

Perspectives in Drug Development
 CTSC 5105S (3 credits)
 Thursday Evenings, 4:30-7:30pm
 RWJMS Clinical Academic Building, Room CAB3405, New Brunswick, NJ
 Course Director: Sheldon Brookman, Ph.D.

Date/Lecturer	Class	Topic	Readings
01/28/10 Brookman	1	I. <u>Course Description and Requirements</u> II. <u>Historical Perspectives and Overview of Drug Development</u> a. Evolution of the pharmaceutical industry b. Changing development landscape: biologics, informatics and global communications c. Drug Development Strategy i. Principles and critical considerations: risks, cost & duration of development ii. Establishing a Target Profile iii. Key milestones and critical stages of development d. Managing projects: Workflow and tracking e. Document management	
02/04/10 Brookman	2	<u>Regulatory Strategy & Tactics</u> FDA and Other Guidelines a. Explaining FDA regulations: CFR Title 21 b. Interpreting Guidance documents c. Pathways to FDA approval d. Mandate of CDER & CBER in IND, NDA, BLA review e. Content and format of IND applications f. Amending regulatory applications g. Key regulatory milestones & meetings with the FDA h. Applying principles of GMP, GLP and GCP and achieving regulatory compliance i. Role of EMEA and other international regulatory bodies in global drug development	

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02/11/10	3	<p><u>Innovation in Drug Discovery</u></p> <ul style="list-style-type: none"> a. Traditional approaches to drug discovery and development b. Biopharmaceutical vs. traditional development c. Essentials of pharmacodynamics & aspects of drug action d. Identifying new drug targets e. Discovery pharmacology: screening and lead optimization f. Tools for screening and preclinical testing <ul style="list-style-type: none"> i. Genomics and proteomics ii. High-throughput screening & microarrays in drug discovery and development iii. Bioinformatics iv. Bioanalysis g. Application of combinatorial chemistry and structure activity relationships 	
02/18/10	4	<p><u>Pharmaceutical and Biotechnology Manufacturing</u></p> <ul style="list-style-type: none"> a. Introduction to Good Manufacturing Practice b. Chemistry, Manufacturing and Control issues & compliance c. Drug Substance d. Formulations, routes of administration and dosage designs e. Biopharmaceutical manufacturing & process validation <p><i>Introduce Assignment: Term Paper</i></p>	
02/25/10	5	<p><u>Safety Pharmacology & Toxicology</u></p> <ul style="list-style-type: none"> a. Core Safety pharmacology testing and timing b. Acute and chronic toxicity in relevant species c. Appropriate studies and guidelines for dose selection to support first-in-man exposure d. Conducting carcinogenicity & mutagenicity testing e. Assessing reproductive & developmental toxicology 	

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03/04/10	6	<u>Pre-Clinical</u> <ol style="list-style-type: none"> a. Pharmacokinetics and ADME b. Bioavailability c. Dose and species selection d. Role of metabolites in safety e. Pro-drugs f. Genetic factors and interindividual variability 	
03/11/10 Brookman	7	<u>Principles of Clinical Trial Development</u> <ol style="list-style-type: none"> a. Study phases: purpose and methods b. Ethics: roles of IRB, investigator and informed consent c. Trial design, sample size, randomization and blinding methods d. Clinical endpoints and biomarkers e. Superiority vs. non-inferiority studies 	
03/18/10 Brookman	8	<u>Conducting & Managing Clinical Trials - I</u> <ol style="list-style-type: none"> a. Planning, approval, investigator selection and monitoring: roles and responsibilities b. Documentation for regulatory approval c. Essentials of Human Research Protection d. Establishing Drug Safety Monitoring Boards e. FDA imposed clinical holds f. Fraud 	
03/25/10 Brookman	9	<u>Conducting & Managing Clinical Trials - II</u> <ol style="list-style-type: none"> a. Material planning to initiate a trial b. Data Capture and analysis and reporting results c. Interpreting and reporting results: Final study reports: d. Study closeout requirements e. Audits and the Corrective Action/Preventative action (CAPA) process f. Bridging studies 	

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04/08/10	10	<p><u>Drug Safety</u></p> <ul style="list-style-type: none"> a. Pharmacovigilence <ul style="list-style-type: none"> i. Adverse Events (AEs) ii. Serious Adverse Events iii. Coding AEs iv. Assessing causality v. Safety issues (liver, cardiac, vital signs) vi. Preparing and submitting periodic safety reports vii. Post-marketing surveillance b. Predicting adverse events c. Assessing renal and hepatic function d. Conducting studies in the elderly e. Interpreting drug-drug / drug-food interactions f. Pharmacogenomics g. Drug resistance 	
04/15/10	11	<p><u>Clinical trial challenges</u></p> <ul style="list-style-type: none"> a. Special populations b. Assessing QTc effects c. Pediatric subjects d. Oncology drug development e. Genotyping f. Drug resistance <p><i>Term Papers due</i></p>	

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04/22/10	12	<u>Special Topics in Clinical Research</u> a. Managing potential risks associated with non-compliance during drug development b. Outsourcing elements of the development process: pros & cons c. Post-approval adverse effects & drug withdrawals d. Subject recruitment practices and issues	
04/29/10 Brookman	13	<u>Case Studies:</u> a. When things go wrong: TGN1412 b. Creating a drug development plan (Selected drugs to be discussed)	
05/06/10 Brookman	14	I. <u>Intellectual Property and Patent Policy</u> a. Patent applications and types of claims b. Patents extensions in the product life cycle c. Managing patent expiration d. Data exclusivity II. <u>Risks and Rewards of Drug Development</u> a. Pharmacoeconomics in clinical trials b. Product valuation & financial considerations c. Calculating Net Present Value d. Estimating risk	
05/13/10 Brookman	15	Student Seminars on Selected Papers from the Literature (mini-journal club) Course Feedback and Assessment	

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Reference Articles:

The following will be provided electronically

- James R. Harris, GOOD MANUFACTURING PRACTICES (GMP) AND RELATED FDA GUIDELINES in “Pharmaceutical Manufacturing Handbook: Regulations and Quality”, edited by Shayne Cox Gad, John Wiley & Sons, Inc. publ
- Chapter 1, entitled STRATEGY AND PHASING FOR DRUG SAFETY EVALUATION IN THE DISCOVERY AND DEVELOPMENT OF PHARMACEUTICALS in Drug Safety Evaluation, authored by Shayne Cox Gad
- Aaron S. Kesselheim, INTELLECTUAL PROPERTY POLICY IN THE PHARMACEUTICAL SCIENCES: THE EFFECT OF INAPPROPRIATE PATENTS AND MARKET EXCLUSIVITY EXTENSIONS ON THE HEALTH CARE SYSTEM, in AAPS Journal 2007; 9 (3) Article 33, E306-E311.
- John Goffi, INTRODUCTION TO CLINICAL TRIALS in “Clinical Trials Handbook”, edited by Shayne Cox Gad, John Wiley & Sons, Inc. publ.
- Congressional Budget Office study, RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY, October 2006.
- Thomson Reuters in conjunction with the Biotechnology Industry Organization report entitled, THE OUTLOOK AND ISSUES FOR THE BIOTECHNOLOGY SECTOR: AN INVESTOR PERCEPTION STUDY, July 2009

Required Textbooks:

On-line Resources:

- <http://www.emea.europa.eu/htms/human/humanguidelines/nonclinical.htm>
- <http://www.emea.europa.eu/htms/human/humanguidelines/efficacy.htm>
- <http://www.FDA.gov>

Assignments for Evaluation:

- 1) **Take home exam 50%**
- 2) **Project – creation of a clinical development plan 40%**
- 3) **Student Presentation of oral report 10%**