

PubH 6161
Regulatory Toxicology
Spring 2016

Credits: 2
Meeting Days: Thursday
Meeting Time: 5:00 P.M. - 7:00 P.M.
Meeting Place: 1250 Mayo

Instructor: Silvia Balbo, PhD, Assistant Professor
Division of Environmental Health Sciences
Masonic Cancer Center
University of Minnesota

Office Phone: 612-624-4240
E-mail: balbo006@umn.edu

Office address: CCRB, 2231 6th St. SE – Room 2-145
Minneapolis, MN 55455

Office Hours: e-mail to make an appointment with instructor

I. Course Description

How do we define what is safe? How do regulatory agencies decide to include red meat in the list of carcinogens to humans, how do we know what is a reasonable level of Radon in our basement, how do we define what levels of contaminants in the water are considered to be acceptable? Using active learning techniques based on case studies and group discussions and presentations, this course will focus on understanding the regulatory framework that helps us evaluate the safety of chemicals and guides their use and handling in the context of both ecotoxicology and human toxicology. The tools used for the practical evaluation of the principles for protection of the environment and of its population will be examined. The course will include an overview of the methods used to evaluate risk and produce safety guidelines, including laboratory testing, epidemiological studies and evaluation of the literature and of the online resources available to gather this information.

II. Course Prerequisites

Coursework or knowledge of general chemistry, biology, biochemistry and toxicology is highly recommended.

III. Course Goals and Objectives

- Develop awareness of how toxicology is applied in real world regulatory situations;
- Develop knowledge of the complexities and competing interests that are part of the regulatory decision-making;
- Learn how to critically evaluate test data and summarize results to be used for regulatory purposes;
- Learn how to access the relevant information and to connect and interpret data from various sources to produce safety guidelines.

IV. Methods of Instruction and Work Expectations

The method of instruction is a series of lectures on key topics instrumental for the class activities which include active discussion, and in-class exercises. Extra credit projects will not be accepted to improve a grade or as a substitute for assignments. Grading Criteria will be discussed in class. Course grades will be determined by the following:

Class participation and attendance (10 pts)

Students are expected to attend all classes and participate in class discussions and exercises. Students must notify the instructor ahead of time and provide documentation that verifies the reason for the absence from class. Absences are allowed in the case of scheduled activities of an official University student organization, a religious holiday, a verifiable illness, a serious family emergency, jury duty or subpoenas. Students are also expected to prepare for class by completing the reading listed for each class.

Exercises (40 pts)

The purpose of the exercises is to prepare students to complete the Biocompatibility Assessment assignment, described below. There will be four exercises provided either as homework or in class:

- Evaluation of the health impact of a life style factor (10 pts)
- Evaluation of the health impact of a pesticide (10 pts)
- Evaluation of the health impact of a naturally occurring exposure (10 pts)
- Evaluation of the health impact of a natural product present in a food supplement (10 pts)

Final Assessment (50 pts)

The students will complete their work with a safety assessment on an exposure of choice. This document will include the compilation and synthesis of information on the exposure levels, the toxicity information on mechanistic studies and epidemiologic studies focusing on the effects on health of the exposure and some conclusion on safety guidelines developed in light of the information collected. The purpose of the Assessment is to document the acquisition of knowledge on the process that is followed to gather information on the safety of exposure and to produce recommendations for the population. Students will choose a topic of interest at the beginning of the class.

Grading of the exercises and Assessment will be based on inclusion of key elements and the application of principles that will be presented in the class.

V. Course Text and Readings

Reading material will be made available throughout the class and it will be predominantly based on peer-reviewed articles from scientific journals.

The following toxicology resource is available at the Biomedical Library if you do not have a background in toxicology or if you need a review.

Principles and Practice of Toxicology in Public Health by Ira S. Richards. This provides an introduction to toxicology. Review chapters 1 – 11 and 18 – 24.

Basic Toxicology: Fundamentals, Target Organs, and Risk Assessment by Frank C. Lu. This provides an introduction to toxicology. Review chapters 1 – 9 and 22.

Casarett and Doull's Toxicology. The Basic Science of Poisons by Curtis D. Klaasen. This is a useful reference for in depth descriptions of toxicology concepts. This reference is available online through the University of Minnesota Biomedical Library: <http://www.knovel.com/knovel2/Toc.jsp?BookID=95>

If you need further review of basic concepts in toxicology, or if you need further explanation of some of the concept illustrated in class fell free to contact the instructor (balbo006@umn.edu) to set up additional meeting time to go over doubts and questions.

Useful Web Sites

Regulatory Frameworks

USFDA

<http://www.fda.gov/RegulatoryInformation/Guidances/default.htm>

European Commission

http://ec.europa.eu/consumers/consumers_safety/product_safety_legislation/general_product_safety_directive/index_en.htm

Reach:

http://ec.europa.eu/environment/chemicals/reach/reach_en.htm

echa database:

<http://echa.europa.eu/>

GLP and Quality Assurance

US FDA Good Laboratory Practices Regulation:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=58>

Society of Quality Assurance:

<http://www.sqa.org/>

Animal Welfare and Alternative Test Methods

European Centre for the Validation of Alternative Methods (ECVAM): <http://ecvam.jrc.ec.europa.eu/>

Johns Hopkins Center for Alternatives to Animal Testing (CAAT): <http://caat.jhsph.edu/>

Institute for In Vitro Sciences: <http://www.iivs.org/>

Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC):

<http://www.aaalac.org/>

United States Animal Welfare Act and related information:

http://awic.nal.usda.gov/nal_display/index.php?info_center=3&tax_level=3&tax_subject=182&topic_id=1118&level3_id=6735&level4_id=0&level5_id=0&placement_default=0

IACUC.org: <http://www.iacuc.org/aboutus.htm>

Development and Recognition of Consensus Standards

International Organization for Standardization (ISO):

www.iso.org

Association for the Advancement of Medical Instrumentation (AAMI):
<http://www.aami.org/standards/>

FDA Recognized Consensus Standards:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

Consensus Standards - Guidance for Industry and FDA Staff:
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077295.pdf>

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
<http://www.ich.org>

University of Minnesota Center for Writing provides free writing support for all University of Minnesota students.
<http://writing.umn.edu/>

VI. Course Outline/Weekly Schedule

Thursday, January 21: *Course Introduction.*

Thursday, January 28: *Introduction to general principles of Regulatory toxicology*

Thursday, February 4: Examples of agencies and institutes of reference for regulatory toxicology

Thursday, February 11: REACH

Thursday, February 18: The Echa database

Thursday, February 25: Invited speaker: Kelly P Coleman (Medtronic)
ISO 10993 standards that govern biocompatibility and toxicity testing of medical devices.

Thursday, March 3: *How to evaluate the information deriving from epidemiological studies for regulatory purposes*

Thursday, March 10: *Specific Toxicology tests*

Thursday, March 17: *No class, Spring break*

Thursday, March 24: The Human Toxome project, animal experiments vs *in vitro* testing

Thursday, March 31: *Regulatory toxicology of a lifestyle factor* (student presentation and discussion)

Thursday, April 7: *Regulatory toxicology of a natural occurring compound* (student presentation and discussion)

Thursday, April 14: *Regulatory toxicology of a pesticide* (student presentation and discussion)

Thursday, April 21: *Regulatory toxicology of a natural product present in food supplements* (student presentation and discussion)

Thursday, April 28: *New Directions in regulations on Biomaterials: Nanomaterials, Biologics*

Thursday, May 5: Competing factors in *Regulatory toxicology*

VII. Evaluation and Grading

Grading Criteria: To be discussed in class.

Course Evaluation

Beginning in fall 2008, the SPH will collect student course evaluations electronically using a software system called CoursEval: www.sph.umn.edu/courseval. The system will send email notifications to students when they can access and complete their course evaluations. Students who complete their course evaluations promptly will be able to access their final grades just as soon as the faculty member renders the grade in SPHGrades: www.sph.umn.edu/grades. All students will have access to their final grades through OneStop two weeks after the last day of the semester regardless of whether they completed their course evaluation or not. Student feedback on course content and faculty teaching skills are an important means for improving our work. Please take the time to complete a course evaluation for each of the courses for which you are registered.

Incomplete Contracts

A grade of incomplete "I" shall be assigned at the discretion of the instructor when, due to extraordinary circumstances (e.g., documented illness or hospitalization, death in family, etc.), the student was prevented from completing the work of the course on time. The assignment of an "I" requires that a contract be initiated and completed by the student before the last official day of class, and signed by both the student and instructor. If an incomplete is deemed appropriate by the instructor, the student in consultation with the instructor, will specify the time and manner in which the student will complete course requirements. Extension for completion of the work will not exceed one year (or earlier if designated by the student's college). For more information and to initiate an incomplete contract, students should go to SPHGrades at: www.sph.umn.edu/grades.

University of Minnesota Uniform Grading and Transcript Policy

A link to the policy can be found at onestop.umn.edu.

VIII. Other Course Information and Policies

Grade Option Change (if applicable)

For full-semester courses, students may change their grade option, if applicable, through the second week of the semester. Grade option change deadlines for other terms (i.e. summer and half-semester courses) can be found at onestop.umn.edu.

Course Withdrawal

Students should refer to the Refund and Drop/Add Deadlines for the particular term at onestop.umn.edu for information and deadlines for withdrawing from a course. As a courtesy, students should notify their instructor and, if applicable, advisor of their intent to withdraw.

Students wishing to withdraw from a course after the noted final deadline for a particular term must contact the School of Public Health Office of Admissions and Student Resources at sph-ssc@umn.edu for further information.

Student Conduct Code

The University seeks an environment that promotes academic achievement and integrity, that is protective of

free inquiry, and that serves the educational mission of the University. Similarly, the University seeks a community that is free from violence, threats, and intimidation; that is respectful of the rights, opportunities, and welfare of students, faculty, staff, and guests of the University; and that does not threaten the physical or mental health or safety of members of the University community.

As a student at the University you are expected adhere to Board of Regents Policy: *Student Conduct Code*. To review the Student Conduct Code, please see:

http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf.

Note that the conduct code specifically addresses disruptive classroom conduct, which means "engaging in behavior that substantially or repeatedly interrupts either the instructor's ability to teach or student learning. The classroom extends to any setting where a student is engaged in work toward academic credit or satisfaction of program-based requirements or related activities."

Use of Personal Electronic Devices in the Classroom

Using personal electronic devices in the classroom setting can hinder instruction and learning, not only for the student using the device but also for other students in the class. To this end, the University establishes the right of each faculty member to determine if and how personal electronic devices are allowed to be used in the classroom. For complete information, please reference:

<http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Scholastic Dishonesty

You are expected to do your own academic work and cite sources as necessary. Failing to do so is scholastic dishonesty. Scholastic dishonesty means plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; altering, forging, or misusing a University academic record; or fabricating or falsifying data, research procedures, or data analysis. (Student Conduct Code:

http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf) If it is determined that a student has cheated, he or she may be given an "F" or an "N" for the course, and may face additional sanctions from the University. For additional information, please see:

<http://policy.umn.edu/Policies/Education/Education/INSTRUCTORRESP.html>.

The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: <http://www1.umn.edu/oscai/integrity/student/index.html>. If you have additional questions, please clarify with your instructor for the course. Your instructor can respond to your specific questions regarding what would constitute scholastic dishonesty in the context of a particular class-e.g., whether collaboration on assignments is permitted, requirements and methods for citing sources, if electronic aids are permitted or prohibited during an exam.

9

Makeup Work for Legitimate Absences

Students will not be penalized for absence during the semester due to unavoidable or legitimate circumstances. Such circumstances include verified illness, participation in intercollegiate athletic events, subpoenas, jury duty, military service, bereavement, and religious observances. Such circumstances do not include voting in local, state, or national elections. For complete information, please see:

<http://policy.umn.edu/Policies/Education/Education/MAKEUPWORK.html>.

Appropriate Student Use of Class Notes and Course Materials

Taking notes is a means of recording information but more importantly of personally absorbing and integrating the educational experience. However, broadly disseminating class notes beyond the classroom community or accepting compensation for taking and distributing classroom notes undermines instructor interests in their intellectual work product while not substantially furthering instructor and student interests in effective learning. Such actions violate shared norms and standards of the academic community. For additional information, please see: <http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Sexual Harassment

"Sexual harassment" means unwelcome sexual advances, requests for sexual favors, and/or other verbal or physical conduct of a sexual nature. Such conduct has the purpose or effect of unreasonably interfering with an individual's work or academic performance or creating an intimidating, hostile, or offensive working or academic environment in any University activity or program. Such behavior is not acceptable in the University setting. For additional information, please consult Board of Regents Policy:

<http://regents.umn.edu/sites/default/files/policies/SexHarassment.pdf>

Equity, Diversity, Equal Opportunity, and Affirmative Action

The University will provide equal access to and opportunity in its programs and facilities, without regard to race, color, creed, religion, national origin, gender, age, marital status, disability, public assistance status, veteran status, sexual orientation, gender identity, or gender expression. For more information, please consult Board of Regents Policy: http://regents.umn.edu/sites/default/files/policies/Equity_Diversity_EO_AA.pdf.

Disability Accommodations

The University of Minnesota is committed to providing equitable access to learning opportunities for all students. Disability Services (DS) is the campus office that collaborates with students who have disabilities to provide and/or arrange reasonable accommodations.

If you have, or think you may have, a disability (e.g., mental health, attentional, learning, chronic health, sensory, or physical), please contact DS at 612-626-1333 to arrange a confidential discussion regarding equitable access and reasonable accommodations.

If you are registered with DS and have a current letter requesting reasonable accommodations, please contact your instructor as early in the semester as possible to discuss how the accommodations will be applied in the course.

For more information, please see the DS website, <https://diversity.umn.edu/disability/>.

Mental Health and Stress Management

As a student you may experience a range of issues that can cause barriers to learning, such as strained relationships, increased anxiety, alcohol/drug problems, feeling down, difficulty concentrating and/or lack of motivation. These mental health concerns or stressful events may lead to diminished academic performance and may reduce your ability to participate in daily activities. University of Minnesota services are available to assist you. You can learn more about the broad range of confidential mental health services available on campus via the Student Mental Health Website: <http://www.mentalhealth.umn.edu>.

The Office of Student Affairs at the University of Minnesota

The Office for Student Affairs provides services, programs, and facilities that advance student success, inspire students to make life-long positive contributions to society, promote an inclusive environment, and enrich the University of Minnesota community.

Units within the Office for Student Affairs include, the Aurora Center for Advocacy & Education, Boynton 10

Health Service, Central Career Initiatives (CCE, CDes, CFANS), Leadership Education and Development –Undergraduate Programs (LEAD-UP), the Office for Fraternity and Sorority Life, the Office for Student Conduct and Academic Integrity, the Office for Student Engagement, the Parent Program, Recreational Sports, Student and Community Relations, the Student Conflict Resolution Center, the Student Parent HELP Center, Student Unions & Activities, University Counseling & Consulting Services, and University Student Legal Service.

For more information, please see the Office of Student Affairs at <http://www.osa.umn.edu/index.html>.

Academic Freedom and Responsibility: for courses that do not involve students in research

Academic freedom is a cornerstone of the University. Within the scope and content of the course as defined by the instructor, it includes the freedom to discuss relevant matters in the classroom. Along with this freedom comes responsibility. Students are encouraged to develop the capacity for critical judgment and to engage in a sustained and independent search for truth. Students are free to take reasoned exception to the views offered in any course of study and to reserve judgment about matters of opinion, but they are responsible for learning the content of any course of study for which they are enrolled.*

Reports of concerns about academic freedom are taken seriously, and there are individuals and offices available for help. Contact the instructor, the Department Chair, your adviser, the associate dean of the college, or the Vice Provost for Faculty and Academic Affairs in the Office of the Provost.

OR:

Academic Freedom and Responsibility, for courses that involve students in research

Academic freedom is a cornerstone of the University. Within the scope and content of the course as defined by the instructor, it includes the freedom to discuss relevant matters in the classroom and conduct relevant research. Along with this freedom comes responsibility. Students are encouraged to develop the capacity for critical judgment and to engage in a sustained and independent search for truth. Students are free to take reasoned exception to the views offered in any course of study and to reserve judgment about matters of

opinion, but they are responsible for learning the content of any course of study for which they are enrolled.*
When conducting research, pertinent institutional approvals must be obtained and the research must be consistent with University policies.

Reports of concerns about academic freedom are taken seriously, and there are individuals and offices available for help. Contact the instructor, the Department Chair, your adviser, the associate dean of the college, or the Vice Provost for Faculty and Academic Affairs in the Office of the Provost.

* Language adapted from the American Association of University Professors "Joint Statement on Rights and Freedoms of Students".