Spring 2021

PHEN 618-102: Principles of Pharmacokinetics and Drug Delivery

Piero Armenante

Dr. Piero M. Armenante
New Jersey Institute of Technology
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Principles of Pharmacokinetics and Drug Delivery
PhEn 618

Syllabus

Term: 2021 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: None. Course is conducted synchronously online

Course Instructor:

Piero M. Armenante, Ph.D.
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Otto H. York Department of Chemical and Materials Engineering
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Availability of Instructor and WebEx Sessions:
Students can contact the instructor for questions in different ways:

- Through WebEx sessions: One-on-one or group WebEx question/answer sessions will be held as needed. Please contact Prof. Armenante to schedule such meetings.
- Via telephone: Students can contact the Prof. Armenante at the mobile number above, but only after a first contact is established via email to avoid that the call is perceived as spam.

Teaching Assistant (TA): TBA

TA's Office Hours: TBA

Computer Hardware and Software Requirements
In order to follow the course, students will require the following:

- NJIT e-mail account, including UCID and password, to access:
  - Canvas (https://canvas.njit.edu/)
  - WebEx (https://njit.webex.com/)
  - Respondus Lockdown Browser (to be downloaded at any time, but to be used only for exams and quizzes from within Canvas) (https://download.respondus.com/lockdown/download.php?id=264548414)
- Web browser (Chrome, Firefox, 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.)

Mobile Phone App Requirements:

- Office Lens (free) and/or CamScanner Apps (free)
- Cisco WebEx Meeting App (free)

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

- **Course Lectures**: Armenante, P. M., 2021, *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., 2021, *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 Canvas 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 Notes, Homework Assignments, Textbook, and References:

- Links to the *Course Lectures* are available to the students through Canvas. Students can access Canvas directly by going to (https://canvas.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 Canvas, 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 Canvas 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 Canvas as appropriate
- If students experience problems and they are unable to log in or access the course material, they should contact the NJIT Helpdesk at 973-596-2900
- The textbook is available in the NJIT bookstore (973-596-3200; http://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 long distance conference calls, conducted via computer, that will enable students to meet for distance learning classes with the course instructor and the other students in the class

- Since this course will be conducted **synchronously online**, WebEx sessions will be held synchronously with the class.
- In addition, WebEx sessions may be conducted as needed as a **forum to discuss topics covered in class, address questions, review selected homework, clarify examples, etc**. WebEx sessions may replace **office hours** for long-distance students
- In order to familiarize themselves with WebEx, students should first visit https://ist.njit.edu/webex, to **learn more about WebEx sessions in general**
- At the time of the meeting, students should go to https://njit.webex.com/ (notice the similarity but also the difference between this link and the previous one)
- The date and time of a WebEx session will be announced via e-mail or through Canvas, and invitations to join a WebEx meeting will be sent to students, together with the **appropriate web link**, as needed
- 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 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
- All exams are typically open-book and open-note. However, changes could be made and will be announced by the instructor prior to the exams
- Under the current circumstances (convergent learning mode) it is likely that all exams will be **conducted remotely** for **all students** at the same time
- A detailed procedure on how to take the exam is described in a separate document
- ***During exams, students will not be able to use computers or mobile phones to communicate with anyone or access any sites.*** Instead students will use their computer **only** to access exams (through **Respondus LockDown Browser**) and use their mobile phone to be proctored and to scan and upload their final answers (and, again, a detailed procedure on how to take the exam is described in a separate document)
- Possible additional exam policy changes will be announced by the instructor prior to the exams
- 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:

- Homework assignments will be posted on Canvas
- Assignments 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 as a **single** PDF file with their phone (using Office Lens and/or CamScanner free apps) and upload it to Canvas
- 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 Canvas 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 the NJIT Office of Accessibility Resources and Services. For further information, students should visit https://www.njit.edu/studentsuccess/accessibility.

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 2021):

January	18	Monday	Martin Luther King, Jr. Day
January	19	Tuesday	First Day of Classes
January	23	Saturday	Saturday Classes Begin
January	25	Monday	Last Day to Add/Drop a Class
January	25	Monday	Last Day for 100% Refund, Full or Partial Withdrawal
January	26	Tuesday	W Grades Posted for Course Withdrawals
February	2	Tuesday	Last Day for 90% Refund, Full or Partial Withdrawal - No Refund for Partial Withdrawal after this date
February	15	Monday	Last Day for 50% Refund, Full Withdrawal
March	8	Monday	Last Day for 25% Refund, Full Withdrawal
March	14	Sunday	Spring Recess Begins - No Classes Scheduled - University Open
March	21	Sunday	Spring Recess Ends
April	2	Friday	Good Friday - No Classes Scheduled - University Closed
April	**5**	**Monday**	**Last Day to Withdraw**
May	4	Tuesday	Friday Classes Meet
May	4	Tuesday	Last Day of Classes
May	5	Wednesday	Reading Day 1
May	6	Thursday	Reading Day 2
May	7	Friday	Final Exams Begin
May	13	Thursday	Final Exams End
May	15	Saturday	Final Grades Due
TBA			Commencement

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

Course Outline (Spring 2021)

Week	Date	Topic
1	January 25-31	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 1-7	Routes of administration; enteral and parenteral routes
3	February 8-14	Drug transport in biological systems - Transport across cell membranes: osmosis, passive diffusion
4	February 15-21	Drug transport in biological systems (continued) - Transport across cell membranes: ion channels facilitated transport, active transport
5	February 22-28	Drug transport in biological systems (continued) - Transport across endothelial cell layers and epithelial cells layers
6	March 1-7	Drug distribution; transcapillary exchange of drugs; perfusion-limited and permeability-limited distribution; binding of drugs to proteins; physiological barriers
7	March 8-14	Renal excretion; renal clearance. Drug metabolism
	March 15-21	*Spring Break – No class*
8	**March 22**	**Midterm exam**
9	March 29-April 4	Mathematical approach to pharmacokinetic modeling
10	April 5-11	One-compartment models and data analysis – IV Injections
11	April 12-18	One-compartment models and data analysis (continued) - Oral dosage models; method of residuals
12	April 19-25	One-compartment models and data analysis (continued) - Oral dosage models; Wagner-Nelson model. Models for other routes of administration
13	April 26- May 2	Multiple-dose models
14	May 3-9	Two-compartment models and data analysis
15	**May 10**	**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 43–NF 38, Pharmacopeial Convention Inc., 20120.*
- 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.
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- 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.