ChE/Pharm 519 Modern Pharmaceutical Engineering W, 2007

URL: https://ctools.umich.edu/portal (you need to log in first and then go to ChE 519 web site)

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Lecture: MW 4:00 – 5:30 pm
Rm 1018, H. H. Dow

References (on reserve):

A. Praxel's Pharmaceutical R & D Statistical Sourcebook 2006/2007, Parexel International Corp., Boston, 2006.

B. Smith C.G. and J.T. O'Donnell (ed.) "The Process of New Dug Discovery and Development" 2nd ed., Informa Healthcare, New York, 2006.

C. Van de Waterbeemd H. et al "Drug Bioavailability" in Methods and Principles of Medicinal Chemistry, Vol. 18, Wiley-VCH, 2003.

D. Pisano, G.P. "The Development Factory" HBS Press, 1997.

E. Hickey A.J. and D. Ganderton "Pharmaceutical Process Engineering" Marcel Dekker, New York., 2001.

F. Levin, M. (ed.) "Pharmaceutical Process Scale-Up" Marcel Dekker, New York, 2002.

G. Niazi S.K. "Handbook of Pharmaceutical Manufacturing Formulations" Vol.1-6, CRC Press, Boca Raton, 2004.

H. Bakeev K. "Process Analytical Technology" Blackwell Publishing, 472 pp., 2005.

I. Vesper J.L. "Risk Assessment and Risk Management in the Pharmaceutical Industry" PDA Bookstore, 292 pp., 2006

This is one of the two core courses in the new Pharmaceutical Engineering program. It is also served as a gateway course covering science and engineering fundamentals and concepts essential to drug discovery support, pharmaceutical development and manufacturing equipment design and operation. The primary goal of this course is to help students (particularly chemical engineering and chemistry/pharmaceutical science students) to gain familiarity with various concept(s) and functions involved in HT drug discovery, process and product development and robust pharmaceutical manufacturing processes. This course will serve as an introduction of the pharmaceutical and related industries for students to understand, identify and develop their professional interests in pursuing further study in any of the particular subject matters covered in this course through additional learning in other advanced courses and/or in research training. The students will be exposed to different computational and analytical tools used in various drug discovery support and development functions. Only simple mathematical tools and models will be used throughout this course. We intend to develop a system approach in introducing product quality with process efficiency in the pharmaceutical discovery, development and manufacturing pipeline.

The first part of the course will be structured to give some background information on drug discovery support functions with a particular emphasis on bioinformatics and high throughput/virtual screening used in drug discovery. The students are encouraged to take a course in basic biochemistry (Biol 311 or equivalent) and a course in organic chemistry so that they should have no trouble in understanding various technical terms used. Additional reading assignments may be required to enhance the students' knowledge in cellular and molecular biology through the use of Internet. The second part of the course shall focus on chiral chemical synthesis and pharmaceutical development with emphasis on solid state science and engineering. Pharmaceutical process development is quite unique since batch processing and the concept of validation are often used. Various issues on chiral drug synthesis and separation, pharmaceutical solid characterization, solid processing such as mixing, drying, blending, granulation and other unit operations will be discussed. Every effort will be tried to relate fundamental engineering principles such as material and energy balances, thermodynamics, transport phenomena, reaction kinetics etc. in the discussion of these topics.

The emphasis of the remainder of the course will be on manufacturing of various drug products and their delivery systems. Only oral and solids based delivery systems will be covered. The main emphasis will be on process scale up and cGMP manufacturing of a few industrially important drugs and biopharmaceuticals. Specific issues related to pharmaceutical manufacturing and operations such as sterile processing, clean-in-place validation will be emphasized throughout this course to illustrate the differences and importance of pharmaceutical processing versus conventional commodity/special chemical based production.

Examinations will be based on, but not restricted to, materials presented in the lecture notes, reading assignments, homework, and computer exercises. Examinations will be given under the provision of the Engineering Honor Code.

Grading:

There will be two, hourly or take home examinations during the course in combination with a term project (teamwork between Engineering and non-Engineering students are preferred) to be completed with a report. Summary of the final reports will then be presented by the students to the entire class by the end of the semester. There will be a series of homework problems, computer programs, and laboratory exercises (optional). Each of these will affect the final grade as follow:

Take home exams	25%
Homework/Comp problems	25%
Term project & oral presentation	40%
Classroom performance	10%
Total	100%

Field trips:

A. Pfizer Global R & D (Ann Arbor, Mich.) Date: TBD
Drug Discovery and Early Development groups

B. Pfizer Global R & D (Ann Arbor, Mich.) Date: TBD
Pharmaceutical Development and Clinical Manufacturing groups

An overall outline and various assignments for the course as follows:

Lecture number	Date	Subject/topic	Assignment
1	01/08	Introduction to the course Global and US Health Care Systems Current Status and Future Trends in Pharmaceutical Business	Course outline and grading HW #1 Drugs versus biologics exercise
2	01/10	Future of Pharmaceutical Innovation Characteristics of Various Drugs, Biologics, and Combination Therapies Brand names and Generics	
3	01/15	MLK Day (No class)	
4	01/17	Basics in Cellular and Molecular biology: Bioinformatics Primer	HW #2 NCBI tutorial and exercise

5	01/22	Systems Biology for Drug Discovery Search and Validate Molecular Targets for Diseases	HW #3 Search for molecular targets of various diseases
6	01/24	New Discovery Science and Technology HT and Virtual Screening of Bioactive Molecules (Lead Identification)	
7	01/29	Rational Drug Design Drugability Issues Cheminformatics Primer	David Wild (IU) HW #4 SMILE exercise
8	01/31	FDA's Critical Path Initiative Computational Pharmaceutics: Physico-chemical Properties Estimation and Prediction (Rule of 5)	HW #5 ACD exercise LogP, pKa, Solub. etc.
9	02/05	Biopharmaceutical Classification System (BCS) Bioavailability (BA)/Bioequivalence (BE), IVIVC and Dissolution Testing	HW#6 e-ADME exercise
10	02/07	Pre-Clinical Toxicology and Toxicogenomics Risk Assessment in Drug Safety	Mark Vogel (PGRD)
11	02/12	Pharmaceutical Product and Process Development Science Chemical Drugs versus Biologics	G. Pasano's book chapters Term project assignment
	02/14	Pfizer Field Trip – 1 (to be confirmed)	
12	02/19	Clinical Development and Manufacturing of Various Health Care Products Science based GMP Initiative Process Analytical Technology (PAT) Initiative	Term project discussion
13	02/21	Take Home Exam #1	
	02/24-03/04	Winter Recess	
14	03/05	Overview of Chemical (API) Development Science	Brian Swierenga (PGRD)
15	03/07	Crystallization and Polymorphic Control in Pharmaceutical Systems Thermodynamics vs Kinetics	HW #7 Cooling Crystallization

16	03/12	Drug Stability Issues Spray and Freeze-Drying Kinetics Sterile Fill Operations	HW #8 Drying Kinetics
17	03/14	Overview of Pharmaceutical Development Science Pharmaceutical Solids: Amorphous versus Crystalline State	Gregory Amidon (PGRD)
	03/19	Pharmaceutical Solids: Particle Size and Shape Analysis Particle Size Distribution (PSD)	HW #9 Particle and PSD analysis
18	03/21	Pharmaceutical Solids Processing -1 Particle Size Alteration Milling and Granulation	Term project discussion
19	03/26	Pharmaceutical Solids Processing - 2 Powder Flow and Mixing Blend Uniformity Considerations	David Pipkorn (Merck) HW#10 Content uniformity analysis
20	03/28	Pharmaceutical Manufacturing–1 Tablets and Capsules Solid Dosage Forms and Formulations	Paul Nkansah (TBD)
21	04/02	Pfizer Field Trip – 2 (to be confirmed)	
22	04/04	Pharmaceutical Manufacturing-2 Continuous Pharmaceutical Manufacturing Lean Global Pharmaceutical Operations Manufacturability of Drug Delivery Systems	Mayur Lodaya (PGRD)
	04/09	Review	
	04/11	Exam #2	
	04/16	Oral presentations of term projects	
	04/18	Oral presentations of term projects	

*This course schedule is subject to change.