BIOL/BCHM 536 Biological & Structural Aspects of Drug Design and Action

Spring, 2019
MWF 9:30 to 10:20 am
Biochemistry Building Room 105

Course Coordinator
Professor Andrew Mesecar
Office: BCHM 120 and HOCK 311
Phone: 494-1924
Email: amesecar@purdue.edu
Office Hours:
MW: 7:30am - 9:00am
or by appointment

Teaching Assistant
Emma Lendy
Office: HOCK 221
Phone: 765-404-7712
Email: elendy@purdue.edu
Office Hours:
TBD
or by appointment

Course Description
This course will provide a general overview of the modern-day drug discovery pipeline process and an in-depth look at the basic biology, structure, and mechanisms-of-action behind currently marketed therapeutics. The course will start with a historical account of the discovery of natural product drugs such as aspirin and penicillin and will then venture into the modern-day era of the drug discovery pipeline with an emphasis on the general principles of target selection, assay development, high-throughput screening and structure-based drug design. We will explore different classes of antibiotics, antiviral, and anti-cancer drugs and their interactions with molecular targets. The majority of the course will be on small molecule drugs with some examples of modern biologics-based drugs near the end of the semester. Students will learn the fundamental properties of protein structure, enzyme kinetics and mechanisms, and will then learn how to apply these principles to drug interactions and design.

Prerequisites
BIOL 23100 or 23000 and CHM 25600 or 26605 or MCMP 20500. Note: A course in Biochemistry such as BCHM 36100, 46200 or CHM 53300, and/or a course in Structural Biology such as BIOL 39500 (Macromolecules), BIOL 44207 or BCHM 46300 is helpful but not required.
Course Goals & Outcomes

As part of the general course outcomes for the Department of Biochemistry, which is also applicable to all students, the following outcomes are expected for students taking BCHM/BIOL 536.

1. Biochemistry students will understand the molecule principles of life based on the core disciplines of biology, chemistry and physics.
   a. Able to describe the chemical structures of the building blocks of biological macromolecules, including amino acids, nucleotides, sugars and fatty acids. (BL4, E, H, Q, CD)
   b. Demonstrate knowledge of the higher order structures of proteins. (BL4, E, H, Q, CD)
   c. Understand the principles of enzyme catalysis and regulation. (BL4, E, H, Q, CD)

2. Biochemistry students will communicate scientific knowledge, experiments and conclusions effectively as speakers and writers.
   a. Describe research projects in an oral presentation that can be readily understood by a general scientific audience (BL4, OP, PR, WR)

3. Biochemistry students will acquire information literacy: the ability to locate, evaluate, and utilize information in the disciplines of biochemistry and molecular biology that is required for research, data analysis, and communication. (BL6, OP, PR, WR)

4. Biochemistry students will appreciate the ethical issues facing professionals in the life sciences.
   a. Understand scientific ethical principles of research including scientific honesty, experimental rigor, intellectual freedom, openness, the principle of credit and the principle of public responsibility. (BL4, CD)

5. Biochemistry students will understand the contributions of our discipline to society, including improvements to medicine, agriculture, the economy and the environment. (BL4, CD)

Note: BL refers to the Bloom’s level of taxonomy, which is a measure of cognition. BL2=knowledge and comprehension, BL4=application and analysis, BL6=synthesis and evaluation. The other symbols refer to the mode of assessment in each course. E=exam, H=homework, LR=lab report, Q=quizzes, CD=class discussion, OP=oral presentation, IR=instructor review, PR=peer review and WR=written report.
In addition to the outcomes above, students in the course will be able to do the following;

From the **biological/pharmacological aspects** of drug action, students will be able to:

1. understand and communicate the sites and mechanism-of-action of a drug
2. understand and communicate the relationship between the pharmacologic mechanism and the therapeutic use of a drug
3. understand and communicate the scientific basis for the therapeutic use of a drug

From the **chemical/structural aspects** of drug action, students should be able to:

1. predict, verbally or in writing, the biological response, if any, from a given chemical structure
2. communicate and describe the relationship between the structural features of a compound and the physicochemical properties that might influence biological response or the design of new agents
3. predict, verbally or in writing, the biochemical mechanism-of-action of a biologically active substrate or compound from its chemical structure
4. communicate and describe the relationship between the chemical structure of a biologically active compound and the receptor or active binding site, using enzyme or receptor models
5. predict, verbally or in writing, the biological response resulting from the chemical alteration or biochemical pathways
6. understand and communicate the relationship between *in vitro* reaction mechanisms and the structural features that alter the *in vivo* biotransformation of a drug

From the **therapeutic aspects** of drug action, students should be able to:

1. describe the pathophysiologic processes associated with a particular disease state, and how they might be affected by drug therapy

*NOTE: structures, compounds, drugs, & disease state therapeutics refer to those discussed within this course or as part of a homework assignment, reading assignment or course project.*
Required Texts
For the Spring 2019 semester, there are no required textbooks to purchase. Every attempt will be
made to provide students with reading material electronically, in print form, or on reserve in a
library.

Material from the following books will be utilized:

Evaluation of Enzyme Inhibitors in Drug Discovery: A Guide for Medicinal Chemists by Robert
A. Copeland

Enzymes: A practical Introduction to Structure, Mechanism and Data Analysis by Robert A.
Copeland.

General Biochemistry Text Books.

Primary Literature Reading Assignments and Utilization
This course utilizes a number of peer reviewed papers from the primary literature in addition to
review articles. We will utilize various journal articles throughout the course as reading material
to fill in your knowledge, as discussion material for class or as part of your team assignment.

You will need to heavily utilize the primary literature and material available via the internet for
your final project. You will need to gather the appropriate material on your enzyme drug target,
interpret and analyze the data available, and then present it in your final oral presentation to
argue your case. You will also need to utilize these references in your final written proposal.

Lecture Notes and Other Paper Handouts
Due to the tuition freezes at Purdue and the necessary budget cuts to implement these freezes, the
Departments have put a ban on distribution of any printed material with the exception of the
Course Syllabus, Quizzes and Exams. Students are responsible for bringing notes (printed or
electronic) to class for annotation during lecture. Lecture notes and material will be uploaded to
Black Board ~1 day prior to the lecture.
General Course Policies

1. Students are required to attend class and actively participate in each scheduled lecture, group activity, quiz or examination at the time specified.

2. The Course Instructor and Teaching Assistant(s) will inform you of their office hours. Questions concerning lecture content should be discussed directly with the given lecturer during classroom time or at a mutually agreed upon time. All other questions, including any questions concerning grading, should be discussed with the Course Instructor.

3. All examinations and quizzes are closed notes, closed book and closed smart phone unless stated otherwise by the instructor. For quizzes and exams that require calculations, a standard scientific calculator that is unable to connect to the internet (no Wi-Fi, no 3G/4G/5G or Bluetooth connections etc.) are to be used.

4. All requests for corrections to an exam, quiz, homework or project score should be made to the Course Instructor within 5 class days after your exam, quiz, homework or project score has been returned to you. You will have 5 class days after the start of the summer term for requests for corrections in the final examination score. It is your responsibility to notify the course instructor of any grading error. No correction of any error in addition or subtraction will be made after the final grade has been submitted.

5. **Make-up examinations will be given only for an excused absence.** Any student who misses an exam must notify the Office of the Dean of Students of his/her absence prior to the scheduled examination to obtain an excused absence from the instructor/course coordinator. Failure to comply with this policy will result in a score of a zero for the missed examination. **The course instructor will set the day and time of the make-up examination.**

6. **Make-up Quizzes, Homework or Team Projects.** You will not be allowed to make-up quizzes or homework assignments if you miss them or fail to hand them in at the specified or scheduled class date and time. If you are unable to attend class to hand in a homework assignment, you must arrange to have the homework assignment delivered to the Course Instructor or Teaching assistant before the scheduled due date and time. One lowest, or missing, quiz or homework score will be dropped from the final calculation of each student’s final grade. Make-up times, dates, etc. on Team Projects will not be allowed. Missed presentations or late submission of written proposals or projects will receive a grade of zero.

7. **Academic Dishonesty**, as defined in the Purdue University “Academic Integrity: A Guide for Students” [https://www.purdue.edu/odos/academic-integrity/](https://www.purdue.edu/odos/academic-integrity/) will not be tolerated. Students caught cheating will, at a minimum, receive a zero or letter grade of F for the assignment. The student may also receive a grade of an F for the course. Additionally, the circumstances surrounding the event will be reported to appropriate administrative officials for further action [https://www.purdue.edu/odos/osrr/resources/documents/responding_to_academic_dishonesty.html](https://www.purdue.edu/odos/osrr/resources/documents/responding_to_academic_dishonesty.html)

8. The course instructor reserves the right to make alterations in the course schedule at any time for new course material, snow days etc.
Purdue’s Honor Pledge—Written by Purdue Students!

You can use this link to a web page for Purdue’s Honor Pledge

“As a boilermaker pursuing academic excellence, I pledge to be honest and true in all that I do. Accountable together - we are Purdue.”

Policy on Student Conduct

Purdue University has a formal description of the “Purdue University Student Conduct Code” that can be found on the Office of the Dean of Students website in the section of Office of Student Rights and Responsibilities.

*Students are responsible for observing the policies, rules, and regulations of Purdue University. These, in general, state the expectation that Purdue students will at all time conduct themselves as responsible citizens. Failure to show respect for duly established laws or University regulations will be handled by the Office of Student Rights and Responsibilities in conformance with the various policies and regulations.*

Additional details can be found at the website which is: http://www.purdue.edu/studentregulations/student_conduct/regulations.html

Students in Biological & Structural Aspects of Drug Design and Action are expected to behave in a civil fashion toward instructors, staff, and their fellow students. Sometimes we fail to realize that our behavior disrupts or offends others. It is important to be sensitive to the goals and feelings of your instructors and classmates.

Please attend to the business of the class while in the classroom. It is rude to talk with a friend, read a newspaper, or engage in non-class activities during class. Help to build a good classroom environment by being a supportive listener and making relevant contributions to the topics being discussed. Please make every attempt to arrive in the classroom and be prepared for lecture and/or recitation at the proper time. Walking in after the bell has sounded and the lecture and/or recitation have begun disrupts the other students and the faculty. Please be courteous at all times.

Policy on Diversity and Nondiscrimination

In accordance to Purdue’s Nondiscrimination Policy Statement, BIOL/BCHM 536 Students, Teaching Assistants and Instructors will be committed “to maintaining a community which recognizes and values the inherent worth and dignity of every person; fosters tolerance, sensitivity, understanding, and mutual respect among its members; and encourages each individual to strive to reach his or her own potential”. In addition, in pursuit of our goal of academic excellence in BIOL/BCHM536, Students, Teaching Assistants and Instructors will seek to develop and nurture diversity. Purdue University believes that diversity among its many members strengthens the institution, stimulates creativity, promotes the exchange of ideas, and enriches campus life and BIOL/BCHM536 will be a reflection of those values. For more information, please see http://www.purdue.edu/purdue/ea_eou_statement.html.
Purdue University prohibits discrimination against any member of the University community on the basis of race, religion, color, sex, age, national origin or ancestry, genetic information, marital status, parental status, sexual orientation, gender identity and expression, disability, or status as a veteran. The University will conduct its programs, services and activities consistent with applicable federal, state and local laws, regulations and orders and in conformance with the procedures and limitations as set forth in Purdue’s Equal Opportunity, Equal Access and Affirmative Action policy which provides specific contractual rights and remedies. Additionally, the University promotes the full realization of equal employment opportunity for women, minorities, persons with disabilities and veterans through its affirmative action program.

Anti-Harassment Policy
Strictly following and interpreting existing University Policy: Purdue University is committed to maintaining an environment that recognizes the inherent worth and dignity of every person; fosters tolerance, sensitivity, understanding and mutual respect; and encourages its members to strive to reach their potential. The most effective way to work toward preventing Harassment is through education that emphasizes respect for every individual.

Students with Disabilities
Purdue University is required to respond to the needs of the students with disabilities as outlined in both the Rehabilitation Act of 1973 and the Americans with Disabilities Act of 1990 through the provision of auxiliary aids and services that allow a student with a disability to fully access and participate in the programs, services, and activities at Purdue University.

If you have a disability that requires special academic accommodation, please make an appointment to speak with me within the first three (3) weeks of the semester in order to discuss any adjustments. It is important that we talk about this at the beginning of the semester.

It is the student’s responsibility to notify the Disability Resource Center http://www.purdue.edu/studentsuccess/specialized/drc/ of an impairment/condition that may require accommodations and/or classroom modifications. Students with disabilities can find more information on available resources at the Disability Resource Center (DRC) website.

Counseling and Psychological Services (CAPS) Information
Purdue University is committed to advancing the mental health and well-being of its students. If you or someone you know is feeling overwhelmed, depressed, and/or in need of support, services are available. For help, such individuals should contact Counseling and Psychological Services (CAPS) at (765)494-6995 and http://www.purdue.edu/caps/ during and after hours, on weekends and holidays, or through its counselors physically located in the Purdue University Student Health Center (PUSH) during business hours.

Policy on Class Attendance
BIOL/BCHM 536 will follow the guidelines on attendance provided by Purdue University; http://www.purdue.edu/advocacy/students/absences.html. Students are expected to be present for every meeting of the class. Only the Course Instructor can excuse a student
**from classes or course responsibilities.** In the event of an illness, accident, or emergency, when circumstances permit, students should make direct contact with the Course Instructor, preferably before a class or an exam takes place. If the instructor cannot be reached in person or by telephone, the student should leave a message in the instructor’s department mailbox or with the instructor’s administrative assistant.

When a student is unable to make direct contact with the instructor and is unable to leave word with the instructor’s department because of circumstances beyond the student’s control, the student or the student’s representative should contact the Office of the Dean of Students if the reported absence is expected to be for an extended period of time (normally **more than five days**). A member of the Dean of Students staff will notify the student’s instructor(s) of the circumstances. Only the instructor may excuse class absences. The student should be aware that this intervention does not change, in any way, the outcome of the instructor’s decision regarding the student’s academic work and performance in any given course. The student must make personal contact with the instructor(s) as soon as it is possible to do so. The student may discuss the circumstances of the absence with a member of the Office of the Dean of Students for advice on how to proceed.

If a student will be absent for **more than five days**, has not been able to reach the instructor in person or by telephone, or through leaving notification of the student’s circumstances with the instructor’s secretary, the student or the student’s representative should notify the Office of the Dean of Students, at **765-494-1747** as soon as possible after becoming aware that the absence is necessary. Be advised, the student, or the student’s representative may be asked by the instructor(s) to provide documentation from an authorized professional or agency which supports an explanation for the student’s absence.

**As an incentive, students who attend ~90% of the lectures will be invited to Professor Mesecar’s house for an end of the semester party. This party will likely take place the weekend before finals, usually Sunday evening. Daily attendance sheets will be distributed at each lecture. Since the first time I created and taught this course in the spring of 2011, there has been a strong correlation between the number of lectures missed by a student and their point total (and final grade) for the semester. The more you miss this class, the more points you tend to miss on quizzes and exams. This trend has been consistent since 2011 and I therefore expect this year to be no different.**

**Arrive to Class On-Time**
You are expected to arrive to class on time. Exams will start promptly at 9:30 am and quizzes are often given right at 9:30 am also. You will NOT be given any extra time if you are late. No exceptions. Homework is often collected at the beginning of class also. If you are not there to turn in your homework when collected it will be considered late and will not be counted. It is not my problem that another professor goes over time with his/her lecture before BIOL/BCHM 536, if you are slow walking to class because you have to talk to someone on a cell phone between classes, or if parking is inconvenient. You need to find a way. If you have a documented handicap or have sustained a temporary injury (ruptured Achilles-happened to me one year, broken leg etc.) that is documented by a health care professional then appropriate accommodations will be made.
Policy on Distribution of Course Material from BCHM/BIOL536: No Material or Notes from this Course Should be posted on Commercial Websites

You are not allowed to distribute any course material given to you in class, out of class, or via email or Blackboard etc. to any other entity or posted on Websites such as Course Hero, Chegg, or Quizlet etc. In general, notes are “considered to be ‘derivative works’ of the instructor’s presentations and materials, and they are thus subject to the instructor's copyright in such presentations and materials.” As such, they cannot be sold or bartered without your express written permission. See the policy with regard to commercial note taking in classes that you may wish to include in your syllabus (see part J of the Purdue student misc. conduct regulations).

BIOL/BCHM 536 COURSE MATERIAL DISTRIBUTION AGREEMENT

I , ___________________________________________ fully understand that I am NOT to:
(Print Student’s Name)

distribute, post, upload to the internet, or email any of the course material provided to me by my instructor in class, out of class, via email or BlackBoard. I understand that this material is provided to me for use in BIOL/BCHM 536 and that it is not to be made publically available unless I obtain written permission by my course instructor, Professor Andrew Mesecar, and Purdue University. I understand that all material provided to me is property of Purdue University and that it is subject to certain Copyright laws.

Student’s signature __________________________________________ Date _____________
Policy on Taping or Recording of Lectures in BCHM/BIOL536:

In general, you are not allowed to record any of the lectures via any electronic format (voice or video recorders, cell phones etc. The lectures will be recorded for you via BoilerCast or the Course Instructor and edited if necessary. These recordings will be posted on Blackboard within 1 week of the lecture. However, if necessary, the procedure for taping/recording lectures in BIOL/BCHM 536 is as follows:

A student can only record a class for personal use if they do all of the following:

1. Obtain written consent (see Consent Form below) of the faculty member lecturing BEFORE the student tapes the lecture (this protects the student from having somebody say later that they didn’t give permission); the consent needs to be signed by the student and indicate that it is only for personal use and it won’t be posted on the internet; a copy of the form should be kept by the student and given to the faculty member.

2. Use the recorded material solely for their own use; lecture cannot be duplicated and given to other class members.

3. Recorded material cannot be posted on the internet or disseminated in any way.

BIOL/BCHM 536 LECTURE RECORDING CONSENT FORM

I ___________________________________________ permit ____________________
(PRINT LECTURER’S NAME) (PRINT STUDENT’S NAME)

I understand that:

§ recordings will be used solely for personal note-taking purposes without being duplicated and/or distributed to other individuals;

§ recordings will not be posted on the internet or unlawfully distributed in any other public forum.

Lecturer’s signature _______________________________ Date _____________

Student’s signature _______________________________ Date _____________
GRADING

**Tentative Plan Course Point Distribution:**

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<tr>
<td><strong>First 1-Hour Examination:</strong></td>
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<td>~130</td>
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<tr>
<td>Covers $X$ lectures @ 10 to 15 pts each</td>
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<td><strong>Second 1-Hour Examination:</strong></td>
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<td>~140</td>
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<td>Covers $Y$ lectures @ 10 to 15 pts each</td>
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<td><strong>Third 1-Hour Exam:</strong></td>
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<td>~130</td>
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<td>Covers $Z$ lectures @ 10 to 15 pts each</td>
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<tr>
<td><strong>Final Examination</strong></td>
<td>Cumulative <em>(may be optional- will depend on course performance)</em></td>
<td>200</td>
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<tr>
<td><strong>Announced and Pop Quizzes:</strong></td>
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<td>3 to 5 @ 10 to 15 pts each = 30 to 90 pts</td>
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<td>30 to 90 pts</td>
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<tr>
<td><strong>Homework</strong></td>
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<td>30 to 75 pts</td>
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<td>3 to 5 @ 10 to 15 pts each = 30 to 75 pts</td>
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<tr>
<td><strong>Student Team Projects and Presentations:</strong></td>
<td>Written Proposal (50), Presentation (100), Team Member Evaluation (25)</td>
<td>200</td>
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<tr>
<td>Peer-Evaluation (25)</td>
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<tr>
<td><strong>Lowest Quiz or Homework Score Dropped</strong></td>
<td>-10 or -15</td>
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<td><strong>Total Points for this Course:</strong></td>
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<td>850 - 950</td>
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**Examinations:**
There will be at least three (3) examinations and one (1) two-hour cumulative final examination. Regular exams will be given during our scheduled class hour. This gives us flexibility in scheduling the day of the exam and it eliminates evening scheduling conflicts. Therefore, all students will be able to take the examinations without excuses.

**Type of Examination Questions:**
In general, problem-solving questions requiring short, concise answers that may involve chemical structures, models for drug-receptor/enzyme interactions and therapeutic applications will be given. In addition, matching and/or multiple-choice questions will also be used. In general, about 10 to 15 points will be assigned per lecture to arrive at the amount of points assigned to each exam.

**Quizzes (Scheduled and Pop):**
We will have a few scheduled or unscheduled “Pop” quizzes throughout the semester. The final number is not set at this point and will depend on class progress.

**Homework**
We will have at least 3 homework problem sets during the semester, but more may be given depending on the academic needs of students.
**Team Proposal Project**

We are going to have a team project where each team of 3 to 4 students will select a potential drug target and then “sell” their idea to develop this target to a scientific board of a fictitious pharmaceutical company. The enzyme target will not yet have a marketed therapeutic developed, but there will be enough biological and lead discovery data on the target to enable its further development. It will be the goal of each project team to convince the company that their target is the best one to move forward in the development pipeline. Only 1 or 2 of these targets, depending on the class size, will be selected to move forward. A written proposal and presentation will be required. Individual team member assessments will be performed by each team member, and presentations will be peer-reviewed. More details will follow.

**Grading System**

A minimum of 60% of the total points is required to guarantee that you will receive a passing grade of a D. All students achieving 90% or above of the total points will receive an A for the course. Grades of B and C will be assigned by the instructor/course coordinator for students receiving above 80% and 70% respectively. Plus (+) and minus (-) may also be assigned to grades based on final percentages. The final cut-off for each grade will be determined based on the overall performance of the class.

**Academic Integrity & Dishonesty**

Academic integrity is one of the highest values that Purdue University holds. Individuals are encouraged to alert university officials to potential breaches of this value by either emailing integrity@purdue.edu or by calling 765-494-8778. While information may be submitted anonymously, the more information that is submitted provides the greatest opportunity for the university to investigate the concern.

Academic Dishonesty will not be tolerated. BIOL/BCHM536 will adopt and abide by the rules and policies of Purdue University for Academic Dishonesty.

Purdue prohibits "dishonesty in connection with any University activity. Cheating, plagiarism, or knowingly furnishing false information to the University are examples of dishonesty." [Part 5, Section III-B-2-a, University Regulations] Furthermore, the University Senate has stipulated that "the commitment of acts of cheating, lying, and deceit in any of their diverse forms (such as the use of substitutes for taking examinations, the use of illegal cribs, plagiarism, and copying during examinations) is dishonest and must not be tolerated. Moreover, knowingly to aid and abet, directly or indirectly, other parties in committing dishonest acts is in itself dishonest." [University Senate Document 72-18, December 15, 1972]

Please read a “Guide for Students” on Academic Integrity which can be found at the following website [http://www.purdue.edu/odos/osrr/academic-integrity/index.html](http://www.purdue.edu/odos/osrr/academic-integrity/index.html)
Plagiarism
There are few intellectual offenses more serious than plagiarism in academic and professional contexts. The Purdue Online Writing Lab (OWL) resource offers advice on how to avoid plagiarism in your work. See https://owl.english.purdue.edu/owl/resource/589/02/.

The iThenticate Plagiarism Detection Software resource http://www.ithenticate.com/ and SafeAssign function in Blackboard will be used for plagiarism detection.

Emergencies

In the event of a major campus emergency, course requirements, deadlines and grading percentages are subject to changes that may be necessitated by a revised semester calendar or other circumstances beyond the instructor’s control. Relevant changes to this course will be posted onto the course website or can be obtained by contacting the instructors or TAs via email or phone. You are expected to read your @purdue.edu email on a frequent basis.

Active Shooter(s) and Shelter in Place

Purdue University has issued guidelines for Active Shooters. See the following site; https://www.purdue.edu/ehps/emergency_preparedness/flipchart/activeshooter.html
Our BCHM 105 classroom is capable of being locked. Please familiarize yourselves with how to lock the door.

Purdue Emergency Notification

In encourage all of my students to subscribe to our emergency notification service. Please go to the following website and subscribe. http://www.purdue.edu/newsroom/health_safety/mail.html
I do allow my students to keep their cell phones on vibrate during class so they can get these messages.
Academic Calendar - Spring Semester 2019

January
Monday 7  CLASSES BEGIN
Tuesday 14  Last day for registration without a late fee
Monday 21  Martin Luther King Jr. Day (No Classes)
Monday 21  Last day to cancel a course assignment without it appearing on record

February
Monday 4  Last day to withdraw a course with a grade of W or to add/modify a course with instructor and advisor signature
Monday 18  Last day for grade correction for Fall 2017 semester.

March
Monday 8  Last day to Withdraw from a Course with a W or WF grade
Monday 8  Last day to Add/Modify a course with Instructor, Advisor and Department Head signature.
Mon.-Sat. 11-16  SPRING VACATION

April
Saturday 27  CLASSES END
Monday 29  FINAL EXAMS BEGIN

May
Saturday 4  FINAL EXAMS END
Saturday 4  SEMESTER ENDS
Saturday 4  Deadline for pending incomplete grades to become failing grades
Tuesday 7  Grades Due
Friday 10  Commencement (1st Division) 3 pm
           Commencement (2nd Division) 7:00 pm
Saturday 11  Commencement (3rd Division) 9:30 am
             Commencement (4th Division) 2:00 pm
Sunday 12  Commencement (5th Division) 9:30 am
           Commencement (6th Division) 2:00 am
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<tr>
<th>Wk</th>
<th>Lecture</th>
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<tr>
<td>1</td>
<td>1</td>
<td>Mon</td>
<td>Jan 7</td>
<td>Brief Overview of Syllabus and Course History and Overview of Drug Discovery</td>
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<td>History and Overview of Drug Discovery</td>
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<td>2</td>
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<td>Wed</td>
<td>Jan 9</td>
<td>Protein Structure – Structure of Water, Amino Acid Side Chain Properties, Bonding Forces</td>
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<td>Protein Structure &amp; Molecular Interactions - Basic Forces and Bonding, pKa’s and acid-base chemistry.</td>
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<td>3</td>
<td>4</td>
<td>Mon</td>
<td>Jan 14</td>
<td>Protein Structure &amp; Molecular Interactions - Basic Forces and Bonding, pKa’s and acid-base chemistry.</td>
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<td>6</td>
<td>Fri</td>
<td>Jan 18</td>
<td>HTS at Purdue – Overview &amp; Examples – Dr. Lan Chen, Chemical Genomics Screening Facility</td>
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<td>3</td>
<td>MLK</td>
<td>Mon</td>
<td>Jan 21</td>
<td>Martin Luther King Jr.</td>
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<td>7</td>
<td>Wed</td>
<td>Jan 23</td>
<td>Protein Structure – Peptide Bonds and Primary Structure, Secondary Structures &amp; Motifs</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Fri</td>
<td>Jan 25</td>
<td>Protein Structure – Tertiary &amp; Quaternary Structures</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>Mon</td>
<td>Jan 28</td>
<td>Forces that stabilize Proteins and Their Interactions with Drug Molecules</td>
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<td></td>
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<td></td>
<td></td>
<td>Introduction to Antibiotics</td>
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<td></td>
<td></td>
<td>Principles and Biology of Antibiotic Target Selection</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Wed</td>
<td>Jan 30</td>
<td>Antibiotics - Penicillins</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Fri</td>
<td>Feb 1</td>
<td>Antibiotics – Penicillins</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Beta-Lactamase mechanism and Inhibitors</td>
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BIOL/BCHM 536 Tentative Class Schedule (Weeks 5 thru 8)

<table>
<thead>
<tr>
<th>Wk</th>
<th>Lecture</th>
<th>Day</th>
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<th>Topic</th>
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</table>
|    |         |     |        | **5** Mon Feb 4                                                                                          | Enzymes Kinetics – zero and first order reactions  
|    |         |     |        | Single Substrate Reactions  
|    |         |     |        | Michaelis-Menten Equation  
|    |         |     |        | Briggs-Haldane Equation  
|    |         |     |        | Meaning of Km and Vmax  
|    |         |     |        | (**Last day to withdraw from a course without a grade, to add a course, or change to pass/not-pass option)** |
| EXAM 1 | Wed |     | Feb 6  | **Covers Material to Lecture 11**  
|        |     |     |        | *Note: May be an evening exam*  
|    |         |     |        | 13 Fri Feb 8                                                                                          | Meaning of Vmax/Km and relation to MIC of antibiotics  
|    |         |     |        | Bi-substrate Reactions (Sequential and Ping-Pong)                                                      |
|    |         |     |        | **6** Mon Feb 11                                                                                      | Inhibitor Interactions with Enzymes  
|    |         |     |        | Competitive, non-competitive, uncompetitive  
|    |         |     |        | Meaning of Ki values  
|    |         |     |        | Meaning of IC50 Values  
|    |         |     |        | 15 Wed Feb 13                                                                                         | Chemical Modification of Enzymes by Covalent Inhibitors  
|    |         |     |        | 16 Fri Feb 15                                                                                         | Antibiotics – Beta Lactamases and their Mechanisms of Inhibition and Resistance  
|    |         |     |        | 17 Mon Feb 18                                                                                         | Antibiotics – Sulfonamide Drugs and Their Targets  
|    |         |     |        | 18 Wed Feb 20                                                                                         | Antibiotics – Susceptibility Testing and Trimethoprim  
|    |         |     |        | 19 Fri Feb 22                                                                                         | Antibiotics – Targeting the Ribosome  
|    |         |     |        | **8** Mon Feb 25                                                                                       | Antibiotics – Targeting DNA Gyrase  
|    |         |     |        | **Wed** Feb 27                                                                                         | Antivirals - The Flu Virus and Neuraminidase  
|    |         |     |        | 21 Fri Mar 1                                                                                           | Antivirals -Neuraminidase Mechanism and Inhibitors  
|    |         |     |        | **Desired Team Member Traits Survey**  

<table>
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<tr>
<th>Wk</th>
<th>Lecture</th>
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<th>Topic</th>
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<tbody>
<tr>
<td>9</td>
<td>22</td>
<td>Mon</td>
<td>Mar 4</td>
<td>Antivirals - HIV and Aids Statistics</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HIV Protease</td>
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<td></td>
<td></td>
<td>Assign Teams 1 to 5</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>Wed</td>
<td>Mar 6</td>
<td>Antivirals- HIV Protease Mechanism and Inhibitors</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Drug Resistance and HIV Protease</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>Fri</td>
<td>Mar 8</td>
<td>Antivirals- Finish HIV Protease if Needed</td>
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<tr>
<td></td>
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<td></td>
<td>PharmaX Project Overview</td>
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<td></td>
<td>Pymol and Chimera molecular modeling and visualization software – demonstration</td>
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<td></td>
<td>Team Time – with time remaining</td>
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<td>(Last day to withdraw from a course with a passing W or failing WF grade)</td>
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<tr>
<td>10</td>
<td></td>
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<td></td>
<td>Spring Break March 11 – March 16</td>
</tr>
<tr>
<td>11</td>
<td>25</td>
<td>Mon</td>
<td>Mar 18</td>
<td>Antivirals - SARS Virus and SARS Proteases</td>
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<td></td>
<td></td>
<td>Or Hepatitis C Protease Inhibitors</td>
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<tr>
<td></td>
<td>EXAM 2</td>
<td>Wed</td>
<td>Mar 20</td>
<td>Covers Material to Lecture 24</td>
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<td>Note: May be an evening exam</td>
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<tr>
<td></td>
<td>26</td>
<td>Fri</td>
<td>Mar 22</td>
<td>Antivirals - SARS Virus and SARS Papain-like Protease Inhibitors</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Or Hepatitis C Protease Inhibitors</td>
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<tr>
<td>12</td>
<td>27</td>
<td>Mon</td>
<td>Mar 25</td>
<td>Antivirals - SARS Virus and SARS Papain-like Protease Inhibitors</td>
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<td></td>
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<td></td>
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<td>Or Hepatitis C Protease Inhibitors</td>
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<td></td>
<td></td>
<td>Team Drug Target Choices Due</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>Wed</td>
<td>Mar 27</td>
<td>Anticancer Drugs- Overview of Cancer as a disease and the three stages of carcinogenesis and metastasis</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>Fri</td>
<td>Mar 29</td>
<td>Anticancer Drugs - Thymidylate Synthetase mechanism and design of anti-cancer drugs</td>
</tr>
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</table>
# BIOL/BCHM 536 Tentative Class Schedule (Weeks 12 thru 16)

<table>
<thead>
<tr>
<th>Wk</th>
<th>Day</th>
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<th>Topic</th>
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<tbody>
<tr>
<td>13</td>
<td>Mon</td>
<td>Apr 1</td>
<td>Anticancer Drugs - Dihydrofolate Reductase mechanism and inhibition by methotrexate</td>
</tr>
<tr>
<td></td>
<td>Wed</td>
<td>Apr 3</td>
<td>Anticancer Drugs - Topoisomerase Inhibitors</td>
</tr>
<tr>
<td></td>
<td>Fri</td>
<td>Apr 5</td>
<td>Anticancer Drugs - Protein Kinases in Cancer Mechanism of Gleevec and BCR-ABL</td>
</tr>
<tr>
<td>14</td>
<td>Mon</td>
<td>Apr 8</td>
<td>Anti-inflammatory Drugs Inflammation, Rheumatoid Arthritis and DMARDs</td>
</tr>
<tr>
<td></td>
<td>Wed</td>
<td>Apr 10</td>
<td>Anti-inflammatory Drugs Mechanism of Cox1 and Cox 2 and Non-Steroidal Anti-inflammatory Drugs (NSAIDS)</td>
</tr>
<tr>
<td></td>
<td>Fri</td>
<td>Apr 12</td>
<td>Anti-inflammatory Drugs Biological Drugs – Humira, Embrel, Orecia etc.</td>
</tr>
<tr>
<td>15</td>
<td>Mon</td>
<td>Apr 15</td>
<td>Anti-inflammatory Drugs Biological Drugs - Continued</td>
</tr>
<tr>
<td></td>
<td>Wed</td>
<td>Apr 17</td>
<td>EXAM 3 Covers Material to Lecture 36 Note: May be an evening exam</td>
</tr>
<tr>
<td></td>
<td>Fri</td>
<td>Apr 19</td>
<td>Team PowerPoint Presentations Due (Jump Drives for ALL groups due by 9:00 am to Prof. Mesecar)</td>
</tr>
<tr>
<td>16</td>
<td>Mon</td>
<td>Apr 22</td>
<td>Student Team Presentations C &amp; D (E&amp;F Evening?) Team Project Written Reports Due (by 5 pm to Professor Mesecar)</td>
</tr>
<tr>
<td></td>
<td>Wed</td>
<td>Apr 24</td>
<td>Student Team Presentations G &amp; H (E&amp;F Evening?) Team Member Evaluations Due (by Noon to Professor Mesecar)</td>
</tr>
<tr>
<td></td>
<td>Fri</td>
<td>Apr 26</td>
<td>Student Team Presentations Results and Final Discussion</td>
</tr>
<tr>
<td>17</td>
<td>Mon</td>
<td>Apr 29- May 4</td>
<td>Final Exam Week</td>
</tr>
<tr>
<td>18</td>
<td>Fri- Sun</td>
<td>May 10-12</td>
<td>Commencements</td>
</tr>
</tbody>
</table>

This syllabus is subject to change at any time. Should changes be made, all students will be contacted in-class and/or through the course website.
PharmaX is a large pharmaceutical company that has average annual gross sales of $10 billion dollars. One of its major drugs for neuropathic pain, Lyracula®, which had a total annual sale of over $5 billion in 2017, is going off patent next year, 2019. Currently, there are no new drug molecules in the pipeline of PharmaX that will be approved by the FDA in time to replace their current leading drug that is set to expire. It is estimated that the generic versions of Lyracula®, will capture a market share of $3 billion in the first year of sales thereby reducing PharmaX’s total annual sales by approximately 30%. Fortunately, PharmaX does have a rich set of drug development projects ongoing in its portfolio that could produce a new drug within 2 years after the patent expires. In an effort to accelerate the development of a new drug from the project portfolio of PharmaX, the scientific advisory board and board of directors has decided to focus resources on only 1 of its 5 ongoing projects. To decide on which project to move forward in an accelerated product development pipeline, the scientific board has asked each of the 5 project teams to draft a 10 to 15-page project proposal/description that describes the merits of their project and why they should receive continued but elevated funding for drug development. They have also asked each project team to give a 20-minute presentation on the scientific merits and the potential impact of their project to PharmaX’s bottom line. From these presentations and written proposals, the scientific advisory board will make a recommendation to the board of directors as to which project(s) to invest in by providing additional resources to those projects. The unsuccessful project teams will be terminated to help capture a portion of the anticipated revenue loss of 30% or $3 billion per year.

**Guidelines for Target Selection**

1. Each project team should choose a disease area of focus, e.g. anti-infectives, anticancer, anti-inflammatory, cardiovascular, neurological etc.
2. Each project team needs to choose a specific target enzyme or receptor to develop. This enzyme or receptor target **MUST have an X-ray, NMR or cryo-EM structure available** (PDB file must be available) and there can be NO marketed (FDA Approved) therapeutic for this target. It is ok, however, if there are small molecule drugs in Phase 1 or Phase 2 clinical trials for your target. This may help give validation of the target and will provide important details.
3. PharmaX is only interested in developing small molecule drugs, i.e. non-biological based drugs, so monoclonal antibodies or engineered proteins are not acceptable.
4. In class, we have discussed a number of factors to consider with target selection including potential market, target biology and validation, and available information on the structure and mechanism of the target. You need to utilize all of this information in selected the best target for development.
Written Proposal Guidelines (15 Pages Maximum) 50 Total Points.

1. The written proposal should be typed using single spaces and Arial 11 or 12-point font. Margins should be 1 inch all around.
2. Figures are allowed but must be accompanied by a Figure Legend (10 to 11-point font) underneath the figure. Figures should be utilized effectively in the proposal by describing them in the text of the proposal. Do not put figures in the proposal that are superfluous.
3. The proposal should contain the following elements:
   a. Title Page: Title of Project and Names of Team Members
   b. Abstract/Summary Page (Limit of 1/2 to 1 Page)- Sell your project in this one page summary based on the most important elements to convince the scientific review board as to why your project is “hot”.
   c. Proposal Body (Limit of 15 pages). Give the details of your target of interest and provide the details of the basis for why your team thinks this is the best target to move forward. Some of the elements to be considered for the proposal body could include the following;
      i. Target disease area and target biology background
      ii. Number of people affected in the US and worldwide
      iii. Chronic versus short term therapy
      iv. Market Potential for Sales
      v. Market -share with other products
      vi. Target biology unique or already validated by others
      vii. Target biology validation and methods of validation (siRNA, known small molecule inhibitors etc.)
      viii. Off target effects, e.g. Kinase inhibitors
      ix. Target Structures available and Mechanism-of-Action
      x. Essentiality of target protein in cell and context of essentiality e.g. conditionally essential in the disease state only
      xi. Other isoforms or isozymes of the target e.g. Cox 1 and Cox 2
      xii. Known inhibitors of the target and strengths of interactions
      xiii. New scaffolds for inhibitors of targets and how they were discovered
      xiv. Examples of structure-based drug design against target
      xv. Any clinical trials already in progress
Project Proposal Presentation Guidelines (20 minutes + 5 minutes for Questions) 100 Points Total

1. Each project team will give a PowerPoint Presentation describing their project and why it should move on for advanced drug development. The presentation should include the most important elements from the written proposal necessary to persuade the scientific advisory team. Often times the presentation is what carries the most weight in terms of persuading individuals of the merits of their project versus just a written proposal/description.

2. Each presentation will be given no more than 20 minutes. At the end of 20 minutes, the presenters will be cut off (mid-sentence if necessary) for the question answer period. We only have 50 minutes for the class so we have to stick to the timeline.

3. Presentations should be constructed using Microsoft PowerPoint.

4. Presentations should be given by 1 to four of the team member(s). The number of team members participating in the presentation and the length of their part of the presentation is up to each team.

5. Each team member should be able to answer any question asked. However, you can assign a person(s) to answer questions after the presentation.

6. 20 Points of the 100 points will be given based upon peer review (other project teams) of your presentation.

Team Member Evaluation (50 Points)

1. If you feel that a team member(s) have not done their part in helping the team prepare the written proposal or the presentation, you will be able to state this on the team member evaluation sheets.
BIOL/BCHM 536
PharmaX Team Project Proposal Deadlines (Tentative)
2019

Tentative Target Selection  Monday, March 25th
Each team needs to provide me with a list of their TOP 3 Target Enzymes and/or Receptors that they are interested in pursuing. Please rank order your choices with the Top Choice being number 1.  *The earlier you select your target, the earlier I can approve it.* We cannot have duplicate targets so approval and assignment of targets will be on a first come, first serve basis. The means that you really need to research each of your potential targets and meet to discuss your priorities before Spring Break to get a good start. One target that is off the list is Beta-secretase (BACE 1 and 2) also known as Memepsin 2 and Memepsin 1. I will approve the targets on a rolling basis but all must be approved by Monday, March 30th.

ALL PowerPoint Presentations DUE  Friday, April 20th by 9:30 am
One of your team members needs to bring a Jump Drive with your final presentation to me in my office in Hockmeyer by 9 am on Friday. All 4 presentations will be loaded onto the computers (PC or Mac laptop). Presentation order will be random and will occur by selection on the day of class. All team members should be present for all presentations. You cannot change your PowerPoint presentation after you turn it in. It is what it is.

PowerPoint Presentations - Friday, April 20th, Monday, April 23rd and Wednesday April 25th in Class

Written Project Proposal Descriptions  Wednesday, April 24th by 5 pm
Bring the proposals to me at class time or to my office in Hockmeyer by noon. I want both a Word Document and a PDF file. I will be running an iThenticate plagiarism check on each written report before I read them. If the server scores and analysis indicates the document or parts of the document have been plagiarized, it will be returned to you without evaluation and your score will be zero.

Team Member Evaluation Sheets  Wednesday, April 24th by 5 pm
Bring the evaluations to me at class time or to my office in Hockmeyer by noon 12:00. Alternatively, you can email a PDF file to me by noon (12:00pm)
BIOL/BCHM 536 STUDENT TEAM EVALUATION FORMS

Name of Evaluator ____________________________________________

Team Number _______________

With regards to your personal contribution to the group project, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

1. My attitude contributed positively to the group project. 5 4 3 2 1
2. I showed up for meetings on time and prepared. 5 4 3 2 1
3. I helped the group make important project decisions. 5 4 3 2 1
4. I completed my share of the work in a competent and timely manner. 5 4 3 2 1

Additional comments:

Team Member's Name ____________________________________________

With regard to this team member, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

1. His/her attitude contributed positively to the group project. 5 4 3 2 1
2. He/she showed up for meetings on time and prepared. 5 4 3 2 1
3. He/she helped the group make important project decisions. 5 4 3 2 1
4. He/she completed his/her work in a competent & timely manner. 5 4 3 2 1
5. I would want this person on my team again. 5 4 3 2 1

Additional comments:

Team Member's Name ____________________________________________

With regard to this team member, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

1. His/her attitude contributed positively to the group project. 5 4 3 2 1
2. He/she showed up for meetings on time and prepared. 5 4 3 2 1
3. He/she helped the group make important project decisions. 5 4 3 2 1
4. He/she completed his/her work in a competent & timely manner. 5 4 3 2 1
5. I would want this person on my team again. 5 4 3 2 1

Additional comments:
**Team Member's Name**

With regard to this team member, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

1. His/her attitude contributed positively to the group project. 5 4 3 2 1
2. He/she showed up for meetings on time and prepared. 5 4 3 2 1
3. He/she helped the group make important project decisions. 5 4 3 2 1
4. He/she completed his/her work in a competent & timely manner. 5 4 3 2 1
5. I would want this person on my team again. 5 4 3 2 1

*Additional comments:*

---

**Team Member's Name**

With regard to this team member, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

1. His/her attitude contributed positively to the group project. 5 4 3 2 1
2. He/she showed up for meetings on time and prepared. 5 4 3 2 1
3. He/she helped the group make important project decisions. 5 4 3 2 1
4. He/she completed his/her work in a competent & timely manner. 5 4 3 2 1
5. I would want this person on my team again. 5 4 3 2 1

*Additional comments:*
# BIOL/BCHM 536 PharmaX Presentation Student Evaluation Form

**TEAM __________**

### Disease & Target

**Evaluation Criteria**

(1 = unacceptable; 2 = poor; 3 = acceptable or good; 4 = very good; 5 = excellent)

1. **PRESENTATION OF PERTINENT DATA**
   - Applicable and important disease area, disease state, and target biology. Basic sciences concepts within these areas are adequately covered based on fundamentals learned during the course. Always or nearly always are correctly interpreted. Content matches audience’s needs and is applicable for project.
   - Comments:

2. **CRITICAL THINKING SKILLS**
   - Provides sound assessments and makes original recommendations to the scientific board based on inquiry, extensive analysis, and scientific reasoning. Appropriate citations of current literature are provided.
   - Comments:

3. **COMMUNICATION SKILLS**
   - The presentation is logically organized and the information is clearly explained. Delivery includes direct eye contact, clarity and proper rate of speech, absence of nervousness and distracting habits, and appropriate terminology and pronunciation.
   - Comments:

4. **RESPONSE TO QUESTIONS & KNOWLEDGE**
   - Able to answer questions in logical fashion and has the ability to think on his / her feet. Answers are accurate and correspond with the expected degree of competence.
   - Comments:

5. **AUDIOVISUALS – SLIDES, HANDOUTS**
   - Comments:

6. **OVERALL EVALUATION AND PERSUASION**
   - Did the presentation and proposal convince you that this project should move forward for further development in the PharmaX company?
   - Comments: