Spring 2020

PHEN 618-102: Principles of Pharmacokinetics and Drug Delivery

Piero Armenante

Dr. Piero M. Armenante
New Jersey Institute of Technology
January 17, 2020

Principles of Pharmacokinetics and Drug Delivery
PhEn 618

Syllabus

Term: 2020 Spring Semester

NJIT Course Title: Principles of Pharmacokinetics and Drug Delivery

NJIT Course Number: PhEn 618, Section 102

Course Day and Time: Monday; 6:00-8:50 pm

Classroom: Faculty Memorial Hall (FMH); Room 412

Course Instructor:

Piero M. Armenante, Ph.D.
Distinguished Professor of Chemical Engineering
New Jersey Institute of Technology
Otto H. York Department of Chemical and Materials Engineering
Newark, NJ 07102-9895

Office: YCEES Building - Room 120
Telephone: (973) 596-3548; **Mobile: (908) 347-8734** (**preferred**)
Fax: (973) 596-8436
E-Mail Address: piero.armenante@njit.edu

Availability of Instructor and WebEx Sessions:

Students can contact the instructor for questions in different ways:

- In-person meetings: Monday, 5:00-6:00 pm or by appointment (for students who can come to NJIT: meetings will likely take place in 150 Tiernan Hall – CME Departmental Office). Students are strongly encouraged to contact Prof. Armenante via e-mail to arrange for a meeting. *Please note that Prof. Armenante will **not** be available for consultation when he is on business travel.*
- Via telephone: students can contact the instructor at the mobile number above
- Through WebEx sessions: If needed, WebEx question/answer sessions will be also held as appropriate, as specified below.

Teaching Assistant (TA):

Baran Teoman, Ph.D. Student in Chemical Engineering
Otto H. York Department of Chemical and Material Engineering
New Jersey Institute of Technology
Newark, NJ 07102-9895

Office: Mixing Lab – Tiernan Hall, Room 312
Telephone: (856) 676-4324
E-mail: bt242@njit.edu (preferred rather than telephone)

TA's Office Hours:

Monday and Tuesday, 4:00-5:00 pm
Students can additionally email the TA to set up appointments at other times

Computer Hardware and Software Requirements

In order to follow the course, students will require the following:

- Hardware
  - Computer with internet access (to retrieve course material, access WebEx, etc.)
  - Scanner or access to a scanner (to scan homework and then e-mail it as an attachment)
  - Speakers and microphone (for WebEx access), typically built in already in most laptop computers
- Software and Access
  - NJIT e-mail account, including UCID and password, to access Moodle (http://moodle.njit.edu/)
  - Web browser (Firefox, Chrome, Safari, etc. - Internet Explorer is not recommended)
  - Adobe Acrobat and Adobe Flash installed and up-to-date (freeware)
  - Other software to complete assignments (e.g., Microsoft Word, Microsoft Excel, etc.)

Course Lectures, Notes, Textbooks, and Other Reference Material:

- **Course Lectures**: Armenante, P. M., 2020, *PhEn 618-Pharmacokinetics and Drug Delivery Course Lectures.* The *Lectures* are videos containing course lectures identical in content and length to the face-to-face PhEn 618 lectures routinely offered at NJIT. The *Lectures* are available through Moodle and can be accessed as described below
- **Course Notes**: Armenante, P. M., 2020, *PhEn 618-Pharmacokinetics and Drug Delivery Course Notes - PhEn 618.* The *Notes* are exact duplicates of the overheads used in the lectures. The *Notes* are also available through Moodle and can be accessed as described below
- **Textbooks**: The following books are recommended but not required as textbooks:
  - Shargel, L. and Yu, A. B. C., *Applied Biopharmaceutics and Pharmacokinetics*, 7th Edition, McGraw-Hill, New York, 2015, ISBN-13 number: 978-0071830935
  - Truskey, G. A., Yuan, F. and Katz, D. F., *Transport Phenomena in Biological Systems,* 2nd Edition, Pearson Prentice Hall, Upper Saddle River, NJ, 2009, ISBN-13 numer: 978-013156988
- A list of additional reference books (not required) is attached.

Availability of Course Lectures, Notes, Homework Assignments, Textbook, and References:

- Links to the *Course Lectures* are available to the students through Moodle. Students can access Moodle directly by going to http://moodle.njit.edu/ and following the instructions there. Once the appropriate course is selected, students will be able to watch streaming videos of the *Lectures* for that class period by clicking on the appropriate links
- The *Course Notes* can be downloaded from the NJIT website using Moodle, as described above. The *Course Notes* will be posted on the internet as PDF files
- The homework, homework solutions, and projects will be posted through Moodle as appropriate, depending on the material covered in that week (typically but not always on a weekly basis)
- Additional material (e.g., videos, reading material, etc.) will be posted through Moodle as appropriate
- If students experience problems and they are unable to log in or access course material they should contact the NJIT Helpdesk at 973-596-2900
- The textbooks are available in the NJIT bookstore (120 Summit Street; njit@bkstr.com; 973-596-3200; https://www.bkstr.com/njitstore/home) or from the publishers
- Most additional references (not required as textbooks) as well as the textbooks are available in most university libraries and have been being placed on reserve at the NJIT library.

WebEx Sessions:

- WebEx sessions are web-based conference calls, conducted via computer, that will enable students to interact directly (i.e., talk, show material, discuss examples) with the course instructor and the other students in the class
- WebEx sessions may be held as needed, as a forum to discuss topics covered in class, address questions, review selected homework, clarify examples, etc. In other words, WebEx sessions will replace office hours for long-distance students

- In order to use WebEx students should first visit http://webex.njit.edu, click on the "Participating in a WebEx Session" link, retrieve the PDF file with detailed instructions, and read it
- The date and time of a WebEx session will be announced via e-mail or through Moodle, and invitations to join a WebEx meeting will be sent to students, together with the appropriate web link, as needed
- At the time of the meeting, students should go to http://njit.webex.com (notice the similarity but also the difference between this link and the previous one)
- If a WebEx meeting number is needed, it will made available by the instructor to the students prior to the meeting and will be specified in the e-mail invitation for that meeting
- Remark: students do not need to open a WebEx account to attend a WebEx session

Course Prerequisites:

- **PhEn and ChE Students**: Currently, students are admitted to the PhEn program if they have baccalaureate degree in chemical engineering or equivalent with a minimum GPA of 3.0. This is a satisfactory prerequisite for this course. Students with undergraduate degrees in biology, chemistry, physics, and equivalent who are admitted to the PhEn program on condition that they take additional undergraduate courses, specified at the time of admission, must have taken and successfully completed those courses. Students enrolled in the old PhEn program should have completed the bridge program (PhEn 500, PhEn 501 and PhEn 502) if required in the student's admission conditions, as well as any other undergraduate-level courses, if any. *PhEn students who do **not** have these prerequisites will have to **drop** the course.* Additionally, PhEn 601 is recommended but not required as a prerequisite.
- **Non-PhEn and non-ChE Students**: Students with appropriate engineering backgrounds (e.g., BME, ME) can also take this course. Students with non-engineering background should have the **appropriate background** in math (up to differential equations), mass and energy balances, fluid flow, heat transfer, and mass transfer in order to be able to follow the course. Therefore, they should talk to Prof. Armenante to make sure that they are adequately prepared for this course before taking it. Additionally, PhEn 601 is recommended but not required as a prerequisite.

Course Objectives: This course is one of the common core courses for the Pharmaceutical Engineering and Biopharmaceutical Engineering MS Degree Programs. The main objectives of this course are to: present the different pharmacokinetic principles affecting drug adsorption, distribution, metabolism and excretion; quantitatively study and apply mathematical models used to describe these phenomena, and; provide the students with basic concepts of drug delivery, pharmacokinetics and pharmacodynamics.

Course Description: The course covers the basic principles of pharmacokinetics, including absorption, transport distribution, metabolism, and excretion of drugs and metabolites in the human body, drug transport, parenteral and enteral routes of drug administration, and factors affecting drug absorption, distribution, and metabolism. Mathematical pharmacokinetic models and drug delivery processes are also presented and quantitatively studied. The course also covers basic aspects of drug delivery of different drug delivery systems and dosage forms.

Course Outline by Topic Areas: Introduction; pharmacokinetics and its role in drug discovery; drug development and process development; drug absorption, distribution, metabolism, and excretion; routes of drug administration, drug absorption by different routes of administration; enteral and parenteral routes; drug transport in biological systems, transport across cell membrane: osmosis, passive diffusion, ion channels facilitated transport, active transport; transport across endothelial cell layers and epithelial cells layers; drug distribution; transcapillary exchange of drugs; perfusion-limited and permeability-limited distribution; binding of drugs to proteins; physiological barriers; renal excretion; renal clearance; drug metabolism; mathematical approach to pharmacokinetic modeling; one-compartment open models and data analysis; multiple-dose pharmacokinetics; two-compartment open models; physiological pharmacokinetic models; nonlinear pharmacokinetics; pharmacokinetic-pharmacodynamic modeling.

Course Learning Outcomes: Upon successful completion of this course, students will be able to:

- Identify and compare the different types of administration routes used in drug delivery
- Recognize and describe the different physiological mechanisms responsible for drug adsorption, distribution, metabolic and elimination
- Quantitatively predict key parameters and transfer rates of importance in the description of physiological processes
- Categorize, analyze, and contrast different types of pharmacokinetics models
- Interpret and analyze pharmacokinetic data to determine the underlining compartment model best describing the observed drug distribution behavior among compartments over time
- Regress pharmacokinetic data to determine the compartment model kinetic parameters
- Assemble compartment models best suited for a specific drug based on its adsorption, distribution, metabolic and elimination characteristics
- Determine the most effective drug delivery method to achieve the desired pharmacokinetic effect based on a quantitative analysis of the underlying pharmacokinetic model

Course Requirements:
- Examinations: Two exams, i.e., a midterm exam and a final exam
- Homework: Assigned by the instructor at the end of each class
- Projects: One, or possibly two, short projects will be assigned after the midterm exam (see below for details)

Grading Policy*:
- Midterm exam* 38%
- Final exam* 38%
- Homework.....12%
- Projects 12%

  Total 100%

(*) Students performing very poorly on the exams will **fail** the course *irrespective* of their performance in the homework and projects, as explained below.

Course Final Grade: a tentative guideline for the assignment of final grades is the following:

Cumulative Points	Overall Grade
85-90 to 100%	A
70-75 to 85-90%	B/B+
60 to 70-75%	C/C+
50 to 60%	"D"
0 to 50%	F

The grade of "D" is not assigned to students taking graduate courses. Students averaging a cumulative point score corresponding to a "D" in the above table could receive either a C or an F, depending on their overall performance.

Please remember that this is only a guideline designed to help the students understand how they are performing in the course. Dr. Armenante will feel free to adjust slightly the grading scale (both ways) when assigning the final grades.

Important Remark: Each exam (midterm and final) will be graded on a point scale from 0 to 100 (100 points in an exam=38% of the final grade; see above). However, **failing to achieve a combined average of at least 55/100 in the two exams** will imply **failing the course (F grade) *irrespective* of the points obtained through the homework and the projects.** In other words, students who perform extremely poorly in the exams will not be able to use the homework and the projects to pass the course. If this minimum requirement is satisfied, the final grade will be assigned based on the grading policy outlined above, including homework and projects.

Exams:

- A calendar of exams is included in the Course Outline given below
- All exams are typically 3 hours long unless otherwise stated
- Only the following material can be used during the exams:
  - Recommended Textbooks and other books (printed versions only)
  - Printed version of instructor's *Course Notes* (posted on Moodle), possibly annotated during classes as students take notes on them
  - Calculator
  - No homework, copies of homework solutions, past exams, and similar material will be allowed during the exams
  - **No computers, telephones, i-Pads, etc. will be allowed during the exams**
- Possible exam policy changes will be announced by the instructor prior to the exams, if needed
- The final exam will be on all material covered throughout the course (although the main emphasis of the exam will be on the material covered after the midterm exam)
- Make-up exams will only be given to students who cannot attend the regular exam time, *and only under documented and extraordinary circumstances*. In any case, no student will be allowed to take a make-up exam unless he/she has the prior consent of the instructor. *If a student will simply not come to an exam, the exam grade will automatically be zero*
- Because of confidentiality issues, the Office of the **Dean of Students** now handles all issues related to **medical conditions** (including justification for postponing exams)

Homework:

- The homework will be posted on Moodle
- It will be assigned as appropriate (typically on a weekly basis), depending on the material covered in that week
- Students should turn in the homework by scanning it and attach it as a PDF file to an e-mail message addressed to the TA for the course
- The homework will not be returned to the students unless practical to do so
- No late homework will be accepted unless a valid reason is provided **in advance** (e.g., an upcoming business trip)
- Homework solutions will be posted on Moodle after the homework has been collected.

> ***Important Remark****: Previous experience has clearly shown that those students who do not work on the assigned problems (or at least seriously try to solve them) typically perform very poorly on the exams.*

Homework Grading: The homework will be graded by the TA on the basis of the effort that the student puts into using solving it using a simplified grading scale, i.e., 0 (no or minimal effort); 5 (intermediate effort); 10 (significant effort). Any questions regarding homework grades should be discussed with the instructor.

Projects: Students will complete one, or possibly two, small projects, which will be assigned after the midterm exam and collected on the day of the final exam. The first project will consist of critically reviewing (critiquing) 2 papers published in scientific journals (as if the papers had been submitted for publication to the student). The papers will have to be related to each other and to be within the scope of the course. The students will be asked to write a short review of the papers. The student will have to justify whatever conclusions he/she may reach. The second project (if assigned) will consist of a small case study assigned by the instructor. The problem will be open-ended to allow each student to come up with his/her own analysis of the problem and solution.

Class Attendance: As with all graduate courses at NJIT, attendance is not mandatory, but strongly recommended. Experience shows that students who do not regularly attend class typically perform poorly in the course. In addition, examples are worked out during the lectures. These examples are not in the *Course Notes*. Students are responsible for all material covered in class.

Time Commitment: Students are expected to allocate some three to six hours per week to study and work on the assignments for this course.

Students with Disabilities: NJIT adheres to Section 504 of the Rehabilitation Act (ADA) of 1990. Appropriate accommodations are provided at no cost to the student. Additional questions should be directed to Dr. Phyllis Bolling, Center for Counseling and Psychological Services (C-CAPS), Campbell Hall, (entry level), Room 205, (973) 596-3420. For further information, visit the http://www5.njit.edu/studentsuccess/disability-support-services/ website.

Code of Conduct and Academic Integrity: Academic Integrity is the cornerstone of higher education and is central to the ideals of this course and the university. Cheating is strictly prohibited and devalues the degree that students are working on. As members of the NJIT community, students have the responsibility to protect their educational investment by knowing and following the NJIT University Policy on Academic Integrity that is found at http://www5.njit.edu/policies/sites/policies/files/academic-integrity-code.pdf. The Code will be upheld on all issues related to the course. Students are expected to be familiar with the code and conduct themselves accordingly. Academic integrity is fundamental to the activities and principles of a university. All members of the academic community must be confident that each person's work has been responsibly and honorably acquired, developed, and presented. Any effort to gain an advantage not given to all students is dishonest whether or not the effort is successful. The academic community regards breaches of the academic integrity rules as extremely serious matters. Sanctions for such a violation may include academic sanctions from the instructor, including failing the course for any violation, to disciplinary sanctions ranging from probation to expulsion. When in doubt about plagiarism, paraphrasing, quoting, collaboration, or any other form of cheating, consult the course instructor. If students have additional questions about the code of Academic Integrity, they should contact the Dean of Students Office at dos@njit.edu.

Plagiarism and Academic Integrity: The approved "University Policy on Academic Integrity" is currently in effect for all courses. Should a student fail a course due to a violation of academic integrity, they will be assigned the grade of "XF" rather than the "F," and this designation will remain permanently on their transcript. All students are encouraged to look at the University Code of Academic Integrity and understand this document. Students are expected to uphold the integrity of this institution by reporting any violation of academic integrity to the Office of the Dean of Students. The identity of the student filing the report will be kept anonymous. NJIT will continue to educate top tier students that are academically sound and are self-disciplined to uphold expected standards of professional integrity. ***Academic dishonesty will not be tolerated.***

Important Dates According to the NJIT Calendar (Spring 2020):

January	20	Monday	Martin Luther King, Jr. Day
January	21	Tuesday	First Day of Classes
January	25	Saturday	Saturday Classes Begin
January	31	Friday	Last Day to Add/Drop a Class
January	31	Friday	Last Day for 100% Refund, Full or Partial Withdrawal
February	1	Saturday	W Grades Posted for Course Withdrawals
February	3	Monday	Last Day for 90% Refund, Full or Partial Withdrawal, No Refund for Partial Withdrawal after this date
February	17	Monday	Last Day for 50% Refund, Full Withdrawal
March	9	Monday	Last Day for 25% Refund, Full Withdrawal
March	15	Sunday	Spring Recess Begins - No Classes Scheduled - University Open
March	22	Sunday	Spring Recess Ends
April	**6**	**Monday**	**Last Day to Withdraw**
April	10	Friday	Good Friday - No Classes Scheduled - University Closed
May	5	Tuesday	Friday Classes Meet
May	5	Tuesday	Last Day of Classes
May	6	Wednesday	Reading Day 1
May	7	Thursday	Reading Day 2
May	8	Friday	Final Exams Begin
May	14	Thursday	Final Exams End
May	16	Saturday	Final Grades Due
May	19	Tuesday	Commencement - Undergraduate Ceremonies at Prudential (Tentative)

Additional important dates are available on the web at the following site: http://www.njit.edu/registrar/calendars/.

Course Outline (Spring 2020)

Week	Date	Topic
1	January 27-February 2	Introduction; pharmacokinetics and its role in drug discovery; drug development and process development; drug absorption, distribution, metabolism, and excretion; routes of drug administration
2	February 3-9	Routes of administration; enteral and parenteral routes
3	February 10-16	Drug transport in biological systems - Transport across cell membranes: osmosis, passive diffusion
4	February 17-23	Drug transport in biological systems (continued) - Transport across cell membranes: ion channels facilitated transport, active transport
5	February 24-March 1	Drug transport in biological systems (continued) - Transport across endothelial cell layers and epithelial cells layers
6	March 2-8	Drug distribution; transcapillary exchange of drugs; perfusion-limited and permeability-limited distribution; binding of drugs to proteins; physiological barriers
7	March 9-15	Renal excretion; renal clearance. Drug metabolism
	March 16-22	*Spring Break – No class*
8	**March 23**	**Midterm exam**
9	March 30-April 5	Mathematical approach to pharmacokinetic modeling
10	April 6-12	One-compartment models and data analysis – IV Injections
11	April 13-19	One-compartment models and data analysis (continued) - Oral dosage models; method of residuals
12	April 20-26	One-compartment models and data analysis (continued) - Oral dosage models; Wagner-Nelson model. Models for other routes of administration
13	April 27- May 3	Multiple-dose models
14	May 4-10	Two-compartment models and data analysis
15	**May 11**	**Final exam**

Important: It is conceivable that some changes in the above outline will take place, depending on the overall performance of the class and the time actually required to cover the most important subjects of the course.

Reference Books

- *The United States Pharmacopeia & The National Formulary. The Official Compendia of Standards, USP 42–NF 37, Pharmacopeial Convention Inc., 2019.*
- Amiji, M. M. and Sandmann, B. J., *Applied Physical Pharmacy*, McGraw-Hill, New York, 2003.
- Allen, L. V., Popovich, N. G., and Ansel, H. C., *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*, 9th Edition, Lippincott Williams & Wilkins Publishers, 2010.
- Banker, G. S. and Rhodes, C. T., *Modern Pharmaceutics*, 3rd Edition, Marcel Dekker, New York, 1995.
- Boroujerdi, M. *Pharmacokinetics: Principles and Applications*, McGraw-Hill, New York, 2002.
- Chien, Y. W., *Novel Drug Delivery Systems*, 2nd Edition, Marcel Dekker, New York, 1991.
- Gennaro, A. R. (editor), *Remington: The Science and Practice of Pharmacy*, 20th Edition, Philadelphia College of Pharmacy and Science, 2000.
- Lieberman, H. A., Rieger, M. M., and Banker, G. S., *Pharmaceutical Dosage Forms: Dispersed Systems*, Vol. 1 (1996); Vol. 2 (1996), Vol. 3, (1998), Marcel Dekker, New York.
- Lieberman, H. A., Lachman, L., and Schwartz, J. B., (eds.), *Pharmaceutical Dosage Forms: Tablets*, Vol. 1 (1989); Vol. 2 (1990), Vol. 3 (1990), Marcel Dekker, New York.
- Avis, K. E., Lieberman, H. A., and Lachman, L., (eds.), *Pharmaceutical Dosage Forms: Parenteral Medications*, Vol. 1 (1991); Vol. 2 (1992), Vol. 3 (1993), Marcel Dekker, New York.
- Mitra, A. K., Kwatra, D., Vadlapudi, A. D., *Drug Delivery*, Jones & Bartlett Learning, 2014.
- Martin, A. N., Bustamante, P. and Chun, A. H. C., *Physical Pharmacy: Physical Chemical Principles in the Pharmaceutical Sciences*, Lippincott Williams & Wilkins Publishers, Philadelphia, 1993.
- Notari, R. E., *Biopharmaceutics and Clinical Pharmacokinetics: An Introduction*, Marcel Dekker, New York, 1986.
- Shargel, L., Wu-Pong, S. and Yu, A. B. C., *Applied Biopharmaceutics and Pharmacokinetics*, 6th Edition, McGraw-Hill, New York, 2012.
- Tyle, P. (ed.) *Drug Delivery Devices: Fundamentals and Applications*, Marcel Dekker, New York, 1988.
- Truskey, G. A., Yuan, F. and Katz, D. F., *Transport Phenomena in Biological Systems,* 2nd Edition, Pearson Prentice Hall, Upper Saddle River, NJ, 2009.
- Welling, P. G., *Pharmacokinetics: Processes, Mathematics, and Applications*, American Chemical Society, 1997.
- Welling, P. G. and Tse, F. L. I. (eds.), *Pharmacokinetics: Regulatory-Industrial-Academic Perspectives*; 2nd Edition, Marcel Dekker, New York, 1995.