Alternative Approaches for Identifying Acute Systemic Toxicity: Moving from Research to Regulatory Testing

September 24-25, 2015
Bldg. 35 Porter Neuroscience Center, NIH campus
Bethesda, MD

The goal of this workshop is to explore alternatives to acute toxicity testing requirements, such as the U.S. Environmental Protection Agency's six-pack, that could reduce and replace use of mammalian species for acute systemic testing in North America. To accomplish this goal, experts will discuss experiences using alternative approaches and how to build upon those approaches to develop strategies that regulatory agencies will accept. Working together, experts from industry, government, academia, and NGOs will define integrated predictive testing strategies that can satisfy regulatory needs to protect human health.

Day 1: September 24, 2015

9:00-9:15	Welcome and introduction Kristie Sullivan, M.P.H., Director, Regulatory Testing Issues Physicians Committee for Responsible Medicine
9:15-10:25	**Session 1: The regulatory landscape: When is acute toxicity data required and how is it used?**
9:15-9:25	U.S. Consumer Product Safety Commission Joanna Matheson, Ph.D., Senior Toxicologist
9:25-9:35	U.S. Environmental Protection Agency, Office of Pesticide Programs Elissa Reaves, Ph.D., Acting Deputy Director for the Antimicrobials Division
9:35-9:45	U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics Louis (Gino) Scarano, Ph.D., Chief of Assessment Branch 1
9:45-9:55	U.S. Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Laboratories Ron Brown, M.S., Toxicologist
9:55-10:25	Panel Discussion led by Dan Wilson, Ph.D., Toxicology Consultant Leader, The Dow Chemical Company
10:25-10:40	**Break**

10:40-12:00 Session 2: State-of-the-science for acute toxicity testing methods

10:40-10:55 ***In vitro* alternatives for acute toxicity testing**
Rabea Graepel, Ph.D., Scientific Officer
European Union Reference Laboratory for Alternatives to Animal Testing

10:55-11:10 ***In silico* alternatives for acute toxicity testing**
Hao Zhu, Ph.D., Assistant Professor of Chemistry
Rutgers University - Camden

11:10-11:25 **PBPK/ADME alternatives for acute toxicity testing**
Bas Blaauboer, Ph.D., Emeritus Professor of Toxicology
Utrecht University, The Netherlands

11:25-11:40 **NRC report: Application of Modern Toxicology Approaches for Predicting Acute Toxicity for Chemical Defense**
David Dorman, DVM, Ph.D., Professor of Toxicology
North Carolina State University
Chair, Committee on Predictive-Toxicology Approaches for Military Assessments of Acute Exposures

11:40-12:00 Panel Discussion led by Nancy Beck, Ph.D., Senior Director, Regulatory Science Policy, Regulatory and Technical Affairs, American Chemistry Council

12:00-1:00 Lunch

1:00-2:30 Session 3: Case studies

1:00-1:30 **Vision for animal-free pesticide formulation assessment**
Sean Gehen, Ph.D., DABT, Research Scientist, Dow Agrosciences

1:30-1:45 Discussion

1:45-2:15 **Predicting acute toxicity hazard in the absence of experimental data: Case studies from the alternatives assessment paradigm**
Jay Tunkel, Ph.D., Principal Investigator, SRC

2:15-2:30 Discussion

2:30-2:45 Break

2:45-3:30 Session 3: Case studies (continued)

2:45-3:15 **Zebrafish models for human acute organophosphorus poisoning**
Natalia Garcia-Reyero, Ph.D., Research Biologist, U.S. Army Engineer Research and Development Center

3:15-3:30 Discussion

3:30-5:15 Session 4: Looking ahead: mechanisms and adverse outcome pathways

3:30-3:50 **Mechanisms**
Dan Wilson, Ph.D., Toxicology Consultant Leader, The Dow Chemical Company

3:50-4:10 **Computationally-predicted AOPs**
Shannon Bell, Ph.D., Toxicologist, Integrated Laboratory Systems, Inc.

4:10-4:30 **High-throughput *in vitro* assays at NCATS**
Menghang Xia, Ph.D., Group Leader, Systems Toxicology, NIH National Center for Advancing Translational Sciences (NCATS)

4:30-5:15 **Group Discussion**
Moderated by Kristie Sullivan and Anna Forsby, Ph.D., Associate Professor and Senior Scientist, Stockholm University and Swetox

5:30-6:30 Independently-sponsored reception

Day 2: September 25, 2015

9:00-10:45 Session 5: Policy discussion

9:00-9:15 **Overview**
Warren Casey, Ph.D., Director, NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

9:15-10:45 Discussion led by Warren Casey and Anna Lowit, Ph.D., Senior Scientist, U.S. Environmental Protection Agency

10:45-11:00 Break

11:00-12:00 Breakout groups

- *In silico* (QSARs, databases, computational) approaches
  Moderated by Dave Allen, Ph.D., Principal Investigator, Integrated Laboratory Systems, Inc., and Barun Bhhatarai, Ph.D., Toxicology and Environmental Research and Consulting, The Dow Chemical Company
- *In vitro* and aquatic approaches (two groups)
  Group 1 moderated by Amy Clippinger, Ph.D., Science Advisor, PETA International Science Consortium, Ltd. and Warren Casey
  Group 2 moderated by Kristie Sullivan and Jon Hotchkiss, Ph.D., Senior Inhalation Toxicologist, The Dow Chemical Company

12:00-1:00 Lunch

1:00-2:00 Breakout groups (continued)

- *In silico* (QSARs, databases, computational) approaches
- *In vitro* and aquatic approaches

2:00-2:30 Report-out from breakout groups

- *In silico* (QSARs, databases, computational) approaches (15 minutes)
- *In vitro* and aquatic approaches (15 minutes)

2:30-4:00 Main group discussion and wrap-up