

# PUBH 8160

Advanced Toxicology  
Fall 2018

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## COURSE & CONTACT INFORMATION

**Credits:** 2

**Meeting Day(s):** Thursdays

**Meeting Time:** 4 – 6 pm

**Meeting Place:** TBA

**Instructor:** Lisa Peterson

**Email:** peter431@umn.edu

**Office Phone:** 612-626-0164

**Office Hours:** By appointment

**Office Location:** Rm 2-126 CCRB; 2233 6<sup>th</sup> St SE

**Instructor:** Elizabeth Wattenberg

**Email:** watte004@umn.edu

**Office Phone:** 612-626-0184

**Office Hours:** By appointment

**Office Location:** Rm 1110 Mayo Building

## 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 students to read and critically analyze and interpret current primary literature in toxicology, and integrate the information to develop and analyze adverse outcome pathways.

## COURSE PREREQUISITES

PubH 6159, PubH 6160, one course in biochemistry and one course in molecular biology; or permission of instructors

## COURSE GOALS & 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
- Conduct a literature search to identify key studies for use in the development of Adverse Outcome Pathways
- 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

## METHODS OF INSTRUCTION AND WORK EXPECTATIONS

This course involves a combination of lectures, student presentations, and extensive independent research that takes place outside of the classroom. Students can meet with instructors outside of class to discuss questions on independent research and assignments.

**Project 1. Analyze AOP 15:** *Alkylation of DNA in male pre-meiotic germ cells leading to heritable mutations*  
<https://aopwiki.org/aops/15>

- September 6: Assignment instructions will be discussed in class and posted on the Moodle site
- September 13: Written part of the assignment is due by the beginning of class (15 points)
- September 20: Receive assignment for presentation part of the assignment
- October 4: Give presentations in class (15 points)

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

- September 6: Assignment instructions will be discussed in class and posted on the Moodle site
- September 20: Submit choice of chemical or class of chemicals by the beginning of class
- October 11: Outline of AOP and list of papers that support each step due (10 points)
- October 25: Give a presentation on the background of the chemical or class of chemicals, and analysis of adverse outcomes (15 points)
- November 8: Give a presentation on the analysis initiating events (15 points)
- November 29: Give a presentation on the analysis of key events (15 points)
- December 6: Give a presentation will be on the overall conclusions and analysis of the AOP (15 points)

### Learning Community

Many of our courses also ask students to work in teams or discussion groups. We do not come to our courses with identical backgrounds and experiences and building on what we already know about collaborating, listening, and engaging is critical to successful professional, academic, and scientific engagement with topics.

In this course, students are expected to engage with each other in respectful and thoughtful ways.

In group work, this can mean:

- Setting expectations with your groups about communication and response time during the first week of the semester (or as soon as groups are assigned) and contacting the TA or instructor if scheduling problems cannot be overcome.
- Setting clear deadlines and holding yourself and each other accountable.
- Determining the roles group members need to fulfill to successfully complete the project on time.
- Developing a rapport prior to beginning the project (what prior experience are you bringing to the project, what are your strengths as they apply to the project, what do you like to work on?)

In group discussion, this can mean:

- Respecting the identities and experiences of your classmates.
- Avoid broad statements and generalizations. Group discussions are another form of academic communication and responses to instructor questions in a group discussion are evaluated. Apply the same rigor to crafting discussion posts as you would for a paper.
- Consider your tone and language, especially when communicating in text format, as the lack of other cues can lead to misinterpretation.

Like other work in the course, all student to student communication is covered by the Student Conduct Code (<https://z.umn.edu/studentconduct>).

## COURSE TEXT & READINGS

*OECD Guidance Document on Developing and Assessing Adverse Outcome Pathways*  
Available at: See Moodle site.

*User's Handbook Supplement to the Guidance Document for Developing and Assessing AOPs*  
Available at: [http://aopkb.org/common/AOP\\_Handbook.pdf](http://aopkb.org/common/AOP_Handbook.pdf)

*EPA Adverse Outcome Pathway Factsheet.* See Moodle site.

*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, DL. et al. *Toxicol. Sci.*, 142: 312–320, 2014. Available online through the U of M libraries

*Practical Approaches to Adverse Outcome Pathway Development and Weight-Of-Evidence Evaluation As Illustrated By Ecotoxicological Case Studies* Fay KA et al. *Environmental Toxicology and Chemistry*, 36(6):1429-1449, 2017.  
Available online through the U of M libraries

*Quantitative Adverse Outcome Pathways and Their Application to Predictive Toxicology* Conolly RB et al. *Environ. Sci. Technol.* 51:4661-4672, 2027. Available online through the U of M libraries

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

COURSE OUTLINE/WEEKLY SCHEDULE

Week	Topic	Readings	Activities/Assignments
Week 1 Thursday, September 6	<ul style="list-style-type: none"> <li>• Orientation to class</li> <li>• Overview of Adverse Outcome Pathways</li> <li>• Watch Tox21 video</li> <li>• Receive assignments</li> <li>• Discuss presentation expectations</li> <li>• Explore the AOP list on the AOP WIKI</li> <li>• <a href="https://aopwiki.org/aops">https://aopwiki.org/aops</a></li> </ul>	<ul style="list-style-type: none"> <li>• <i>OECD Guidance Document on Developing and Assessing Adverse Outcome Pathways</i></li> <li>• <i>User's Handbook Supplement to the Guidance Document for Developing and Assessing AOPs</i></li> <li>• <i>EPA Adverse Outcome Pathway Factsheet</i></li> </ul>	<ul style="list-style-type: none"> <li>• Receive instructions for Projects 1 and 2</li> <li>• Explore website for Project 1 <a href="https://aopwiki.org/aops/15">https://aopwiki.org/aops/15</a></li> <li>• Watch the Risk Bites YouTube video: <i>A New Way to Evaluate Chemical Safety - TOX21</i> <a href="https://www.youtube.com/watch?v=vKhn1HXgn8">https://www.youtube.com/watch?v=vKhn1HXgn8</a></li> </ul>
Week 2 Thursday, September 13	<ul style="list-style-type: none"> <li>• Introduction to AOPs</li> <li>• Carlie LaLone, EPA</li> <li>• Introduction to AOPs               <ul style="list-style-type: none"> <li>○ Background</li> <li>○ Principles of AOP-development</li> <li>○ Introduction to the AOP-wiki</li> <li>○ Brief overview of weight of evidence (WoE) for AOPs</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <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</li> <li>• <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</li> <li>• <i>Practical Approaches to Adverse Outcome Pathway Development and Weight-Of-Evidence Evaluation As Illustrated By Ecotoxicological Case Studies</i> Fay KA et al. <i>Environmental Toxicology and Chemistry</i>, 36(6):1429-1449, 2017. Available online through the U of M libraries</li> </ul>	<ul style="list-style-type: none"> <li>• Written part of Project 1 is due by the beginning of class</li> </ul>

<p>Week 3 Thursday, September 20</p>	<p>Case studies in AOP development Dan Villeneuve, EPA</p>	<ul style="list-style-type: none"> <li>• <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</li> <li>• <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</li> <li>• <i>Quantitative Adverse Outcome Pathways and Their Application to Predictive Toxicology</i> Conolly RB et al. <i>Environ. Sci. Technol.</i> 51:4661-4672, 2027. Available online through the U of M libraries</li> </ul>	<ul style="list-style-type: none"> <li>• Receive assignment for the presentation part of Project 1</li> <li>• Submit choice of chemical or class of chemicals for Project 2</li> </ul>
<p>Week 4 Thursday, September 27</p>	<ul style="list-style-type: none"> <li>• Independent work on Project 1 presentations</li> </ul>	<ul style="list-style-type: none"> <li>• <i>OECD Guidance Document on Developing and Assessing Adverse Outcome Pathways</i></li> <li>• <i>User's Handbook Supplement to the Guidance Document for Developing and Assessing AOPs</i></li> </ul>	<ul style="list-style-type: none"> <li>• Develop Project 1 presentations</li> </ul>
<p>Week 5 Thursday, October 4</p>	<ul style="list-style-type: none"> <li>• AOP for Alkylation of DNA in male pre-meiotic germ cells leading to heritable mutations</li> </ul>		<ul style="list-style-type: none"> <li>• Project 1 presentations</li> </ul>
<p>Week 6 Thursday, October 11</p>	<ul style="list-style-type: none"> <li>• Present Project 2 AOP outline and list of papers that support each step</li> </ul>		<ul style="list-style-type: none"> <li>• Outline of Project 2 AOP and list of papers that support each step due</li> </ul>

Week 7 Thursday, October 18	<ul style="list-style-type: none"> <li>Independent work on Project 2 background on the chemical and analysis of adverse outcomes</li> </ul>	<ul style="list-style-type: none"> <li>Develop presentation on Project 2 background on the chemical and analysis of adverse outcomes</li> </ul>	
Week 8 Thursday, October 25	<ul style="list-style-type: none"> <li>Background on the chemical and analysis of adverse outcomes</li> </ul>	<ul style="list-style-type: none"> <li>Presentation of Project 2 background on the chemical and analysis of adverse outcomes</li> </ul>	
Week 9 Thursday, November 1	<ul style="list-style-type: none"> <li>Independent work on Project 2 analysis of initiating events</li> </ul>	<ul style="list-style-type: none"> <li>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</li> </ul>	<ul style="list-style-type: none"> <li>Develop presentation on Project 2 analysis of initiating events</li> </ul>
Week 10 Thursday, November 8	<ul style="list-style-type: none"> <li>Initiating events</li> </ul>	<ul style="list-style-type: none"> <li>Presentation on Project 2 analysis of initiating events</li> </ul>	
Week 11 Thursday, November 15	<ul style="list-style-type: none"> <li>Independent work on analysis of key events and on overall conclusions and analysis of the Project 2 AOP</li> </ul>	<ul style="list-style-type: none"> <li>Develop presentation on Project 2 key events</li> <li>Independent work on analysis and presentation of key events</li> </ul>	
Week 12 Thursday, November 22	<ul style="list-style-type: none"> <li>Thanksgiving</li> </ul>	<ul style="list-style-type: none"> <li>Develop presentation on overall conclusions and analysis of the Project 2 AOP</li> </ul>	
Week 13 Thursday, November 29	<ul style="list-style-type: none"> <li>Key events</li> </ul>	<ul style="list-style-type: none"> <li>Presentations on Project 2 analysis of key events</li> </ul>	
Week 14 Thursday, December 6	<ul style="list-style-type: none"> <li>Overall conclusions and analysis of Project 2 AOP</li> </ul>	<ul style="list-style-type: none"> <li>Presentation of Project 2 overall conclusions and analysis AOP</li> </ul>	

## SPH AND UNIVERSITY POLICIES & RESOURCES

The School of Public Health maintains up-to-date information about resources available to students, as well as formal course policies, on our website at [www.sph.umn.edu/student-policies/](http://www.sph.umn.edu/student-policies/). Students are expected to read and understand all policy information available at this link and are encouraged to make use of the resources available.

The University of Minnesota has official policies, including but not limited to the following:

- Grade definitions
- Scholastic dishonesty
- Makeup work for legitimate absences
- Student conduct code
- Sexual harassment, sexual assault, stalking and relationship violence
- Equity, diversity, equal employment opportunity, and affirmative action
- Disability services
- Academic freedom and responsibility

Resources available for students include:

- Confidential mental health services
- Disability accommodations
- Housing and financial instability resources
- Technology help
- Academic support

## EVALUATION & GRADING

[Enter a detailed statement of the basis for grading here. Include a breakdown of course components and a point system for achieving a particular grade. Include expected turnaround time for grading/feedback. Please refer to the University's Uniform Grading Policy and Grading Rubric Resource at <https://z.umn.edu/gradingpolicy>]

### **Grading Scale**

The University uses plus and minus grading on a 4.000 cumulative grade point scale in accordance with the following, and you can expect the grade lines to be drawn as follows:

<b>% In Class</b>	<b>Grade</b>	<b>GPA</b>
93 - 100%	A	4.000
90 - 92%	A-	3.667
87 - 89%	B+	3.333
83 - 86%	B	3.000
80 - 82%	B-	2.667
77 - 79%	C+	2.333
73 - 76%	C	2.000
70 - 72%	C-	1.667
67 - 69%	D+	1.333
63 - 66%	D	1.000
< 62%	F	

- A = achievement that is outstanding relative to the level necessary to meet course requirements.
- B = achievement that is significantly above the level necessary to meet course requirements.
- C = achievement that meets the course requirements in every respect.
- D = achievement that is worthy of credit even though it fails to meet fully the course requirements.
- F = failure because 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 (Incomplete).
- S = achievement that is satisfactory, which is equivalent to a C- or better
- N = achievement that is not satisfactory and signifies that the work was either 1) completed but at a level that is not worthy of credit, or 2) not completed and there was no agreement between the instructor and student that the student would receive an I (Incomplete).

Evaluation/Grading Policy	Evaluation/Grading Policy Description
<p><b>Scholastic Dishonesty, Plagiarism, Cheating, etc.</b></p>	<p>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 (As defined in the Student Conduct Code). For additional information, please see <a href="https://z.umn.edu/dishonesty">https://z.umn.edu/dishonesty</a></p> <p>The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: <a href="https://z.umn.edu/integrity">https://z.umn.edu/integrity</a>.</p> <p>If you have additional questions, please clarify with your instructor. 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.</p> <p>Indiana University offers a clear description of plagiarism and an online quiz to check your understanding (<a href="http://z.umn.edu/iuplagiarism">http://z.umn.edu/iuplagiarism</a>).</p>
<p><b>Late Assignments</b></p>	
<p><b>Attendance Requirements</b></p>	
<p><b>Extra Credit</b></p>	