Adverse Outcome Pathways: From Research to Regulation

William H. Natcher Conference Center, National Institutes of Health
Bethesda, Maryland, USA
September 3-5, 2014

DRAFT Program

— Day 1 —
Wednesday, September 3, 2014

8:30–8:35: **Welcome**
Warren Casey, NICEATM

8:35–9:05: **Innovation in Toxicology at NCATS**
Christopher Austin, U.S. National Center for Advancing Translational Sciences

9:05–9:35: **From Mode of Action to Adverse Outcome Pathways: Moving Towards Regulatory Applicability**
Bette Meek, University of Ottawa

9:35–10:05: **What is an AOP (and What ISN'T It?)**
Donna Mendrick, U.S. Food and Drug Administration (FDA)

10:05–10:20: **Break**

10:20 **Session 1: Building Upon Other Efforts**

10:20–10:50: **AOP Activities at the OECD**
Joop de Knecht, Organisation for Economic Co-operation and Development (OECD)

10:50–11:20: **AOP Knowledge Base/Wiki Tool Set**
Steven Edwards, U.S. Environmental Protection Agency (EPA)

11:20–11:50: **Outcomes from the March Somma Lombardo Workshop**
Ed Perkins, U.S. Army

12:00–1:00: **Lunch**

1:00 **Session 2: AOPs Under Development**

1:00–1:25: **Embryonic Vascular Disruption and Adverse Prenatal Outcomes**
Nicole Kleinstreuer, ILS/NICEATM

1:25–1:50: **Using Adverse Outcome Pathway Analysis to Identify Gaps in High-Throughput Screening for Thyroid Disruption**
Katie Paul, Bayer CropScience

1:50–2:15: **Application of the Adverse Outcome Pathway (AOP) Concept to Neurotoxicology: A Challenging Approach**
Ellen Fritsche, IUF Dusseldorf

2:15–2:40: **AOP Development: After the Heights of the Mountains – the Hardship of the Plains; the Example of Liver Fibrosis**

Brigitte Landesmann, European Commission Joint Research Center (JRC)

2:40–3:05: **Fish Early Life Stage: Developing AOPs to Support Targeted Reduction and Replacement**

Dan Villeneuve, EPA

3:05–3:30: **Break**

3:30–3:55: **Adverse Outcome Pathway for Effects of Anticoagulant Rodenticides on Predatory Birds**

Barnett Rattner, U.S. Geological Survey, U.S. Department of the Interior

3:55–4:20: **An AOP for Activation of the Aryl Hydrocarbon Receptor**

Ted Simon, Ted Simon LLC

4:20–4:45: **Developing AOPs from PPAR Activation Leading to Reproductive Toxicity**

Malgorzata Nepelska, JRC

4:45–5:10: **Framework for Computationally-Predicted AOPs**

Shannon Bell, EPA

5:10–5:30: **End of Day Wrap-Up**

— Day 2 —

Thursday, September 4, 2014

8:30 **Session 3: Case Studies: Regulatory Uses for Well-Identified AOPs**

8:30–9:00: **Testing of the Predictive Power and Robustness of an AOP Construct for Bile Salt Export Pump Inhibition to Cholestatic Injury**

Mathieu Vinken, Vrije Universiteit Brussel

9:00–9:30: **Using the Estrogen Receptor AOP to Prioritize and Screen Chemicals for EDSP**

David Dix, EPA

9:30–10:00: **Validating New Tools/Assays Against Carcinogenicity AOPs to Support Regulatory Decisions**

Rita Schoeny, EPA

10:00–10:30: **Identifying Integrated *In Vitro/In Silico* Testing Strategies (IATA/ITS) by Mapping to the Skin Sensitization AOP**

Joanna Matheson, U.S. Consumer Product Safety Commission

10:30–10:45: **Break**

10:45 **Session 4: The Risk Context**

10:45–11:15: **Exposure and Dosimetry Considerations for AOPs**

John Wambaugh, EPA

11:15–11:45: Ozone-Induced Lung Inflammation and Injury: From Mechanism to Adversity in Humans

Robert Devlin, EPA

11:45–12:15: Suspected Modes of Action Affected by Pesticides Exposure: Informing an Adverse Outcomes Pathway (AOP) for Cancer

Michael Alavanja, U.S. National Cancer Institute

12:15–1:15: Lunch

1:15–1:30: Introduction to Breakout Groups

1:30–3:00: Breakout Group Discussions (First Rotation)

1. The Process of Regulatory Acceptance

Moderators:
David Dix, EPA
Craig Rowlands, The Dow Chemical Company

Case Study Presentations (8-10 min each plus 20 min discussion):

I. What is the process for AOP development, peer review and application within OECD? How do you go from OECD acceptance to agency acceptance?
Melissa Panger, EPA
Working Group of National Coordinators, OECD Test Guidelines Programme

II. How do we establish scientific confidence in AOPs?
Rick Becker, American Chemistry Council

III. How are the critical relationships between chemical bioavailability, activity, and adversity established within an AOP in a way that protects the most sensitive subpopulations?
Ruthann Rudel, Silent Spring Institute

2. Using AOPs for Regulatory Decisions: Confidence and Criteria

Moderators:
Suzanne Fitzpatrick, FDA
Annie Jarabek, EPA

Case Study Presentations (8-10 min each plus 20 min discussion):

I. Contaminants in the food supply: how the AOP concept can help regulators make decisions using arsenic as a case study
Christina Powers, EPA

II. Considerations for using AOPs in human health risk assessment of environmental contaminants
Annie Jarabek, EPA

III. Using evidence-based toxicology to evaluate AOPs
Thomas Hartung, Center for Alternatives to Animal Testing, Johns Hopkins University

3. Taking Qualitative AOPs to the Next (Quantitative) Level

Moderators:
Nicole Kleinstreuer, ILS/NICEATM
Kristie Sullivan, Physicians Committee for Responsible Medicine

Case Study Presentations (8-10 min each plus 20 min discussion):

I. Case study presentation: a quantitative AOP for skin sensitization
Gavin Maxwell, Unilever

II. A conceptual model that enables quantitative integration of data into an AOP
Catherine Willett, Humane Society of the United States

III. Applying semantic and network methods in AOP knowledge
David Wild, University of Indiana School of Informatics and Computing

3:00–3:15: Break

3:15–4:45: Breakout Group Discussions (Participants rotate to a new group)

4:45–5:00: Break

5:00–6:00: Short Presentations by Junior Investigators With Outstanding Poster Abstracts
End of Day Wrap-Up

6:00–8:00: Poster Session and Independently Sponsored Reception

— Day 3 —
Friday, September 5, 2014

9:00–10:30: Breakout Group Discussions (Third and final rotation)

10:30–10:45: Break

10:45–12:00: Hands-on Demonstration/Training

I. Entering an AOP Into the OECD Wiki
Stephen Edwards, EPA

II. Introduction to Effectopedia
Hristo Aladjov, OECD

12:00–1:30: Lunch

1:30–3:00: Breakout Group Moderator Reports

I. David Dix, EPA, and Craig Rowlands, The Dow Chemical Company
II. Suzanne Fitzpatrick, FDA, and Annie Jarabek, EPA
III. Nicole Kleinstreuer, ILS/NICEATM, and Kristie Sullivan, PCRM

3:00–4:00 Facilitated Whole-Group Discussion

Moderators:
Sharon Munn, European Union Reference Laboratory for Alternatives to Animal Testing
Michelle Embry, International Life Sciences Institute Health and Environmental Sciences Institute

4:00 **Adjourn**