
I  Contact Information

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Associate Professor of Medicinal Chemistry
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       Tu - Th: 11:00-12:00, 4:00-5:30p
       W: 11:00-11:45a, 4:00-5:00p
       F: 11:30-1:00p
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Email: rhill@ulm.edu
Preferred method of contact: e-mail/phone/in person

II  Course Prerequisites/Co-requisites

Credit or registration in PHRD 4020.

III  Course Description

PRINCIPLES OF DRUG ACTION I.  4 cr.  This course focuses on molecular-level function and processes as relates to rational and successful therapeutic intervention with medicinal substances.
IV Curricular Outcomes

Educational outcomes (CAPE 2013 document)

1.1. Learner-Develop, integrate, and apply knowledge from the foundational sciences (pharmaceutical, social/behavioral/administrative, and clinical sciences) to evaluate the scientific literature, explain drug action, solve therapeutic problems, and advance population health and patient-centered care.

ACPE Appendix 1 required element

Biochemistry
Structure, properties, biological functions, applicable kinetics. Application of these concepts to identify endogenous targets for drug therapy and rational drug design strategies.

Medicinal Chemistry
Chemical basis of drug action and behavior in vivo and in vitro, with an emphasis on pharmacophore recognition and the application of physicochemical properties, structure-activity relationships, intermolecular drug-receptor interactions and metabolism to therapeutic decision-making.

Pharmaceutics/Biopharmaceutics
Physicochemical properties of drugs, routes of administration, bioavailability, and biodistribution, excretion.

Pharmacogenomics/genetics
Genetic basis for disease and individual differences in metabolizing enzymes

Pharmacology
Pharmacodynamics, mechanisms of therapeutic and adverse drug actions and interactions

V Course-Level Objectives and Outcomes

The overarching objective for the course is to introduce the student to basic principles underlying the actions of medicinal substances in the human body. More particularly, this course aims to guide students in gaining foundational understandings of the chemical/biochemical logic underlying the molecular design and consequent actions and biohandling of medicinal substances in human patients, which together with corresponding theoretical frameworks encompasses the molecular-level aspects of pharmacology and biopharmaceutics. The molecular structures and corresponding physical and functional characteristics of the medicinal substances (pharmaco/therapeutic agents, or in the vernacular, “drugs”) and also of the biological substrates (enzymes, receptors, and other molecular-level drug targets; binding and transport proteins; drug-metabolizing enzymes) will be considered, focusing on relationships (“correlates”) between molecular structure and (1) biopharmaceutical properties, including routes of administration, bioavailability, and biodistribution; (2) target-level pharmacological actions and off-target-mediated side-effects; (3) biotransformation (“drug metabolism”), and (4) excretion.
Evaluation will largely be based on assessing your understanding of concepts and principles, and your ability to apply this understanding in intelligent and reasonable ways, including higher-order abilities: analysis and evaluation. The content of this course varies in nature, ranging from conceptual to applied mathematical; the expectations and corresponding nature of the assessments will vary accordingly.

**Overall Course-Level Objectives and Competencies:** Upon completion of this course, besides progressing on the general curricular outcome (CAPE 2013) noted in section IV above, students completing this course should be equipped with knowledge and abilities as follows.

- Describe selected structural and functional characteristics of some of the important types of molecular targets of drug action: (1) enzymes and (2) selected receptor types.
- Describe structural and functional characteristics of important macromolecular assemblages and tissue microstructures as affects drug absorption, distribution, biotransformation, and excretion: (1) cellular and intracellular lipid membranes; (2) transporters; (3) enzymes catalyzing biotransformation.
- Given a molecular structure of a drug molecule, demonstrate rudimentary abilities to rationalize and make reasonable structure-based predictions concerning …
  - aqueous solubility and relative hydrophilicity/lipophilicity;
  - useful routes of administration;
  - ease of access to various tissues.
- With respect to acidic and basic properties of structural moieties incorporated within drug molecules and macromolecular drug targets, demonstrate a knowledge of approximate pKₐs for common ionizable structural moieties, and the corresponding molecular species distribution as a function of pH (i.e., approximate proportions of ionized, un-ionized, and–if applicable–amphoteric forms).
- Given a molecular structure of a drug molecule, describe its stereochemical attributes, and potential pharmacological and biopharmaceutical significances thereof.
- As pertains to molecular recognition (including drug-target interactions), describe the significances of conformation changes involved in binding events, the types and strengths of intermolecular forces that occur between a ligand (drug or other) and its macromolecular binding site, the enthalpic and entropic gains and penalties involved in molecular recognition and the relationship of these to binding affinity, rate constants associated with binding interactions and significances thereof with respect to molecular pharmacodynamics, and the basis of hydrophobic interactions.
- Define and differentiate affinity and intrinsic activity (molecular-level efficacy), describe how these concepts relate to the associated concepts of agonism, antagonism, partial agonism, and inverse agonism, and further describe in general how these concepts are related to the patient-level actions (observed clinical pharmacology) of drugs.
- Define the concept of pharmacological selectivity, describe the molecular bases for selectivity from both the drug and target aspects, and describe the general clinical significance of selectivity.
- Define the concept of equilibrium, and how equilibria are affected by Gibbs free energy changes for biochemical transformations.
- Define the basic mathematical terms commonly encountered in descriptions of the kinetic characteristics of enzymes, and their meaning from a biochemical, drug action, and drug biotransformation (drug metabolism) perspective.
Demonstrate an understanding of the distinct types of enzyme inhibitors, and the consequences of these differences in terms of the biochemical pharmacology of drugs that modulate enzymes. Define allosteric cooperativity, and describe the significance of such cooperativity to molecular cellular physiology and the biochemical pharmacology of drug action. Provide a list of drug-associated and tissue-associated factors affecting access by drugs to particular organs of the body, including access to the body (i.e., bioavailability). Describe the general physiological purposes of drug biotransformation (“drug metabolism”), and define and differentiate Phase I and Phase II biotransformation, including the nature of the chemical transformations involved with each. Given a molecular structure of a drug molecule, be able to predict likely routes of biotransformation. Describe, in general terms, the significance of drug biotransformation with respect to pharmacokinetics. List major sources of individual variation and drug-drug interactions that may arise as a result of effects on drug biotransformation, and outline the practical significance of each of these sources.

VI Course Topics

See a listing in the Course Schedule (Section X below).

VII Instructional Methods and Activities

Instructional methods will include: traditional and technology-based content presentations, generally aiming to be highly interactive in nature, and various formative exercises designed to invoke active learning, including outside homework/study assignments that in most cases will not be collected for a grade.

VIII Evaluation and Grade Assignment

| Test 1 | 50 points | (Hill) |
| Test 2 | 50 points | (Hill/H) |
| Test 3 | 50 points | (El Sayed/Hill) |
| Quizzes/active learning | 50 points | (Hill, El Sayed, Jois) |
| Final Exam | 50 points | (Jois ~80%, Hill/El Sayed ~20%) |
| Total | 250 points |

According to university guidelines (as given in The University of Louisiana at Monroe 2017-2018 Graduate Catalog, wherein the Pharm.D. program is currently listed as a professional degree program), grades should reflect the following:

A - EXCELLENT
B - AVERAGE
C - BELOW AVERAGE
D – POOR
F - FAIL

Grading will be straight-scale:

>89.5% = A
79.5%–89.4% = B
69.5%–79.4% = C
59.5%–69.4% = D
<59.5% = F
Mid-term grades will be posted online for students to view via Banner. Mid-term grades indicate a student’s status at mid-semester only.

IX Class Policies and Procedures

At a minimum, all policies stated in the current ULM Student Policy Manual & Organizational Handbook will be followed (see http://www.ulm.edu/studentpolicy/). Additional class policies include:

- **Preparation for class.** For each class period, you will typically be held responsible for varying degrees of prior preparation, involving: (1) viewing any e-presentations as may be assigned in advance; (2) completing one or more advance readings if assigned as preparation for a particular class; (3) answering or attempting to answer any assigned pre-class study questions. Pre-class and post-class study assignments will be constrained to a modest length, and will serve to illustrate and elaborate key concepts, emphasizing application, in accord with specific content objectives provided. **You should plan for a minimum of 7-8 hours per week of outside study time in support of your learning in this class; some students may find that they need more time than this in some topic areas, depending in part on strength of pertinent prior academic preparation.** Assignments and any needed materials (notes, handouts, study questions) will typically be posted on Moodle at least several days in advance. You should, however, habitually check the Moodle page the evening before class for any possible corrections or clarifications.

- **Portable Computers and Clickers.** Exercises conducted on portable computers (“laptops” or equivalent) may occur on any given day to generate grades for certain activities (such as a quiz). Therefore, please bring your computer to every class period; if you do not have it, you may not be afforded an alternative means to provide responses (i.e., you may earn a ‘0’ on the graded activity).

- **Exams.** Four examinations will be administered during the course. The three hourly exams (Tests 1, 2, & 3) will emphasize topics as mentioned in the class schedule, but beginning with Test 2, will have some degree of comprehensive coverage, the nature of which will be communicated to you soon enough for any needed review. The final exam will include a significant comprehensive component.

- **Dropped Test Questions.** When, due to faculty concerns regarding a question appearing on an administered examination, or as the result of a student-generated appeal that is judged to be valid and of merit by course faculty, the question will generally be omitted from the grade calculation for all students—the total points for the course will be reduced, without altering the percentages required to earn a particular course grade given above in section VIII. Course faculty reserve the right to deviate from this general guideline, however, according to their professional judgement as pertains to the specifics of the issue with the question deemed to be flawed.

- Exams will be conducted using ExamSoft/Examplify on your portable computer. All students will be required to download the testing file prior to the time of the scheduled exam. In the
event that a student cannot take an exam that has already been downloaded on the scheduled date and at the scheduled time, the student must reverse-download the exam, without having opened it, at earliest pragmatically possible opportunity (i.e., you are with your computer and an internet connection is available to you). Seating charts will be used for examinations, and screen privacy covers must be used during exams and during any other activity during which computers are used as part of a grade-generating exercise. For examinations and some quizzes, official scratch paper will be issued, and all students will be required to print and sign their name on the scratch paper and return it to the proctor, even if otherwise unused, prior to leaving the room. For exams and some quizzes, when turning in this sheet, students will also be required to show a proctor that the exam/quiz has been irreversibly closed, and also uploaded, before leaving the room; in the event of a power outage or loss of Wi-Fi connection, students are required to upload the exam/quiz at the earliest possible reconnection time.

- During exams as well as during any grade-generating activities, the use of programmable calculators and electronic devices capable of storing, receiving or transmitting data are prohibited unless expressly authorized by the course instructor. Such devices must be turned off and placed in a location that is not readily accessible to you during the activity.

- Early Intervention and Remediation Policies. The School of Pharmacy Early Intervention and Remediation Policies, as revised August 2016, will be followed. In addition, any student earning a non-passing grade of “D” or “F” on an exam, and whose average (exams only, beginning after Test 1) is below 70.0%, will be required to meet with the course coordinator, at earliest mutually possible opportunity, but at latest within one week of when test scores are posted, to (1) review the test, if not already done as part of a group debriefing session (documented attendance); and (2) establish a mandatory academic performance improvement plan that will be undertaken by the student prior to the subsequent exam, which will include adherence to the Early Intervention Policy, but which may also include tutoring sessions offered by course faculty and/or other documented assistance (such as student tutoring and mentoring—Rho Chi tutoring, e.g.) in content areas identified as weaknesses as per a student’s exam performance(s), and continuing until such a time as the student secures a solid passing average in the course.
IX  Class Policies and Procedures, contd.

A.  Textbook(s) and Materials:

In addition to the required textbooks listed below, various materials will be provided online via the Moodle portal.


Purchase of the Examsoft Examplify® software is also required.

B.  Attendance:

The [ULM attendance policy](#) will be followed.
IX Class Policies and Procedures, contd.

C. Make-up Policy:

Exams, Graded In-class Exercises, and Assignment Deadlines: The university requires that you are given a fair opportunity to complete missed grade opportunities when circumstances warrant. For examinations (and in most other instances) such circumstances must be compelling, including: (1) you are sick enough to require medical attention and be confined to bed; (2) there is a death in the immediate family (see ULM policy definition); (3) there is a personal or family emergency. If the absence is predictable (e.g., a scheduled surgery), a prior approval must be obtained from course coordinator (as the Instructor-of-Record). In most instances, physical proof will be needed or you will not be provided the opportunity to make up the grade. If you miss an examination or assignment deadline, and intend to request a makeup under the above policy, The coordinator MUST be informed BY PHONE, by E-mail*, OR IN-PERSON no later than the day following the missed event, unless circumstances are clearly prohibitive. Excuses will be validated. If a makeup is allowed under these guidelines, it will be arranged on an individual basis. *If you choose E-mail, please assure that the course coordinator/co-coordinator acknowledges receipt within 24 hours, else send again.

D. Academic Integrity:

Faculty and students must observe the ULM published policy on Academic Dishonesty (see the ULM Graduate Catalog, ULM Student Policy Manual (http://www.ulm.edu/studentpolicy)). All professional students will adhere to the standards set forth in the ULM College of Pharmacy’s Code of Conduct http://www.ulm.edu/pharmacy/documents/ospa/codeofconduct040617.pdf These policies will be strictly enforced—notably, CHEATING WILL NOT BE TOLERATED, AS ANY ACADEMIC ADVANCEMENT THEREBY GAINED IS CONSIDERED A POTENTIAL THREAT TO THE PUBLIC. Any instances of academic dishonesty will be dealt with vigorously and doggedly, and to the fullest extent possible.

E. Course Evaluation Policy:

At a minimum, students are expected to complete the on-line course evaluation.
IX  Class Policies and Procedures, contd.

F.  Student Services:

Information concerning student services in the College of Pharmacy can be found in the College of Pharmacy Student Handbook. In particular, students should pay special attention to the College’s technical standards and policies concerning students with special needs (http://www.ulm.edu/pharmacy/documents/ospa/specialneeds.pdf). ULM student services, such as the Student Success Center (http://www.ulm.edu/studentsuccess/), Counseling Center (http://ulm.edu/counselingcenter/), and Student Health Services, is available at the following Student Services web site: http://ulm.edu/studentaffairs/.

If you are having problems with emotional, social, and/or behavioral issues please call any of the mental health clinics on the ULM campus to make an appointment. All services are free to ULM students, staff, and faculty, and are strictly confidential.

✓ COP Office of Student and Professional Affairs:  342-3800
✓ ULM Counseling Center:  342-5220
✓ Marriage and Family Therapy Clinic: 342-5678

The University of Louisiana at Monroe strives to serve students with special needs through compliance with Sections 504 of the Rehabilitation Act of 1973 and the Americans with Disabilities Act. These laws mandate that postsecondary institutions provide equal access to programs and services for students with disabilities without creating changes to the essential elements of the curriculum. While students with special needs are expected to meet our institution's academic standards, they are given the opportunity to fulfill learner outcomes in alternative ways. Examples of accommodations may include, but are not limited to, testing accommodations (oral testing, extended time for exams), interpreters, relocation of inaccessible classrooms, permission to audiotape lectures, note-taking assistance, and course substitutions.

Title IX of the Education Amendments of 1972 prohibits sex discrimination against any participant in an educational program or activity that receives federal funds, including federal loans and grants. Furthermore, Title IX prohibits sex discrimination to include sexual misconduct, sexual violence, sexual harassment and retaliation. If you encounter unlawful sexual harassment or gender-based discrimination, please contact Student Services at 318-342-5230, or to file a complaint, visit www.ulm.edu/titleix.

G.  Emergency Procedures:

Please review the emergency escape plan in the classrooms and hallways of the Bienville building. In the event we must evacuate the building, move quickly and in an orderly fashion to the appropriate stairwell and exit the building. The meeting place for this class will be the far end of the north parking lot between Bienville and Broadmoor Blvd. Under no circumstances is the elevator to be used for emergency evacuation. Any student needing assistance should notify the professor immediately. For emergencies, to contact University Police, call 1-911 from landlines and 342-5350 from cell phones.
## X. Course Schedule

*(Note: The instructor/faculty reserves the right to adjust the schedule if needed.)*

Bienville Bldg., **Room 340/350; M&W 8:00-9:50 a.m**

<table>
<thead>
<tr>
<th>Day, Date</th>
<th>Topic</th>
<th>Hrs</th>
<th>Faculty Contrib.</th>
<th>Pts/Questions Due date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASYN</td>
<td>Drug discovery and molecular therapeutics invention/creation (focus on small molecules/non-biologics, with illustrative examples, and embedded introduction to selected pharmacology and biopharmaceutics concepts)</td>
<td>2</td>
<td>Hill Recorded lecture</td>
<td></td>
</tr>
<tr>
<td>ASYN</td>
<td>Drug creation, contd. Lead compound generation</td>
<td>2</td>
<td>Hill Recorded lecture</td>
<td></td>
</tr>
<tr>
<td>1 08/17/20 M</td>
<td>Drug creation</td>
<td>2</td>
<td>Hill</td>
<td></td>
</tr>
<tr>
<td>2 08/19/20 W</td>
<td>Molecular structure as relates to acidity, basicity, and solution ionization of organic molecules; review of ionic equilibria of biochemically and medicinally common structural moieties</td>
<td>2</td>
<td>Hill</td>
<td></td>
</tr>
<tr>
<td>3 08/24/20 M</td>
<td>Solution ionization—drug action and disposition aspects</td>
<td>2</td>
<td>Hill</td>
<td></td>
</tr>
<tr>
<td>4 08/26/20 W</td>
<td><strong>Class Exercise 1</strong>* Active learning Stereochemistry as pertains to drug action and biohandling</td>
<td>2</td>
<td>Hill</td>
<td>10</td>
</tr>
<tr>
<td>08/31/20 M</td>
<td>Conformational equilibria (of drugs and drug targets) as pertains to drug action Molecular recognition (ligand-target interactions)</td>
<td>2</td>
<td>Hill</td>
<td></td>
</tr>
<tr>
<td>5 09/2/20 W</td>
<td>Molecular recognition (ligand-target interactions), contd Class Exercise 2*** Active learning</td>
<td>2</td>
<td>Hill</td>
<td>10</td>
</tr>
<tr>
<td>09/07/20 M</td>
<td>HOLIDAY</td>
<td></td>
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</tr>
<tr>
<td>6 09/9/20 W</td>
<td>Response vs. concentration relationships Review for the test</td>
<td>2</td>
<td>Hill</td>
<td></td>
</tr>
<tr>
<td>7 09/14/20 M</td>
<td><strong>Test 1</strong> (Topics covered from 08/17 to 09/09)</td>
<td>2</td>
<td>Jois/Hill</td>
<td>Questions due</td>
</tr>
<tr>
<td></td>
<td>Date</td>
<td>Day</td>
<td>Topic</td>
<td>Instructor</td>
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<tr>
<td>8</td>
<td>09/16/20</td>
<td>W</td>
<td>Amino acids and Proteins: Brief review/overview of their various biological functions as pertains to drug targets and drug action</td>
<td>Hill</td>
</tr>
<tr>
<td>9</td>
<td>09/21/20</td>
<td>M</td>
<td>Multimeric protein assemblies; allosteric cooperativity and regulation</td>
<td>Hill</td>
</tr>
<tr>
<td>10</td>
<td>09/23/20</td>
<td>W</td>
<td>Enzyme Kinetics</td>
<td>Hill</td>
</tr>
<tr>
<td>11</td>
<td>09/28/20</td>
<td>M</td>
<td>Enzyme kinetics</td>
<td>Hill</td>
</tr>
<tr>
<td>12</td>
<td>9/30/20</td>
<td>W</td>
<td>Physicochemical properties: molecular determinants of membrane transport (passive diffusion emphasis; see transporters coverage below) and other biopharmaceutics-related attributes</td>
<td>Hill</td>
</tr>
<tr>
<td>13</td>
<td>10/05/20</td>
<td>M</td>
<td>Physicochemical properties: molecular determinants of membrane transport</td>
<td>Hill</td>
</tr>
<tr>
<td>14</td>
<td>10/07/20</td>
<td>W</td>
<td><strong>Test 2 (Topics covered from 09/16 to 9/30)</strong></td>
<td>Jois/Hill</td>
</tr>
<tr>
<td>15</td>
<td>10/12/20</td>
<td>M</td>
<td>Biotransformation of xenobiotics (including drugs)</td>
<td>El Sayed</td>
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<td></td>
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<td>Phase I metabolism, including some enzymology</td>
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<td></td>
<td>Phase II metabolism, including some enzymology Biotransformation (continued)</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>10/14/20</td>
<td>W</td>
<td>Biotransformation of xenobiotics (including drugs)</td>
<td>El Sayed</td>
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<tr>
<td></td>
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<td>Phase I metabolism, including some enzymology</td>
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<td></td>
<td></td>
<td></td>
<td>Phase II metabolism, including some enzymology Biotransformation (continued)</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>10/19/20</td>
<td>M</td>
<td><strong>Quiz 1</strong></td>
<td>El Sayed</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Biotransformation (continued)</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>10/21/20</td>
<td>W</td>
<td>Biotransformation (continued)</td>
<td>El Sayed</td>
</tr>
<tr>
<td>19</td>
<td>10/26/20</td>
<td>M</td>
<td>Review of biotransformation</td>
<td>El Sayed</td>
</tr>
<tr>
<td>Week</td>
<td>Date</td>
<td>Day</td>
<td>Topic</td>
<td>Notes</td>
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<tr>
<td>20</td>
<td>10/28/20</td>
<td>W</td>
<td>Test 3 (Topics covered from 10/05 to 10/26)</td>
<td>2 Jois/El Sayed</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Questions due by 10/26/20 50 pt</td>
</tr>
<tr>
<td></td>
<td>ASYN</td>
<td></td>
<td>Enzyme based drug design</td>
<td>2 Jois recorded lecture</td>
</tr>
<tr>
<td>21</td>
<td>11/02/20</td>
<td>M</td>
<td>Enzyme-targeted drug design.</td>
<td>2 Jois</td>
</tr>
<tr>
<td>22</td>
<td>11/04/20</td>
<td>W</td>
<td>Enzyme-targeted drug design with examples</td>
<td>2 Jois</td>
</tr>
<tr>
<td>23</td>
<td>11/09/20</td>
<td>M</td>
<td>Enzyme-targeted drug design with examples</td>
<td>2 Jois 10</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Active learning</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>11/11/20</td>
<td>W</td>
<td>Quiz 2 Enzyme-targeted drug design with examples. Active learning</td>
<td>2 Jois 10</td>
</tr>
<tr>
<td></td>
<td>TBA</td>
<td></td>
<td>Final Examination, 9-11 a.m. (covers topics 11/02–11/11 + comprehensive)</td>
<td>Jois/Hill/El Sayed Questions due by 11/13/20</td>
</tr>
</tbody>
</table>

**Notes:**
- ASYN –asynchronous.
- **practice tests will be posted on Examsoft before each test.

**NOTE:** TEST DATES REMAIN SUBJECT TO CHANGE UNTIL FINALIZED BY THE BEGINNING-OF-THE-SEMESTER REVIEW PROCESS, AND SUCH CHANGES, IF ANY, WOULD REQUIRE FURTHER ADJUSTMENTS TO THE OVERALL COURSE SCHEDULE