Toxicology in Drug Discovery and Development

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Spring 2022

Conference Room C/EOHSI

Fridays 2:30-3:30

Course Directors: Laura Armstrong, PhD (laura.armstrong1@bms.com), Jedd Hillegass, PhD, DABT (jedd.hillegass@bms.com), John Szilagyi, PhD (john.szilagyi@bms.com), and Lauren Aleksunes, PharmD, PhD, DABT (aleksunes@eohsi.rutgers.edu)

Course Description: The purpose of this 1-credit elective course is to provide students an understanding of the drug discovery and development paradigm, from target validation and lead optimization to the numerous preclinical studies conducted to ensure drug safety. To emphasize the multidisciplinary approach needed to accomplish this task, students will learn from and engage instructors with a wide array of expertise, and will participate in case studies designed to improve their understanding of the course material.

Course Objectives: Upon completion of this course, students are expected to:

- Describe the stages of drug development and the timing of various safety studies.
- Demonstrate an understanding of the types of studies performed for regulatory submissions to global regulators.
- Review The International Council for Harmonisation (ICH) safety guidelines that dictate the battery of studies needed for the safety testing of pharmaceuticals.
- Compare and contrast the safety testing of small molecules and biologics.
- Apply knowledge from lectures to solve case study questions.

Course Texts: No textbook is required. However, Casarett & Doull's Toxicology: The Basic Science of Poisons, 9th Edition can used to for background knowledge (accessible on Access Pharmacy at Rutgers Library). The ICH Technical Requirements for Pharmaceuticals for Human Use can be accessed at http://www.ich.org/products/guidelines/safety/article/safety-guidelines.html.

Grading:
Class participation 20%
Attendance 40%
Case study performance 40%

Attendance Policy: JGPT students in Busch campus laboratories are required to attend the class in-person in the EOHSI building. If you need permission to attend online, email Liz Rossi. JGPT students and postdocs on other campuses can attend in-person or via Zoom. Students from other programs are welcome in EOHSI or on Zoom. Make sure to sign in each session.

Academic Integrity: Students are required to be familiar with the University's Policy on Academic Integrity. Violation of academic integrity is a separable offense under the University Code of Student Conduct. Any student who is aware of academic misconduct by another student is obligated to notify a faculty member; failure to do so is also a violation of the Policy on Academic Integrity. Any violations of academic integrity relating to this course will be handled by the student disciplinary process as outlined in the University Code of Student Conduct. **NO LECTURE CONTENT IS PERMITTED TO BE UPLOADED TO PUBLIC DOMAINS ON THE INTERNET – THIS IS A VIOLATION OF COPYRIGHT.**

Weekly Schedule

Date	Topic	Instructors
21 Jan 2022	***Drug Discovery and Development – Overview*** • General timeline of drug development • Considerations for small molecules versus biologics • Pharmacodynamics versus toxicology • Overview of group roles • Regulatory requirements • Discovery through Regulatory toxicology	Lois Lehman-McKeeman
28 Jan 2022	***Target Validation and Lead Optimization*** • Principles of target screening • Technologies utilized • *In vitro* to *in vivo* screenings and model selection	TBD
04 Feb 2022	***Discovery Toxicology*** • Case Study: Early liability assessment	Laura Armstrong
11 Feb 2022	***Investigative Toxicology*** • Identification of early liabilities • Animal model selection rationale • Criteria for conducting investigative studies • Case Study	John Szilagyi
18 Feb 2022	***Anatomic / Clinical Pathology*** • Brief overview of preclinical study clinical pathology testing • Distinguishing spontaneous from test article-related findings • Determination of adverse vs non-adverse findings • Extrapolation of animal data to human risk assessment	Jay Mysore / Paula Katavolos
25 Feb 2022	***Genetic Toxicology*** • Mechanisms of genotoxicity • *In silico / in vitro / in vivo* assays • Regulatory requirements • Case study	Penny Leavitt / Zhiying Ji
04 Mar 2022	***Safety / Cardiovascular Pharmacology*** • Basics of safety pharmacology • Cardiovascular safety assessments • Regulatory requirements	Paul Levesque
11 Mar 2022	***Immunotoxicology*** • Classic assays of immunotoxicology	Rashade Haynes / Courtni Newsome

	• Incorporating pharmacodynamic assessments into toxicology studies • Utilizing vaccine models to assess pharmacodynamics	
18 Mar 2022	***CASE STUDY: Immunotoxicology***	Rashade Haynes / Courtni Newsome
25 Mar 2022	***No class - Spring Break***	
01 Apr 2022	***No class - Society of Toxicology Annual Meeting***	
08 Apr 2022	***Pharmacokinetics / Toxicokinetics / Biotransformation*** • Basic Principles of PK/TK • Calculating exposure multiples to human dose • ADME • Regulatory requirements and study design	Rama Iyer
15 Apr 2022	***CASE STUDY: PK/TK/BT***	Beth Joshi
22 Apr 2022	***Reproductive Toxicology*** • *In vitro* screening in early discovery • Validation of alternative models • Regulatory requirements	Karen Augustine
29 Apr 2022	***Clinical / Translational / Biomarkers***	Francisco Ramirez-Valle