

School of Public Health

Syllabus and Course Information



UNIVERSITY OF MINNESOTA
Driven to DiscoverSM

PubH 8160 Advanced Toxicology Fall 2016

Credits: 2
Meeting Days: Wednesdays
Meeting Time: 4 – 6 pm
Meeting Place: Mayo 1155

Instructor: Lisa Peterson
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I. Course Description

This course will focus on the development and application of Adverse Outcome Pathways as a framework for integrating existing knowledge to construct a biological pathway that links molecular initiating events induced by chemicals and classes of chemicals with specific adverse outcomes, such as cancer, neurotoxicity, and reproductive and developmental toxicity. This course requires to students to read and critically analyze and interpret current primary literature in toxicology, and integrate the information to develop and analyze adverse outcome pathways.

II. Course Prerequisites

PubH 6160, one course in biochemistry and one course in molecular biology; permission of instructors.

III. Course Goals and Objectives

By the end of the semester, students will be able to:

- Explain the basic principles of the development and application of Adverse Outcome Pathways
- Develop strategies to investigate issues in toxicology by integrating publically available data to develop an Adverse Outcome Pathway
- Use databases to identify key studies for use in the development of Adverse Outcome Pathway
- Read and analyze primary literature in toxicology
- Critically analyze experimental design and interpret data
- Apply toxicology principles learned in other courses to real world research questions
- Make scientific presentations to an educated audience

IV. Methods of Instruction and Work Expectations

This course involves a combination of lectures, student presentations, and independent research.

Project 1. Choose an Adverse Outcome Pathway (AOP) from the list on the AOP WIKI to analyze and present to the class. The AOP must be listed as “Ready for Commenting.” <https://aopwiki.org/aops>

- September 14: Submit choice of AOP
- October 5: Give a presentation on the background of the chemical or class of chemicals, and analysis of adverse outcomes
- October 19: Give a presentation on the analysis of the initiating events
- October 26: Give a presentation on the analysis of key events, and overall conclusions and analysis of the AOP

Each presentation should be approximately 30 minutes (no longer than 30 minutes).

October 5: Provide background information on the chemical or class of chemicals for the AOP you have chosen. Why is this chemical or class of chemicals of interest? How would humans be exposed? If humans would not be exposed, why is there interest in this chemical or class of chemicals? Describe the adverse outcome for this chemical or class of chemicals. Why is it important? What is the evidence that this occurs in animals, humans, or other species? Present the key data that support the conclusions.

October 19: For the AOP you have chosen, discuss the molecular initiation event(s). Why is this initiating event important? What is the evidence that this occurs in animals, humans, or other species? Present data from key papers that support the selection of the initiating event. Present data that demonstrate the initiating event is linked to the adverse outcome. Discuss the strengths and weaknesses of the support for the molecular initiation event(s).

October 26: For the AOP you have chosen, discuss the key events and the overall conclusions and analysis of the AOP. Why are these events important? What is the evidence this occurs in animals, humans, or other species? Present evidence that demonstrate that these events link the initiating event to the adverse outcome. Discuss the strengths and weaknesses of the support for the key events. Then, discuss the overall AOP and its strengths and weaknesses? What data gaps have been identified? Propose future experiments to address these gaps. Include a discussion of how the AOP can be used to protect human health.

Project 2: Develop an AOP for a chemical or class of chemicals of your choice, and present it to the class.

- October 12: Submit choice of chemical or class of chemicals
- November 2: Give a presentation on the background of the chemical or class of chemicals, and analysis of adverse outcomes
- November 16: Give a presentation on the analysis initiating events
- December 7: Give a presentation on the analysis of key events

- December 14: Give a presentation will be on the overall conclusions and analysis of the AOP

Use the AOP template from OECD guidelines as a guide for your analyses and presentations (GUIDANCE DOCUMENT ON DEVELOPING AND ASSESSING ADVERSE OUTCOME PATHWAYS, pages 27-30.)

Each presentation should be approximately 30 minutes (no longer than 30 minutes).

November 2: Provide background information on the chemical or class of chemicals you have chosen for your AOP. Why is this chemical or class of chemicals of interest? How would humans be exposed? If humans would not be exposed, why is there interest in this chemical or class of chemicals?

Describe the adverse outcome for this chemical or class of chemicals. Why is it important? What is the evidence that this occurs in animals, humans, or other species? Present data from key papers that support your conclusions.

November 16: Define the molecular initiation event(s) for your AOP. Why is this initiating event important? What is the evidence that this occurs in animals, humans, or other species? Present data from key papers that support your conclusions. Present data from papers that the initiating event is linked to the adverse outcome. Discuss the strengths and weaknesses of the support for the molecular initiation event(s).

December 7: Define the key events for your AOP. Why are these events important? What is the evidence this occurs in animals, humans, or other species? Present evidence that these events link the initiating event to the adverse outcome. Discuss the strengths and weaknesses of the support for the key events.

December 14: Present an overall conclusion regarding the AOP. Identify strengths and weaknesses, and identify gaps in knowledge. Propose future experiments to address these gaps. Discuss how the AOP can be used to protect human health.

V. Course Text and Readings

OECD Guidance Document on Developing and Assessing Adverse Outcome Pathways

Available at:

[http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2013\)6&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2013)6&doclanguage=en)

User's Handbook Supplement to the Guidance Document for Developing and Assessing AOPs

Available at: http://aopkb.org/common/AOP_Handbook.pdf

Development of an Adverse Outcome Pathway for Acetylcholinesterase Inhibition Leading to Acute Mortality

Russom CL, LaLone CA, Villeneuve DL, Ankley GT. *Environ Toxicol Chem.* (2014), 10:2157-69.

Available online through the U of M libraries

The adverse outcome pathway concept: A pragmatic tool in toxicology. Vinken M. *Toxicology.* (2013),

312:158-165. Available online through the U of M libraries

Defining molecular initiating events in the Adverse Outcome Pathway framework for risk assessment. Allen

TEH, Goodman JM, Gutsell S, PJ Russell. *Chem. Res. Toxicol.* (2014), 27:2100-2112. Available online

through the U of M libraries

Adverse Outcome Pathways: A Conceptual Framework to Support Ecotoxicology Research and Risk

Assessment Ankley, G.T. et al. *Environ. Toxicol. Chem.*, 29: 730–741, 2010. Available online through the U

of M libraries

Adverse Outcome Pathway (AOP) Development I: Strategies and Principles Villeneuve, D. et al. *Toxicol.*

Sci., 142: 312–320, 2014. Available online through the U of M libraries

Additional reviews and readings from the primary literature may be added during the course.

VI. Course Outline/Weekly Schedule

September 7, 2016	<p>Orientation to class: Overview of Adverse Outcome Pathways Watch Tox21 video Discuss presentation expectations Explore the AOP list on the AOP WIKI https://aopwiki.org/aops</p>
September 14, 2016	<p>Introduction to AOPs Dan Villeneuve, EPA</p> <p>Readings:</p> <p><i>Adverse Outcome Pathways: A Conceptual Framework to Support Ecotoxicology Research and Risk Assessment</i> Ankley, G.T. et al. <i>Environ. Toxicol. Chem.</i>, 29: 730–741, 2010. Available online through the U of M libraries</p> <p><i>Adverse Outcome Pathway (AOP) Development I: Strategies and Principles</i> Villeneuve, D. et al. <i>Toxicol. Sci.</i>, 142: 312–320, 2014. Available online through the U of M libraries</p> <p>Submit choice of AOP from the AOP WIKI for initial analysis and presentation</p>
September 21, 2016	<p>Case study in AOP development-Acetylcholinesterase inhibition leading to acute mortality Carlie LaLone, EPA</p> <p>Reading: <i>Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS): A web-based tool for addressing the challenges of cross-species extrapolation of chemical toxicity</i>, Lalone, C.A. et al. <i>Toxicol Sci.</i> Jun 30, 2016. Available online through the U of M libraries</p> <p><i>Adverse Outcome Pathway (AOP) Development I: Strategies and Principles</i> Villeneuve, D. et al. <i>Toxicol. Sci.</i>, 142: 312–320, 2014. Available online through the U of M libraries</p> <hr/> <p>Strategies for Literature Searches Frank Sayre, Health Science Librarian</p>
September 28, 2016	Week off to work on presentations
October 5, 2016	<p>Presentation on background on the chemical and analysis of adverse outcomes</p> <p>Reading: <i>OECD Guidance Document on Developing and Assessing Adverse Outcome Pathways</i></p> <p><i>User's Handbook Supplement to the Guidance Document for Developing and Assessing AOPs</i></p>
October 12, 2016	<p>AOPs in ecotoxicology Mark Jankowski, EPA</p>

	<p>Reading: <i>Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses</i>, C.E. Stephen et al., (read the main document, you do not need to read the appendices), available at: https://www.epa.gov/wqc/guidelines-deriving-numerical-national-water-quality-criteria-protection-aquatic-organisms-and</p> <p><i>Adverse Outcome Pathways: A Conceptual Framework to Support Ecotoxicology Research and Risk Assessment</i> Ankley, G.T. et al. Environ. Toxicol. Chem., 29: 730–741, 2010. Available online through the U of M libraries</p> <p><i>Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS): A web-based tool for addressing the challenges of cross-species extrapolation of chemical toxicity</i>, Lalone, C.A. et al. Toxicol Sci. Jun 30, 2016. Available online through the U of M libraries</p> <p>Submit choice of chemical for AOP development</p>
October 19, 2016	<p>Presentation and analysis initiating events</p> <p>Reading: <i>Defining molecular initiating events in the Adverse Outcome Pathway framework for risk assessment</i>. Allen TEH, et al. Chem. Res. Toxicol. (2014), 27:2100-2112.</p>
October 26, 2016	<p>Presentation and analysis of key events. Overall conclusions and analysis of the Adverse Outcome Pathway</p>
November 2, 2016	<p>Presentation on background on the chemical and analysis of adverse outcomes for project 2</p>
November 9, 2016	<p>Week off to work on AOP</p>
November 16, 2016	<p>Presentation and analysis initiating events for project 2</p>
November 23, 2016	<p>Week off to work on AOP</p>
November 30, 2016	<p>Presentation and analysis of key events for project 2</p>
December 7, 2016	<p>Week off to work on AOP</p>
December 14, 2016	<p>Overall conclusions and analysis of the Adverse Outcome Pathway for project 2</p>

VII. Evaluation and Grading

A/F letter grade will be determined by total effort as follows:

A = 92-100%	(4.0) Represents achievement that is outstanding relative to the level necessary to meet course requirements.
A- = 88-91.5%	
B+ = 84-87.5%	
B = 80-83.5%	(3.0) Represents achievement that is significantly above the level necessary to meet course requirements.
B- = 76-79.5%	
C+ = 72-75.5%	
C = 68-71.5%	(2.0) Represents achievement that meets the minimum course requirements.
C- = 64-67.5%	
D+ = 60-63.5%	
D = 56-59.6%	(1.0) Achievement below minimum course expectations but sufficient to be awarded credit.
D- = 52-55.5%	
F = <51.5	Represents failure (or no credit) and signifies that the work was either (1) completed but at a level of achievement that is not worthy of credit or (2) was not completed and there was no agreement between the instructor and the student that the student would be awarded an I.

S/N option must complete all assignments to a C- level (70%):

S	Achievement that is satisfactory will be expected to complete all assignments and receive a minimum of 70% to receive a passing score (achievement required for an S is at the discretion of the instructor but may be no lower than a 70%).
F	Represents failure (or no credit) and signifies that the work was either (1) completed but at a level of achievement that is not worthy of credit or (2) was not completed and there was no agreement between the instructor and the student that the student would be awarded an I.

Course Evaluation

Beginning in fall 2008, the SPH will collect student course evaluations electronically using a software system called CourseEval: www.sph.umn.edu/courseeval. 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.

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>.

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. *[Customize with names and contact information as appropriate for the course/college/campus.]*

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

Template update 9/2013