

# Mind the gaps: Prioritizing activities to meet regulatory needs for acute systemic lethality

October 30-31<sup>st</sup>, 2019

Porter Neuroscience Center, NIH campus

Bethesda, Md, USA

Purpose: A workshop to discuss the evaluation of acute lethality associated with chemicals and chemical mixtures with the purpose of designing comprehensive strategies to predict their toxicity while avoiding animal tests. The envisioned key outcomes include: defining how to calculate the LD50 of a chemical mixture/formulated product; identifying gaps where model (or assay) development or optimization is needed; understanding regulatory needs for model (or assay) outputs; pinpointing the types of mechanistic information that would be useful, and establishing the feasibility of using artificial intelligence in model development. Workshop participants will be expected to outline and continue to be involved in specific plans for testing and other follow up.

## Agenda:

### October 30, 2019

- 8:30 – 8:45** Welcome and introductions  
*Kristie Sullivan, Physicians Committee for Responsible Medicine (PCRM) & David Allen, Integrated Laboratory Systems, Inc. (ILS)*
- 8:45 – 9:15** **Presentation:** Summarizing output of previous acute tox workshops and charting the course ahead  
*Amy Clippinger, PETA International Science Consortium*
- 9:15 – 9:45** **Presentation:** Regulatory needs: Can existing data be used to derive acute lethality estimates without animal tests? CATMoS WoE and the Additivity Equation as example approaches  
*Warren Casey, NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)*
- 9:45 – 10:00: BREAK**
- 10:00 – 10:30** **Case study presentation and discussion:** Calculating the toxicity of pesticide mixtures  
*Raja Settivari, Corteva*
- 10:30 – 11:45** **Group Discussion:** Evaluating mixtures for acute lethality  
**Discussion leader:** Raja Settivari, Corteva
- 11:45 – 12:45 LUNCH**

- 12:45 – 1:15**    **Demonstration:** Structure-based approaches to predicting acute toxicity: CATMoS  
*Kamel Mansouri, NICEATM*
- 1:15 – 1:45**    **Case study presentation and discussion:** Integration of *in vitro* and *in silico* tools for acute toxicity prediction  
*Kyle Glover, US Army*
- 1:45 – 2:15**    **Group Discussion:** Leveraging AI to identify acutely toxic substances  
**Discussion leader:** *Kamel Mansouri, NICEATM*
- 2:15 – 3:15**    **Group discussion:** Information gaps and how to address them in a systematic fashion  
**Discussion leader:** *Dan Wilson, Dow Chemical*
- 3:15 – 3:30**    **BREAK**
- 3:30 – 4:30**    **Group discussion:** Where can we predict acute lethality with mechanistic *in vitro* models?  
**Discussion leader:** *Dan Wilson, Dow Chemical*
- 4:30 – 5:00**    **Group discussion:** How should ADME be considered?  
**Discussion leader:** *Sanjeeva Wijeyesakere, FMC*

**October 31**

- 8:30 – 9:00**    **Group discussion:** What does the AOP framework contribute?  
**Discussion leader:** *Steve Edwards, RTI International*
- 9:00 – 10:00**    **Group discussion:** How you would supplement existing model predictions/methods with information specific to particular classes of chemicals?  
**Discussion leader:** *Warren Casey, NICEATM*
- 10:00 – 11:30**    **Group discussion:** Regulatory applicability: How do we prioritize our next activities?  
**Discussion leader:** *Kristie Sullivan, PCRM*
- 11:30 – 12:30**    **Group discussion:** Operationalizing findings and recommendations  
**Discussion leader:** *David Allen, ILS*
- 12:30**            **Close of meeting**