

E520 FALL 2004 SYLLABUS
(Graduate) Environmental Toxicology
SECTION: 10815
ROOM: WH106

TIME: T Th 2:30 - 3:45 PM

Web Page: <http://www.spea.indiana.edu/dhenshel/toxicology>

PROFESSOR: Diane Henshel, e-mail: dhenshel@indiana.edu

Office Location: SPEA 357; Laboratory Location: SPEA 379

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Office Hours: T 4 - 5 pm (except Nov 16), R 10 - 11 am (except Nov 18),
and by appointment (email or phone me to set up the appointment).

Office Secretary: Kathy Perry, Room 340

DESCRIPTION:

In Environmental Toxicology we will cover basic principles of toxicology, the basics of different body systems, and the effects of exogenous chemicals upon those systems. We will review these effects and synthesize the responses of the integrated whole (the body) in response to the different classes of chemicals. Finally, we will consider how these chemicals present in our environment impact on the animals (including humans) so exposed. In one take home homework/test, we will explore the policy implications of one aspect of the toxicological impacts of some form of pollution. This year, the focus for the policy brief will be on toxic chemicals in consumer products.

In addition to the basic learning in the class, students will also gain a familiarity with the current literature and toxicological or epidemiological research methods by conducting a semester-long project. There are two options for this project:

a) The student will write a research proposal during the course of the semester. During the semester, then, the student will carry out the steps of writing a research proposal, handing in the appropriate midpoint documents. Each student choosing this option will write a research grant proposal that is based on the research literature. The grant proposal will demonstrate the student's ability to recognize what are the important research questions pertaining to that topic that are still unanswered. Writing this proposal will enable the student to explore a toxicological topic of their choosing in more depth, and will give the student experience in writing a product-oriented research proposal.

or

b) The student will conduct an environmental toxicologically-oriented research project. Using a health database from one of a number of states (preferably the midwestern states around the Great Lakes), the student will choose potential environmentally-linked endpoints to be assessed in at least three subregions of the state. The student will then analyze the database to evaluate the relative incidence of these endpoints relative to: a reference city/locale, the state, AND the nation. The student will then compare this data to environmental pollution data using either statistical and/or GIS modeling methods. The student will then write up the results in a formal

research paper including Introduction, Methods, Results, Discussion and Conclusions using the format defined by an appropriate peer-reviewed journal. In the discussion section the student will demonstrate his/her ability to identify the implications of the results and will point out the important relevant research questions that are still unanswered.

The project should be carried out in pairs, and the students will have to demonstrate equal sharing of the work.

PREREQUISITES:

Some college level biology is virtually essential. Cell Biology, Biochemistry, and Physiology are all relevant background and strongly recommended. If you have not had any biology, please come see me or call me. It is possible to catch up on the material, but it will add to the time commitment for the course. I will help you obtain appropriate background material if you need it.

- TEXTS:
- 1 *Casarett and Doull's Toxicology* 6th Ed, Klaassen CD, McGraw-Hill 2001
[This is the classic reference book that you will use for years. There are chapters that are relatively poorly written - and I have on reserve copies of these chapters from older editions that are more clearly organized and written.]
 - 2 *Casarett and Doull's Essentials of Toxicology* - the companion handbook to *Casarett and Doull's Toxicology* by JB Watkins and CD Klaassen, McGraw-Hill 2003.
[Read the chapters in here first to get the gist of the most important concepts. However, this text will not provide the details you will need to clarify and provide examples for each concept we cover. Therefore, you will need to use the main text to fill in the details that this text lacks.]
 - 3 *Our Stolen Future* by T Colborn, JP Myers, and D Dumanosky,
[Read this book throughout the semester. It is very readable. It needs to be completely read by Nov 18, so the class can talk about it during the endocrine toxicology lecture. Ronnie Yeager will lead the class discussion.]
 - 4 Recommended optional texts for background reading:
 - Goldberg, S., *Clinical Physiology Made Ridiculously Simple*, MedMaster, Inc., Miami, 1997.
 - Stewart, J., *Clinical Anatomy and Physiology for the Angry Health Professional*, MedMaster, Inc., Miami, 1997.
 - Goldberg, S., *Clinical Biochemistry Made Ridiculously Simple*, MedMaster, Inc., Miami, 2001.
 - Kapit, W. et al, *The Physiology Coloring Book*, Addison, Wesley, Longman, 2nd Edition, NYC, 2000
 - Kapit, W. et al, *The Anatomy Coloring Book*, Addison, Wesley, Longman, 2nd Edition, NYC, 2002.

[The two coloring books are formally recommended for E410, but they may be helpful to you - check them out and decide for yourself.]
 - 4 Also recommended for background material, should you need it, is:

- a) a good biochemistry book--I like Lehninger et al. or Stryer
- b) a good cell biology book--*Molecular Biology of the Cell* by Alberts et al. is very good.

5. The following web sites are helpful:

Haz-Map: <http://hazmap.nlm.nih.gov>

Haz-Map is an occupational health and toxicology database, links jobs and hazardous job-related tasks to exposure to chemicals. The database also includes occupational diseases and their symptoms.

TOXNET: <http://toxnet.nlm.nih.gov>

TOXNET is a cluster of databases on toxicology, environmental health and hazardous chemicals.

And two IU search pages:

<http://www.indiana.edu/~libfind/scimedlist.html>

This is the main IU library Science and Medicine databases access page.

<http://www.indiana.edu/~liblife/ejournal.html>

This is the search page for the full text journals accessible through the Life Sciences Library web pages. More full text journals are available here than through the main library search page.

In addition to the text and the notes you take in class, I have also provided toxicology notes on the web page. THESE NOTES ARE AN ACCUMULATION OF MY NOTES FOR TEACHING CLASS OVER THE PAST DECADE. THEY WERE DEVELOPED FOR BOTH THE GRADUATE AND THE UNDERGRADUATE CLASSES AND ARE NOT MODIFIED TO BE SPECIFIC FOR YOUR CLASS THIS SEMESTER. In the end, for the tests, **you are responsible for the material covered in class AND the material in the text assigned in the syllabus.** My goal is that you become a critical educated reader of the technical toxicologically-related literature that you will use and critique through your career. You will always be able to look up the details from the book or the literature if you have a good sense of the basic material, and know where to look and what kind of information you are looking for. Therefore, in general, I expect you to know the basic concepts and definitions, the types of responses expected from specific cells and organ systems (and WHY), as well as key information about major chemicals and chemical classes we cover. I will tend to allow you to choose what specific examples you want to memorize that will cover the key concepts and types of responses I expect you to learn. I will cover many examples. You will read about more in the texts and in the web notes (should you choose to use them too).

Re: CLASS STUDY NOTES:

Many Casarett and Doull references are from the 4th Edition, unless another edition is specified. I have been correcting this over time.

I have also provided additional articles that are available through the library reserve readings pages. You can access our articles through the following:

Web Address: <http://www.spea.indiana.edu/reserves/>

Course: E520

Password:

These readings will be useful in explaining background material, and in providing examples which may be used in the tests. These readings are for reference, to help you understand the information, and to provide further information into specific topics. They are not required readings, but you may well find them useful throughout the class. The readings include good basic introductions to the anatomy, physiology and biochemistry of body systems. If you are not sufficiently well-versed in biology, these background readings will be very helpful. Please see the list at the end of the syllabus.

GRADING: Test 1: 20%
Policy Brief: 20%
Final: 20%
Class Participation, and Attitude: 15%
Final Project/Grant: 25%:
Grant: 2% bibliography, 5% section 1/intro [2.5% first draft/outline, 2.5% second draft], 3% framing the question and hypothesis, 5% research proposed section [2.5% first draft/outline; 2.5% second draft], 2% evaluation and what could go wrong; 8% final version.
Project: 2% background research and initial bibliography, 3% problem formulation, 4% database analysis, 4% environmental comparison, 4% evaluation of the results, 8% final paper.

Note: as all material in the class is based on previous material, **all tests and the final are cumulative.**

Class attendance is mandatory. If you can not come to class, please let me know why/what happened. Failure to do so **will** affect your grade. Three unexcused absences will reduce your grade by a half grade. Five unexcused absences will reduce your grade by a full grade. Studying for another class or finishing a project or paper for another class is not an excuse for skipping a class and will not be excused. Medical emergencies or family illness require a doctor's note, with his or her phone number for follow-up. Funerals require that you provide the name of the funeral home and the phone number and name of the funeral home's director.

EXPECTATIONS FOR CLASS:

Students are expected to have read the assignments and the material for that day **PRIOR TO COMING TO CLASS.** Such class preparation will greatly enhance your ability to learn and understand the vast quantity of material in the class, and will increase the likelihood that the class can explore issues and sub-topics of special interest to the students in the class. Students are expected to review material after class, and ask me about any questions or uncertainties you have

about the reading material and the material covered in class. I can not guess when you are confused about the information you are expected to learn. I am happy to answer questions by email, as well as in person. Please put "E520" in the subject line of your emails so that when I scan my email I know to open it immediately. I consider class email high priority.

REGARDING TESTS, HOMEWORK ASSIGNMENTS AND THE HONOR CODE:

This course benefits, in general, from students working and studying together. However, I expect students will not take or write tests together. If cheating is indicated from the work handed in, the students involved will be given a 0 for the exam or homework. Additionally, if duplicate answers on tests are found both the copier and the copyee will be considered guilty and both will flunk that test. Even if the cheater knows of other persons who cheated but who were not caught, I reserve the right to prosecute the person(s) I catch cheating. Repeat offenders will automatically flunk the course.

Plagiarism (*to steal and pass off [the ideas or words of another] as one's own without crediting the source: present as new and original an idea or product derived from an existing source [Webster's New Collegiate Dictionary]*) is against the *Code of Student Ethics, Indiana University* [August 15, 1990]. Anyone who plagiarizes to any extent will fail that assignment, and potentially the class. This includes "borrowing" information from the internet or the text (without proper attribution or appropriate paraphrasing - see the handout on writing which includes guidance on paraphrasing), which can, and will be double checked. **Please sign and hand in the last page of this syllabus indicating that you have read and will comply with this honor code.**

E520—FALL SCHEDULE 2004—T Th 2:30-3:45 a.m. SPEA 275

DATE	DAY	LECTURE	READINGS*
Aug 31	T	Introduction/What is Toxicology/Definitions	Ch 1,2
Sept 2	Th	Principles of Toxicology/Dose-Response Curves	Ch 2
Sept 7	T	Mechanisms 1: Step 1	Ch 3
Sept 9	Th	Mechanisms 2: Step 2	Ch 3
Sept 14	T	Mechanisms 3: Step 3	Ch 3
Sept 16	Th	Mechanisms 4: Step 4	Ch 3
Sept 21	T	Mechanisms 4: Step 5	Ch 3
Sept 23	Th	Disposition 1/Membrane Transport/Absorption	Ch 5
Sept 28	T	Disposition 2/Distribution/Elimination	Ch 5
Sept 30	Th	Disposition 3/Biotransformation 1 - Intro and Phase 1	Ch 6 + Handout
Oct 5	T	Disposition 4/Biotransformation 2 - Phase 2 and Factors Affecting Biotransformation	Ch 6 (better in 4 th edition)
Oct 7	Th	Carcinogenesis	Ch 8
Oct 12	T	Mutagenesis	Ch 9
Oct 14	Th	Developmental Toxicology	Ch 10
Oct 19	T	Test (through Developmental Toxicology)	-----
Oct 21	Th	Hepatotoxicity (Liver)	Ch 13
Oct 26	T	Nephrotoxicology (Kidney)	Ch 14
Oct 28	Th	Pulmonotoxicology (Respiratory System)	Ch 15
Nov 2	T	Neurotoxicology 1 (Nervous System)	Ch 16
Nov 4	Th	Neurotoxicology 2	Ch 16
Nov 9	T	Male Reproductive Toxicity	Ch 20
Nov 11	Th	Female Reproductive Toxicity	Ch 20
Nov 16	T	No class - Work on your policy brief	-----
Nov 18	Th	Endocrine Toxicology - Discussion of <i>Our Stolen Future</i>	Ch 21
Nov 23	T	PCBs/Dioxins (includes immunosuppression)	use text index + handout
Nov 25	Th	THANKSGIVING RECESS	-----
Nov 30	T	Pesticides	Ch 22
Dec 2	Th	Metals	Ch 23

Dec 7	T	Solvents	Ch 24
Dec 9	Th	Air Pollution	Ch 28
Dec	T	FINAL EXAM (12:30 pm - 2:30 pm)	-----

*All readings are chapters in **Klaassen, Casarett and Doull's Toxicology, 6th Ed.** and the companion text

PROJECT OPTION 1: THE RESEARCH (grant) PROPOSAL, Bibliography, and the PRE-PROPOSAL

All students will write a 10 page (single-spaced; 20 pages double-spaced) research proposal (i.e. a grant proposal) through the course of the semester. The grant proposal will be due THURSDAY December 9. Proposals handed in after that date **may not** get graded in time for grades to be handed in and the student may get an “I” for the semester, depending on the date the grant is handed in. Late proposals may affect your final grade.

The proposal will be focused on a toxicology sub-topic of your choosing. Briefly, the sequence is as follows:

1. **The annotated bibliography** is due Thursday, September 16. Start by researching the topic. To find the topic, scan science journals (Life Sciences Library in Jordan Hall, or SPEA/Business Library), MedLine, ToxLine, Biological Abstracts, Science News, New Scientist, Discover, or other popular or research-oriented science news magazines in the library or on the Internet. Once you have found a topic that interests you, do a complete science database and journal search. You will find yourself using the web a lot. Do not rely exclusively on the web, as there are still many valuable journals that are not readily accessible on the web. Look up the articles and select the relevant articles that characterize and define the topic. A few review articles will be helpful to you as you try to narrow your interest down to a specific research question. Most of the articles you include must be primary research articles. If you are not sure if the articles are appropriate - check with me. Each article should include a one sentence summary of the articles and a one sentence explanation of it's relevance to your topic. At the end or the beginning of the annotated bibliography include a brief paragraph defining the topic you are interested in and the general research question you are planning to focus on for the grant proposal.

2. **Section 1: Introduction**
Outline of section 1 + hypothesis + question to be asked due October 7. Full version of Section 1 due November 11, along with the outline for the Proposed Research section. The question to be asked will focus you on where you are going with the introduction. What question is there left unanswered about this topic that you propose to answer via the research proposed in your proposal? This is where you want to lead the reader to in the introduction. First introduce the topic and discuss why it is relevant or important. (Why should the reader care?) Next introduce the issues or topics that will be relevant to the work to

be proposed later. The reader should not come across any new background information on the topic after the introduction section. Now lead the reader through the relevant literature to the point where there's a gap in the knowledge base that your proposed work is intended to fill. At the end of this, your proposed question to be addressed should be obvious. In short, what you are doing is step by step building a logical argument for your question and hypothesis. The hypothesis is your working hypothesis that you will test via the proposed experiments. It is best to end this section with the hypothesis and the research question.

3. **Section 2: Proposed Research**

The outline of the second section is due Nov 11. The first draft of this section is due Nov 23 or Nov 30. In this section you will propose the research needed to confirm the hypothesis and answer the proposed question. You will briefly present the research scheme and study design. Then you will discuss the methods to be used in the study, providing enough detail to make it clear that you understand the methods. Include such details as the number of animals or replicates or people to be included in each part of the study, the dose groups, controls, housing conditions, special considerations, methods for data analysis and quality control, and a brief (but accurate) summary of the methods to be used. Explain how you will analyze the data, and discuss how you will interpret the potential results and how you would address results that are not the predicted results. Also include a section that discusses what kind of problems could occur, and what you could do to address these problems.

4. **The full grant proposal** is due Thursday, December 9. The full grant proposal is a logical unfolding of the work you have done so far. You will have been able to rewrite the proposal through the semester, so I expect good quality writing.

The structure of the grant will be:

- * Introduction to the topic, significance and logical development of the ideas and known information which leads to the ...
- * Question to be asked and hypothesis.
- * Proposed research -
 - * introduce the logic of the proposed research which will find the answers to the question of concern
 - * detail the methods in sufficient detail that it is clear to the reader that you have some sense of the techniques, how they work, and their

weaknesses

- * discuss expected results
- * What can go wrong and what you can do to address these problems and ...
- * Conclusion
- * Full bibliography of references cited in context.

Remember the entire proposal will be approximately 10 single-spaced pages, not including the references.

I suggest you look at some of the grant-writing briefs that are linked to the class web page and are on reserve in the library. They will help you think through the logic of the writing and grant development process. The web page also has links to web pages with good grant writing information.

References

Cite all your references (including methodological references) in full, including: authors (with initials), year, title, journal or source, publisher (if a book), pages.

If you use a web reference, you **must** cite the author of the page(s), the web address (in full) *and the date you accessed the page*. Web resources can change.

Grading

You will be graded on organization, clarity, understanding of the material, innovation in your thinking [i.e. is this really a new research direction, or has this already been published], appropriate detail in the research plan and introduction, and depth. Excessively long proposals may be down-graded and are likely to be less clearly written and less well organized. Plagiarism is sufficient cause for an "F," as is not appropriately citing your sources (in context, and in the bibliography).

NOTE REGARDING GRANT PROPOSALS: = WARNING = CHOOSE YOUR TOPICS AND DO THE RESEARCH EARLY. Much of the material you need will NOT BE AVAILABLE ON-LINE but will have to be ordered (or may be in hardcopy only at IUPUI or Purdue) and not to be found on this campus. You will need up to 2 weeks to get requested articles through the library system. **KNOW TO EXPECT THIS!!** I will not accept anyone having a poor choice of articles due to their inability to plan ahead.

PROJECT OPTION 2: THE RESEARCH PROJECT

Students choosing this option will carry out a research project using environmental and public health databases. The goal of this project will be to evaluate in some way the linkage between environmental exposures and health effects. In general, expect to be evaluating effects at a population level, as individual level databases are difficult to obtain. The final project will be due THURSDAY December 9. Project reports handed in after that date **may not** get graded in time for grades to be handed in and the student may get an “I” for the semester, depending on the date the grant is handed in. Late proposals will affect your final grade. Students will work in pairs on the research project. This allows the students to split the work load, and enables the students to use brainstorming as an essential part of the project planning and work.

The timing of expected due dates is as follows.

1. **The annotated bibliography and statement of the research topic** is due Thursday, September 16. Start by researching the topic. To find the topic, scan science journals (Life Sciences Library in Jordan Hall, or SPEA/Business Library), Medline, ToxLine, Biological Abstracts, Science News, New Scientist, Discover, or other popular or research-oriented science news magazines in the library or on the Internet. It is also critical that you evaluate what potential databases will be available for your use, since data availability will help you define your specific research question. Try using Google to find relevant database sources. Also look at state health department websites, NGO sites, and NHIS (National Health Information and Statistics???) website to find appropriate data.

Once you have found a topic that interests you, do a complete science database and journal search. You will find yourself using the web a lot. Do not rely exclusively on the web, as there are still many valuable journals that are not readily accessible on the web. When choosing your background literature, look up the articles and select the relevant articles that characterize and define the topic. A few review articles will be helpful to you as you try to narrow your interest down to a specific research question. At least some of the articles you include must be primary research articles. Try to find articles that evaluate and compare environmental and health databases. If you are not sure if the articles are appropriate - check with me. Each article should include a one sentence summary of the articles and a one sentence explanation of it's relevance to your topic. At the end or the beginning of the annotated bibliography include a brief paragraph defining the topic you are interested in and the general research question you are planning to focus on for the grant

proposal.

Do not neglect to spend some time looking for relevant databases during this initial phase. The availability of databases will help you define your research question. I have been building up data that will be made available to those doing research projects. Be sure to talk to me about what data I can make available to you.

2. **Section 1: Introduction**

Outline of your background information section + the specific problem formulation guiding your research is due October 7. By this date you should also have your databases in hand, or know where you are getting most of your information from. The research problem that you will be focused on will guide you in choosing what information needs to be included in your background information (introduction) section. You will need to include information about both the topics to be investigated as well as about the analysis methods that you intend to use. Do not forget to include specific information about your sources of data (ie the databases).

3. Full version (first draft) of the introduction with preliminary analyses of your data due November 11. At the same time you will hand in an outline of the analysis and (potential) conclusions sections. I fully expect to see a lot of you throughout October and early November, as you start to figure out how to analyze the data that you are pulling together.

4. First draft of the data analysis and conclusions section due Nov 23 or Nov 30. I may (am likely to) suggest additional analyses to try. If you have been conferring with me regularly, you are less likely to get surprised with many new suggested analyses to test, or with requests to find additional data.

5. **The full research report** is due Thursday, December 9.

The structure of the Project Report will be:

- * Introduction to the topic, significance and logical development of the ideas, known information, and previous use of the analytical methods and databases which leads to the ...
- * Problem Formulation.
- * Research Methods

- * Discuss the databases and the kind of information available in the databases you use. Then detail the statistical, graphical and GIS-based methods that you use to analyze the data.
- * Results
 - * Present your results in whatever forms are most appropriate, including graphical, GIS and tabular presentation styles.
 - * Summarize and discuss the results. What were the problems and weaknesses of this analysis? What kinds of conclusions can you draw? What are the implications of these results?
 - * Full bibliography of references cited in context. Cite all your references (including methodological references) in full, including: authors (with initials), year, title, journal or source, publisher (if a book), pages. If you use a web reference, you **must** cite the author of the page(s), the web address (in full) *and the date you accessed the page*. Web resources can change.

Write your research paper in the format of a journal article, adding supporting information as appendices. Use *Environmental Health Perspectives* or *Environmental Research* as potential models for what to include in your paper, and the depth of the analyses that need to be done. If the paper is sufficiently complete, I will help you get it into final publishable form and help you publish the paper.

E520 Information Form

Hi -

In order for me to better help you learn, I need to know what you know and what specifically you are all interested in. Please fill out this form to help me teach you better.

Name:

What is your concentration?

Why are you taking Toxicology?

What do you expect to do with this information?

General Science (biology, chemistry, esp) Classes Taken in College [Please include names, not just numbers]:

Other SPEA or Environmental Science/Policy Classes taken or enrolled in now (course #s ok):

Please look at the syllabus schedule. Please list specific sub-topics that interest you that you want us to cover this semester:

I have read the syllabus for E520, Environmental Toxicology, including the information about the Honor Code. I understand that I will get a 0 on any test that I cheat on, regardless of whoever else is or is not caught cheating. I also understand that if my test is copied from, I will also get a 0 on the test. I agree not to plagiarize, and understand that plagiarizing will also result in a 0 on the assignment.

I agree that I will comply with the Honor Code, as laid out in both this syllabus and in the Indiana University *Code of Student Ethics* [August 15, 1990]. I understand and agree with the penalties of cheating on tests and on copying or plagiarizing on the written projects.

Name: _____

Date: _____