinical trials in drug development.
- Deduce why so many experimental compounds fail to ever reach the market.

Assignments and Grading:

4 Short Reflections @ 5 pts each	20 pts	(10 %)
4 quizzes @ 10 pts each	40 pts	(20%)
Discussion Board Participation:	20 pts	(10%)
1 midterm exam	50 pts	(25 %)
<u>1 final exam:</u>	<u>70 pts</u>	<u>(35 %)</u>
Total:	200 pts.	

Short Reflections and Attendance (20 pts):

Attendance at all classes is expected. Participation will be evaluated by accepting “short reflections” throughout the semester (5 pts per submission/ total of 4 maximum) and will include evaluating the class material and the method of delivery for any given week. That is, I want you to tell me what is working and what is not working during the semester so I can continue to improve the class in real time. It is expected that the students read the assigned papers prior to the lecture and be prepared to discuss background, current understanding, treatments, and gaps in knowledge for the topic in each lecture.

Quizzes (40 pts):

There will be 4 quizzes over the course of the semester that will primarily be based on questions pulled from the textbook and lectures.

Discussion Board (20 pts):

Each student will also participate in Discussion Board posts during the semester or other deliverable assignments on Blackboard. Further information regarding the Discussion Board assignments will be provided during the first week of class.

Participation Assignment	Due Date	Points
Blackboard Assignment 1	February 1, 2024	10
Blackboard Assignment 2	April 23, 2024	10

Exams:

The midterm (50 points) will include multiple choice questions T/F questions fill-in the blank questions, and short answers.

Final Exam (70 points): The final exam will include multiple choice and T/F questions as well as a series of questions involving short answers. The final exam will be cumulative but will emphasize material covered after the midterm.

Additional details will be presented during week one of the class and included in the Week 1 PPT slides.

Notes, books, calculators, electronic dictionaries, regular dictionaries, cell phones or any other aids are not allowed during exams.

Students will be asked to complete an anonymous critical evaluation of the course at its completion.

Course Readings

Required Readings

Drug Discovery and Development: Technology in Transition, 2nd Edition

Raymond G. Hill & Humphrey P. Rang; ISBN-13: 978-0702042997

Although not mandatory, it is strongly suggested that the students purchase the textbook for this course as it will greatly improve the students grasp on the Drug Discovery/Development process. The students will be able to use identified chapters in the text to support their learning process throughout the semester.

Other course materials including but not limited to the syllabus, supplemental reading assignments and additional handouts will be posted on <http://blackboard.usc.edu/>. The students will also be encouraged to use the online discussions among students via Blackboard.

Recommended

- Adman Bernstein and Patricia Sullivan. “Frances Oldham Kelsey, FDA scientist who kept thalidomide off U.S. market, dies at 101.” *Washington Post*. August 7, 2015
https://www.washingtonpost.com/national/health-science/frances-oldham-kelsey-heroine-of-thalidomide-tragedy-dies-at-101/2015/08/07/ae57335e-c5da-11df-94e1-c5afa35a9e59_story.html

- Christine M. Clovis, PhD and Christopher P. Austin, MD. The NIH-Industry New Therapeutic Uses Pilot Program: Demonstrating the Power of Crowdsourcing. *Drug Repurposing, Rescue and Repositioning*. VOL. 1 NO. 1 (March, 2015)
- Cynthia Fox, Reading Leaves a Dramatic Imprint on the Brain: <http://www.biosciencetechnology.com/articles/2014/12/reading-leaves-dramatic-imprint-brain?location=top>
- [Hepatitis C cure eludes patients as states struggle with costs](https://www.nbcnews.com/health/health-news/hepatitis-c-cure-eludes-patients-states-struggle-costs-n870846)
<https://www.nbcnews.com/health/health-news/hepatitis-c-cure-eludes-patients-states-struggle-costs-n870846>
- Dr. Timothy Scott discusses some of the history of the FDA and how it shaped the industry. <https://youtu.be/TXAVCaOSi-s>
- Free magazine “Translational Science” <https://www.youtube.com/watch?v=9Cw9v-LnrRU&feature=youtu.be>
 - [Newsletters such as: Drug Discovery Online Newsletter <info@DrugDiscoveryOnline.com>](mailto:info@DrugDiscoveryOnline.com)
 - [Pharmaceutical Processing: https://www.rdmag.com/topics/pharmaceutical-processing](https://www.rdmag.com/topics/pharmaceutical-processing)

Course Content Distribution and Synchronous Session Recordings Policies

USC has policies that prohibit recording and distribution of any synchronous and asynchronous course content outside of the learning environment. Recording a university class without the express permission of the instructor and announcement to the class, or unless conducted pursuant to an Office of Student Accessibility Services (OSAS) accommodation. Recording can inhibit free discussion in the future, and thus infringe on the academic freedom of other students as well as the instructor. ([Living our Unifying Values: The USC Student Handbook](#), page 13).

Distribution or use of notes, recordings, exams, or other intellectual property, based on university classes or lectures without the express permission of the instructor for purposes other than individual or group study. This includes but is not limited to providing materials for distribution by services publishing course materials. This restriction on unauthorized use also applies to all information, which had been distributed to students or in any way had been displayed for use in relationship to the class, whether obtained in class, via email, on the internet, or via any other media. ([Living our Unifying Values: The USC Student Handbook](#), page 13).

Course Outline

This course will be in the format of a directed seminar/lecture under the guidance of the instructor for the specific session. During each weekly session the instructor will engage the

students with questions and draw comments or interpretations primarily based on the assigned reading. Students are expected to ask questions and participate in an interactive fashion.

Week & Date	Topic	Subtopics to be Included	Assigned and Supplemental Reading
Introduction and Background			
Week 1 Tues. Jan. 9 Thur. Jan. 11	Introduction: expectations and goals of this class. General overview of drug development process from therapeutic target to marketable drug.	Pharmacological principles and definitions: Efficacy (EC ₅₀), potency, MTD, ADME, etc. Drug discovery and development: facts and figures	Additional readings to enrich subject matter will be posted on Blackboard. Hill/Rang, Chapter 22.
Week 2 Tues. Jan. 16 Thur. Jan. 18	Development of Pharmaceutical Industry- History of the Discovery and Development of Modern Medicines Quiz 1 Jan 18	History of drug development (where and how it all got started). Case studies illustrating why we have the FDA. What is Translational Science? https://www.youtube.com/watch?v=rAbIbUmyQgk	Hill/Rang, Chapter , Chapter 2 Hill/Rang, Chapter 3
Week 3 Tues. Jan. 23 Thur. Jan. 25	Nature of Disease Daryl Davies Reflection Paper 1 Jan. 25	Etiology, pathology, research highlights, current drug treatments and future drug development. Therapeutic Interventions; Therapeutic modalities Novel use of Ketamine: https://youtu.be/GnL4p-35Grg	Hill/Rang, Chapter 4
Drug Discovery			
Week 4 Tues. Jan. 30 Thur. Feb. 1	An Overview of Modern-Day Drug Discovery Good Research Practices DD Hovik Gukasyan Blackboard Assignment 1, Due Feb. 1	Brain Games: an example of challenges of Academic science https://www.science.org/content/article/misc/duct-concerns-possible-drug-risks-should-stop-stroke-trial-whistleblowers-say General Principles; Case Histories	Hill/Rang, Chapter 4
Week 5 Tues. Feb. 6 Thur. Feb. 8	DD Defining a Market DD Project Management of Drug Quiz 2 Feb 8th	Defining the Market. Where and how does it start. The role of Project Management in Drug Discovery	Hill/Rang, Chapters 5-6
Week 6		Drug Discovery, where does it all start?	

Tues. Feb 13 Thur. Feb 15	Pharmaceutical Development Hovik Gukasyan	“Drugable” Property Space: Desired properties and qualities of an ideal candidate? Safety, Efficacy, Delivery Confidence In Chemical Matter: Drug Discovery Implications	Hill/Rang, Chapter 16
Week 7 Tues. Feb. 20 Thurs. Feb. 22	Dr. Ashutosh Kulkarni Reflection Paper 2 Feb. 22	Understand the role of drug metabolism and pharmacokinetics (DMPK) and early stage toxicology studies as major hurdles in the drug discovery process; Role of pharmacology (specifically confirmation in vitro assays, target selectivity testing and in vivo pharmacological profiling) in the drug discovery process;	Hill/Rang, Chapters 10-11;13-14
Week 8 Tues. Feb. 27 Thurs. Feb. 29	The Components of Drug Discovery Mary Ellen Cosenza Midterm Feb 29th	Biopharmaceuticals; Midterm Feb 29th	
Week 9 Tues. Mar. 5 Thurs. Mar. 7	Mary Ellen Cosenza Dr. Robert Pacifici, CHDI	Assessing Drug Safety; Identifying the Project; Identifying the Target	Hill/Rang, Chapters 10-12;13-14
Spring Recess Sunday, March 10, 2024 to Sunday, March 17, 2024			
Drug Development			
Week 10 Tues. Mar. 19 Thurs. Mar. 21	Hovik Gukasyan Dr. Robert Pacifici Reflection Paper 3 Due Mar. 21	Development products for clinical testing and comparability Role of CROs in new drug development	
Week 11	Larisa Yedigarova	"Clinical development of novel therapeutics"	Hill/Rang, Chapter 17

Tues. Mar. 26		For Assignment #2 Phases of Clinical Trials explained https://www.youtube.com/watch?v=k40iNSRzdEU&t=13s	
Thurs. Mar. 28			
Week 12	Hovik Gukasyan	Development Strategies and Considerations for Combination Products—Drug+Drug combinations, Drug:Device combinations; drug eluting stents.	Hill/Rang, Chapter-20
Tues. Apr. 2	Quiz 3 Apr 2		
Thurs. Apr. 4	Hovik Gukasyan	Future research directions. Channeling gene-therapy and Crispr cas9	
Week 13	Michael R. Hamrell, PhD	Regulation of Advertising and Promotion for Prescription Drugs	
Tues. Apr. 9	Reflection Paper 4 Due Apr. 11		
Thurs. Apr. 11			
Week 14	Repurposing	The use of a drug repurposing strategy to accelerate new opportunities for currently approved drugs in the pharmaceutical industry	Examples from DD laboratory
Tues. Apr. 16	DD: Patents: Importance of IP in Academia		Hill/Rang, Chapter 19
Thurs. Apr. 18	Quiz 4 Apr 18		
Week 15	Hovik Gukasyan	Comprehend different drug delivery systems Scale-up /formulation challenges	
Tues. Apr. 23	Blackboard Assignment 2 due April 23		
Thurs. Apr. 25			
Final Exam: Tuesday, May 7, 2024 from 8 am to 10 am			

Academic Integrity

The University of Southern California is foremost a learning community committed to fostering successful scholars and researchers dedicated to the pursuit of knowledge and the transmission of ideas. Academic misconduct is in contrast to the university's mission to educate students through a broad array of first-rank academic, professional, and extracurricular programs and includes any act of dishonesty in the submission of academic work (either in draft or final form).

This course will follow the expectations for academic integrity as stated in the [USC Student Handbook](#). All students are expected to submit assignments that are original work and prepared specifically for the course/section in this academic term. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s). Students suspected of engaging in academic misconduct will be reported to the Office of Academic Integrity.

Other violations of academic misconduct include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university 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](#).

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Distribution or use of notes, recordings, exams, or other intellectual property, based on university classes or lectures without the express permission of the instructor for purposes other than individual or group study. This includes but is not limited to providing materials for distribution by services publishing course materials. This restriction on unauthorized use also applies to all information, which had been distributed to students or in any way had been displayed for use in relationship to the class, whether obtained in class, via email, on the internet, or via any other media. ([Living our Unifying Values: The USC Student Handbook](#), page 13).

Course Evaluations

Course evaluation occurs at the end of the semester university-wide. It is an important review of students' experience in the class.

Respondus Lockdown Browser for Exams

Exams will be administered through Respondus. You will not be able to open the exam without downloading the browser. Please follow the instructions from **USC ITS** below prior to the exam.

Students **MUST** download the Respondus Lockdown Browser on the computer they will be using to take the test. Respondus does not automatically update, so students are encouraged to check their version on the download page below to ensure they have the most up-to-date version. If **USC** computer lab computers are being used the Respondus Lockdown Browser must be installed on them before the test. The download instructions for the Respondus Lockdown Browser, are as follows:

1. On the computer you will be taking the test from, click this link:
<https://download.respondus.com/lockdown/download.php?id=945755274>
2. If desired, watch the “**Before you install**” video.
3. Click “**Install Now**”.
4. Follow online instructions to install the Respondus Lockdown Browser on your computer.
 1. If asked, type the admin name and password for your computer. **NOTE:** This is the information you use to log into your computer.

Please download the browser ahead of time, it will save time during your exam.

Use of Artificial Intelligence

There is an expectation about AI (e.g., ChatGPT and image generation tools) use for this class. Learning to use AI is an emerging skill, and discussions about appropriate use are welcome. It is recommended that you take the opportunity to meet with your professor to get guidance with the use of these tools during office hours or after class. Keep in mind the following:

- AI tools are allowed to help you brainstorm topics or revise work you have already written.
- If you supply minimum-effort prompts, you will get low-quality results. You will need to refine your prompts to get good outcomes. This will take work.
- Proceed with caution when using AI tools and do not assume the information provided is accurate or trustworthy. If it gives you a number or fact, assume it is incorrect unless you either know the correct answer or can verify its accuracy with another source. You will be responsible for any errors or omissions provided by the tool. It works best for topics you understand.

- AI is a tool, but one that you need to acknowledge using. Please include a paragraph at the end of any assignment that uses AI explaining how (and why) you used AI and indicate / specify the prompts you used to obtain the results what prompts you used to get the results. Failure to do so is a violation of academic integrity policies.
- Be thoughtful about when AI is useful. Consider its appropriateness for each assignment or circumstance. The use of AI tools requires attribution. You are expected to clearly attribute any material generated by the tool used.

Statement on Academic Conduct and Support Systems

Academic Integrity:

The University of Southern California is a learning community committed to developing successful scholars and researchers dedicated to the pursuit of knowledge and the dissemination of ideas. Academic misconduct, which includes any act of dishonesty in the production or submission of academic work, compromises the integrity of the person who commits the act and can impugn the perceived integrity of the entire university community. It stands in opposition to the university's mission to research, educate, and contribute productively to our community and the world.

All students are expected to submit assignments that represent their own original work, and that have been prepared specifically for the course or section for which they have been submitted. You may not submit work written by others or “recycle” work prepared for other courses without obtaining written permission from the instructor(s).

Other violations of academic integrity include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), collusion, knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage. 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.

Students and Disability Accommodations:

USC welcomes students with disabilities into all of the University's educational programs. [The Office of Student Accessibility Services](#) (OSAS) is responsible for the determination of appropriate accommodations for students who encounter disability-related barriers. Once a student has completed the OSAS process (registration, initial appointment, and submitted documentation) and accommodations are determined to be reasonable and appropriate, a Letter

of Accommodation (LOA) will be available to generate for each course. The LOA must be given to each course instructor by the student and followed up with a discussion. This should be done as early in the semester as possible as accommodations are not retroactive. More information can be found at osas.usc.edu. You may contact OSAS at (213) 740-0776 or via email at osasfrontdesk@usc.edu.

Support Systems:

[Counseling and Mental Health](#) - (213) 740-9355 – 24/7 on call

Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

[988 Suicide and Crisis Lifeline](#) - 988 for both calls and text messages – 24/7 on call

The 988 Suicide and Crisis Lifeline (formerly known as the National Suicide Prevention Lifeline) provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week, across the United States. The Lifeline is comprised of a national network of over 200 local crisis centers, combining custom local care and resources with national standards and best practices. The new, shorter phone number makes it easier for people to remember and access mental health crisis services (though the previous 1 (800) 273-8255 number will continue to function indefinitely) and represents a continued commitment to those in crisis.

[Relationship and Sexual Violence Prevention Services \(RSVP\)](#) - (213) 740-9355(WELL) – 24/7 on call

Free and confidential therapy services, workshops, and training for situations related to gender- and power-based harm (including sexual assault, intimate partner violence, and stalking).

[Office for Equity, Equal Opportunity, and Title IX \(EEO-TIX\)](#) - (213) 740-5086

Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants.

[Reporting Incidents of Bias or Harassment](#) - (213) 740-5086 or (213) 821-8298

Avenue to report incidents of bias, hate crimes, and microaggressions to the Office for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

[The Office of Student Accessibility Services \(OSAS\)](#) - (213) 740-0776

OSAS ensures equal access for students with disabilities through providing academic accommodations and auxiliary aids in accordance with federal laws and university policy.

[USC Campus Support and Intervention](#) - (213) 740-0411

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

[Diversity, Equity and Inclusion](#) - (213) 740-2101

Information on events, programs and training, the Provost's Diversity and Inclusion Council,

Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

[USC Emergency](#) - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call

Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

[USC Department of Public Safety](#) - UPC: (213) 740-6000, HSC: (323) 442-1200 – 24/7 on call

Non-emergency assistance or information.

[Office of the Ombuds](#) - (213) 821-9556 (UPC) / (323-442-0382 (HSC)

A safe and confidential place to share your USC-related issues with a University Ombuds who will work with you to explore options or paths to manage your concern.

[Occupational Therapy Faculty Practice](#) - (323) 442-2850 or otfp@med.usc.edu

Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.