

FUNDAMENTALS OF TOXICOLOGY – BIOL. SCI. 432-01; 432-02 (Lab)
Spring, 2012: Tues, Thurs, 8:25 – 9:40 am, BS 335; Lab, Thurs, 9:50 am– 12:20 pm, BS 236

Instructor: Dr. Michael Chen, Office Location: BS 235; email: mchen@calstatela.edu,
 Office Hours are Tues, Thurs, 12:45-3:00 pm.

Course Objective: The chief objective of this course is to introduce you to the field of toxicology. The course will help you develop a strong foundation in some of the general principles of toxicology. Each of you will understand factors that influence the interpretation of toxicological data from microorganisms, animals, plants and humans, and how this information relates to human and ecological risk assessment. You will also understand some of the biochemical mechanisms involved in cellular and organ specific toxic effects caused by a variety of chemical compounds including drugs and environmental toxicants.

Course Pre-requisites: BiolSci 380: Cell Biology; Chem 301c: Organic Chemistry;
 Chem 302b (Organic Chem Lab).

Textbook: Klaassen, C.D., Watkins, III, J.B. *Casarett and Doull's Essentials of Toxicology*. McGraw-Hill, 2010, ISBN 978-0-07-162240-0.

Lecture Topics and Relevant Chapters from Klaassen and Watkins

Lecture Portion of Course

Lectures can be found on my faculty web-page at: <http://www.calstatela.edu/faculty/mchen/>

As the Instructor, I reserve the right to make changes in the following schedule or final course evaluation in assigning final grades. Topics and Student Learning Outcomes/Objectives:

Week 1 - April 3⁽²⁾, 5⁽²⁾

General Introduction / Dose-Response Relationships: An assessment of dose response data for both non-carcinogenic and carcinogenic compounds. An analysis of acute, sub-chronic and chronic tests and the toxicological parameters that are obtained from these tests. Agonist, antagonist, inducer, potency, efficacy, LD50, ED50, and therapeutic index are among just some of the terms/concepts that will be introduced (Chapters 2, 7, 8, 9).

Week 2 - April 10⁽²⁾, 12⁽²⁾

Risk Assessment: The major components of a human and ecological risk assessment will be presented. (Chapters 4, 29)/ **Disposition of Chemicals Including Absorption, Distribution and Excretion:** Specific examples of how different chemicals are absorbed into the body, distributed within the body, and excreted from the body will be considered. The importance of chemical structure in these processes will be examined (Chapters 5).

Week 3 - April 17⁽²⁾, 19⁽²⁾

Phase I Metabolism: Students will examine various phase I reactions including oxidation, reduction and hydrolysis. Students will be exposed to an in-depth consideration of cytochrome P450 enzymes including structure and function of the enzyme system (Chapter 6). **Worksheet Assignment 1 Due (Chloroform (CHCl₃)).**

Week 4 – April 24⁽²⁾, 26

Phase II Metabolism: Students will examine various phase II reactions. The integration of phase I with phase II metabolism will be considered. (Chapter 6)/ **Factors Affecting Metabolism and Disposition:**

The influence of factors such as species, gender, genotype, nutritional status, and site of absorption on toxicity will be considered.

Midterm 1 is tentatively scheduled on Thursday, April 26.

Week 5 - May 1⁽²⁾, 3⁽²⁾

Mechanisms of Toxicity: Specific examples of toxic mechanisms including DNA adducts, nucleotide base transversions, reactive oxygen species and lipid peroxidation will be considered (Chapters 3). Specific mechanisms of toxicant delivery, reactions of the ultimate toxicant, development of toxicity, and cellular/molecular repair mechanisms will be presented in detail. **Worksheet Assignment 2 Due (Disposition).**

Week 6 - May 8⁽²⁾, 10⁽²⁾

Mechanisms of Toxicity: Continued from Week 5. **Worksheet Assignment 3 Due (Metabolism).**

Week 7 – May 15⁽²⁾, 17

Toxicology of Metals: Students will learn how mercury, lead, selenium, cadmium, and other metals produce toxic effects. An analysis of how animals and humans are exposed to these metals will also take place (Chapters 14, 16, 23). **Midterm 2 is tentatively scheduled on Thursday, May, 17.**

Week 8 - May 22⁽²⁾, 24⁽²⁾

Toxicology of Pesticides: Students will be presented with mechanisms of organochlorine, organophosphate, and carbamate pesticides. The molecular basis of action will be considered. (Chapter 22). **Worksheet Assignment 4 (Chromium) Due.**

Week 9 - May 29⁽²⁾ 31⁽²⁾

Polycyclic Aromatic Hydrocarbons: Students will examine the sources, structure, metabolism, and mechanism of toxic action for these important environmental carcinogens. The importance of stereoisomerism and structure-activity relationships will be stressed/ **PCBs, PBBs and Dioxins**: Students will examine the sources, structure, metabolism, and mechanism of toxic action for these compounds. Structure-activity relationships will be stressed **Worksheet Assignment 5 Due (CH₃Hg).**

Week 10 - June 5⁽²⁾, June 7⁽²⁾

Endocrine Disrupting Compounds: Students will examine the sources, structure, metabolism, and mechanism of toxic action for these important environmental compounds that are affecting reproduction in animal species such as fish. Students will also examine how these compounds may affect humans (Chapters 20, 21). **Toxic Effects of Selected Natural Venoms and Poisons of Animals and Plants** (Chapters 26, 27).

The **final exam** for this class is scheduled for **Tuesday, 6/12/12, at 8:00 – 10:30 am.** The final exam will be cumulative in the sense that general concepts covered during the first half of the course will be necessary for the understanding of material covered during the second half of the course. A verifiable excuse must be provided for any missed exam and the instructor reserves the right not to give make-up exams.

Course Requirements and Grading:

Assignment	Points
Midterm Exams (2)	150 (75 points each)
Final Exam	85
Risk Assessment Document	100
Worksheets (5)	100 (average 20 points each)
[Attendance	32 (2 points per lecture indicated above)]
TOTAL POINTS	~ 467

Criteria that will be used to assign grades include the level of knowledge of the toxicological concepts presented in lecture; the performance on worksheet assignments related to the use of information from computer databases; the demonstration of thorough research on and understanding of the risk assessment topic; the demonstration of logical and critical thought; the clarity of writing; correct spelling, grammar, and sentence structure; ability to give a good presentation of the scientific literature.

As the instructor, I reserve the right to give some or all of the following grades: A, A-, B+, B, B-, C+, C, D and F. Final grades will be based on percentage: 91-100%, "A" range; 81-90%, "B" range; 71-80%, "C" range; 61-70%, "D" range; and < 60% will be an "F".

Worksheet Assignments

To help you cement the concepts in your mind as well as provide some real-life examples, there will be 5 worksheet assignments that will be completed throughout the quarter. These can also be found on my faculty webpage at <http://www.calstatela.edu/faculty/mchen/>. These must be turned in *sometime* during the stipulated week, definitely by the end of class on Thursday, but not on Fridays. On Fridays of that week and thereafter, they will be considered late and **3 points** will be deducted for every weekday they are late. **Except under dire circumstances, I will not accept worksheet assignments electronically. Only hardcopies.**

Risk Assessment Document

Students will work in pairs. Then, in cooperation with each other, each student will choose a chemical in which s(he) is interested. Each person should then research his/her particular chemical to the point that you are familiar with its *interactive* ability with the chemical your partner chose. For example, suppose Person A chose alcohol and Person B chose valium. Each person will then research and answer the questions I ask about that particular chemical. Then, the 2 partners will characterize their interactive potential and mechanism(s). The 2 partners should corroborate early in choosing their chemicals to establish that there is evidence that these 2 chemicals do indeed interact at all. **So, one very important criterion for choosing your chemical is that there must be literature evidence that it interacts in some way with your partner's chemical.**

Then, characterize in-depth, each chemical separately according to the criteria provided at the end of the syllabus. The completed document can be about 20-30 double spaced typed **text** pages, not including references, figures, and tables. The document **must include additional** graphs and/or tables.

The completed Risk Assessment Document **must** be given to me, in its entirety, in person on Thursday of Week 10. This means that the entire document must be handed in – not only 1 partner's part 1 week (or day) and another partner's part on another day. Documents turned in after Thursday of Week 10 will be considered late. I will deduct 10 (10 %) points for every weekday it is late. **I do not accept RA documents electronically – You must hand in a hardcopy.**

However, if the Risk Assessment document is turned in to me Week 9, then you will get 10 (10 %) extra credit points.

LAB SCHEDULE

Week 1	Introduction to Computer Databases Related to Toxicology – Students will acquaint themselves with the various toxicology-related websites they will need to complete their Risk Assessment projects.
Week 2	Risk Assessment and Introduction to Computer Databases Related to Toxicology/Worksheet Assignment 1 – Chloroform.
Week 3	Selection of Risk Assessment Projects/Worksheet Assignment 2 - Disposition.
Week 4	Work on Risk Assessment Projects.

Week 5	Use of Computer Databases/Library Resources / Worksheet Assignment 3 - Metabolism.
Week 6	Work on Risk Assessment Projects using Computer Databases/Library Resources.
Week 7	Work on Risk Assessment Projects using Computer Databases/ Library Resources/Worksheet Assignment 4 - Chromium.
Week 8	Work on Risk Assessment Projects using Computer Databases/Library Resources/ Worksheet Assignment 5 – Methyl Mercury.
Week 9	Turn in Risk Assessment Documents for 12 extra credit points
Week 10	Turn in Risk Assessment Documents.

ADA: Reasonable accommodation will be provided to any student who is registered with the Office of Students with Disabilities and requests needed accommodation.

Student Learning Outcomes:

DEPARTMENT OF BIOLOGICAL SCIENCES UNDERGRADUATE STUDENT LEARNING OUTCOMES

M/S/P by Assessment Committee: February 11, 2008

1. The student will acquire the following attitudes:
 - 1.1. Learning about both living micro and macro systems is relevant and essential for understanding life.
 - 1.2. All areas of science are integrated and interconnected.
 - 1.3. Scientific ethical conduct and ethical implications of scientific issues in society are important.
2. The student will be able to demonstrate that he/she is skilled at:
 - 2.1. Applying the processes and methods of scientific inquiry, including the search and retrieval of scientific information, the formulation of scientific hypotheses, the design and conduct of experiments, and the analysis and interpretation of data;
 - 2.2. Understanding and critically evaluating the scientific work of others;
 - 2.3. Communicating scientific information effectively using oral presentations and written reports;
 - 2.4. Performing laboratory techniques that are appropriate to the major, with an understanding of the principles of laboratory safety;
 - 2.5. Working collaboratively on group projects.
3. The biology student will be able to demonstrate knowledge of the following:
 - 3.1. Molecular and cellular structure and function;
 - 3.2. Basic principles of anatomy, physiology, and development;
 - 3.3. Taxonomy and phylogenetic and evolutionary relationships of major groups of organisms;
 - 3.4. Ecological interactions among organisms and their relationships with their environments;
 - 3.5. Careers and professions available in the biological sciences.
4. The microbiology student will be able to demonstrate knowledge of the following:
 - 4.1. Microbiological techniques and handling of biohazardous materials;
 - 4.2. Microbial diversity, evolution of microorganisms and transmissible agents;
 - 4.3. Microbial physiology and genetics including cellular structure and function;
 - 4.4. Interactions of microorganisms with multicellular organisms and the environment;
 - 4.5. Applications of microbiology and career opportunities in the field.

DEPARTMENT OF BIOLOGICAL SCIENCES GRADUATE STUDENT LEARNING OUTCOMES

M/s/p by Assessment Committee: May 15, 2008.

At the completion of the Masters of Science degree in Biology a graduate student will have acquired:

- The analytical, communication, problem solving, interpersonal, and technical skills that will provide a strong foundation for scientific productivity and progressive career development.
- An in-depth understanding of biological concepts that apply to the student's area of concentration.
- Experience with the peer scientific review process.

The following are specific objectives in the areas of attitudes, skills, and knowledge.

1. The student will acquire the following attitudes:

- 1.1. Scientific research plays a crucial role in the development of policy and decision-making for the benefit of society.
- 1.2. Scientific progress should be based on the unbiased collection, analysis, and interpretation of evidence.
- 1.3. The biological sciences, by their nature, are interdisciplinary.
- 1.4. Understanding science is a life-long learning process.
- 1.5. Scientific ethical conduct and ethical implications of scientific issues in society are important.

2. Upon completion of the Master of Science degree, the student will be able to demonstrate that he/she is skilled at:

- 2.1. Developing a coherent research prospectus.
- 2.2. Carrying out a research project which includes mastery of appropriate techniques and the collection, organization and analysis of data.
- 2.3. Synthesizing the results of their work in a master's thesis.
- 2.4. Understanding and critically evaluating the scientific work of others and discussing new results in the context of what is already known and what should still be done.
- 2.5. Communicating his/her work, as well as that of others, in a seminar and thesis defense.
- 2.6. Developing teaching skills.

3. Upon completion of the Master of Science degree, the student will be able to demonstrate knowledge in:

- 3.1. Scientific concepts, recent developments, and areas for future research efforts in his or her chosen field.
- 3.2. Traditional, modern, and emerging techniques and approaches used to conduct research in his or her chosen field of research.
- 3.3. Practical applications of his or her research field and potential career opportunities.

ACADEMIC HONESTY: Students are expected to abide by the University's Academic Honesty Policy, which can be found at http://www.calstatela.edu/univ/stuaffrs/Academic_Honesty.htm.

Students who violate this policy will be subject to disciplinary action, and may receive a failing grade in the course for a single violation.

BioSci 432: Fundamentals of Toxicology
RISK ASSESSMENT DOCUMENT

Four Parts to the Risk Assessment Document

1. Hazard Assessment overview of the chemical being researched. This must be done for each of the 2 chemicals separately.
2. Dose-response assessment for each chemical. This must be done for each of the 2 chemicals separately.
3. Exposure assessment for each chemical. Here, you will set up one real-world scenario you may find interesting. For example, what are the effects of exposure of a tiny town lying downstream of a plant dumping high levels of the chemical into their runoff? Or, what are the effects of someone taking a low concentration of a pain reliever, but has also been feeding a cocaine addiction? Or, what are the effects of medium exposure of some pollutant to, say, young children? Elderly? This must be done for each of the 2 chemicals separately.
4. For each of your chemicals, *calculate* the risks. This is the corroborative part between the 2 partners. What are the risks of the interactions of the two chemicals. Additivity? Synergistic? Antagonism? Cytochrome P-450?

RISK ASSESSMENT – CRITERIA TO BE COMPLETED IN YOUR DOCUMENT

Be sure you use each of these as **Headings** and **Subheadings** in your document.

Hazard Identification: (Heading)

The following are to be Subheadings:

1. Presentation of the innate toxic effects of the compound.
2. Presentation of appropriate human and/or animal studies.
3. Presentation of cellular level studies for cytotoxicity, mutations, and DNA damage (if appropriate?).
4. Distinguish appropriately among acute, subchronic, and chronic effects.
5. Presentation of appropriate information related to chemical fate, metabolism of the chemical, and various forms of the chemical.

Dose Response Assessment: (Heading)

The following are to be Subheadings:

1. Distinguish appropriately between non-carcinogenic and carcinogenic effects (if applicable).
2. Presentation of appropriate human and/or animal dose-response studies.
3. Distinguish among acute, subchronic, and chronic dose-response studies.
4. Presentation of the RfD, ADI, or MRL for the appropriate subpopulation(s).
5. Description in sufficient detail how the RfD, ADI, or MRL was/were calculated.
6. Utilization of data related to the appropriate mode of absorption or various modes of absorption.

7. Included the appropriate Cancer Assessment Category (if appropriate).
8. Included the appropriate slope factor or factors, risk levels, or unit risk levels (if appropriate)?

Exposure Assessment: (Heading)

The following are to be Subheadings:

1. Adequate characterization of the exposure setting by selecting realistic scenarios and subpopulations?
2. Adequate identification of the applicable exposure pathways by giving literature values for amounts of the chemical that can be obtained through various exposure pathways
3. Adequate quantification of the exposure levels for the appropriate exposure pathways using the realistic scenarios and subpopulations.
 - a) Show how the calculated Maximum Daily Exposures related to non-carcinogenic chemicals for these subpopulations were calculated.
 - b) Show how the LADD for these subpopulations were calculated.

Risk Characterization: (Heading)

The following is to be Subheading:

1. Integrated the dose and exposure assessments to yield a probability of an adverse health effect for both non-carcinogenic and carcinogenic events.

General:

1. Follow the Heading/Subheading format indicated above?
1. Overall adequacy of coverage of the compound
2. Clarity of presentation: organization?
3. Grammar, page numbers.
4. Literature background throughout the document, liberal use of citations (either [the authors of the study + year of publication] or the URL): In addition to the toxicology databases, I provide, also search MEDLINE > PubMed for peer-reviewed journal articles.