UNITED STATES ICCVAM Advancing Alternatives to Animal Testing

Interagency Coordinating Committee on the Validation of Alternative Methods

Report on ICCVAM and NICEATM Activities

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SACATM Meeting, September 27, 2016
Research Triangle Park, NC

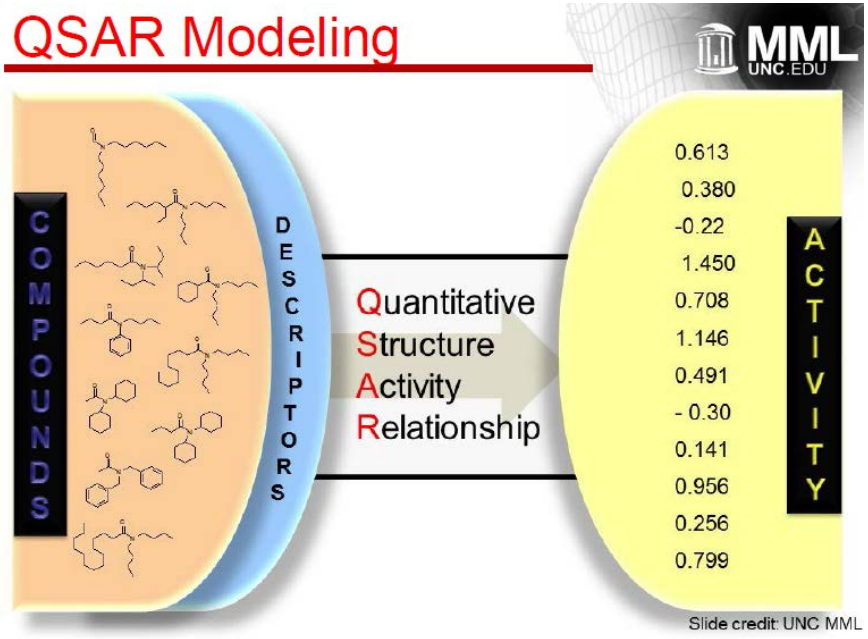
Agency for Toxic Substances and Disease Registry • Consumer Product Safety Commission • Department of Agriculture
Department of Defense • Department of Energy • Department of the Interior • Department of Transportation
Environmental Protection Agency • Food and Drug Administration • National Institute for Occupational Safety and Health
National Institutes of Health • National Cancer Institute • National Institute of Environmental Health Sciences
National Library of Medicine • Occupational Safety and Health Administration

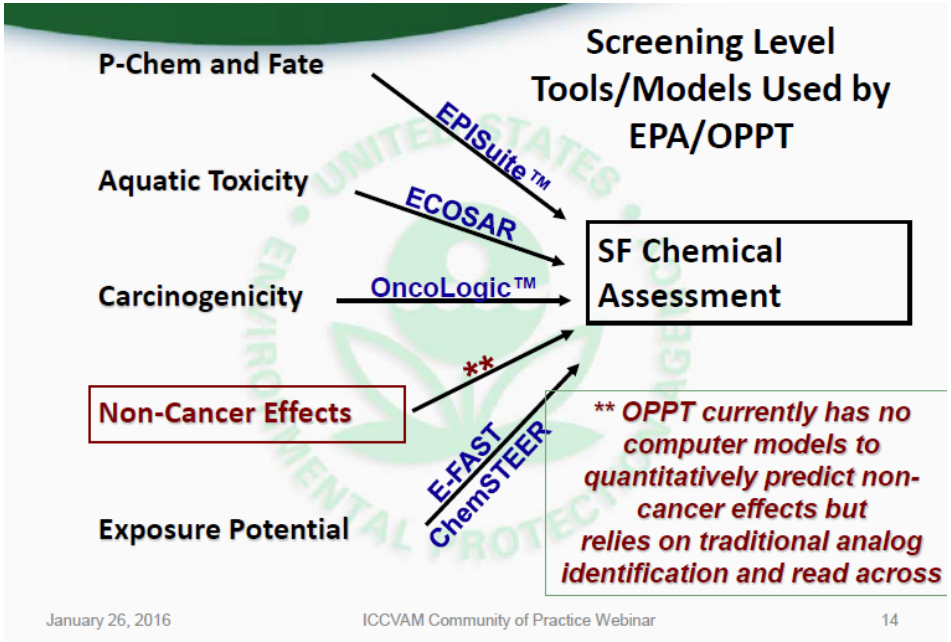
ICCVAM Biennial Progress Report

- Congressionally mandated
- Comprehensive summary of member agency activities (2014-2015) relevant to the ICCVAM mission
- This and future editions will be published as searchable websites; downloadable PDF available
- Published August 2016

Communities of Practice Webinar

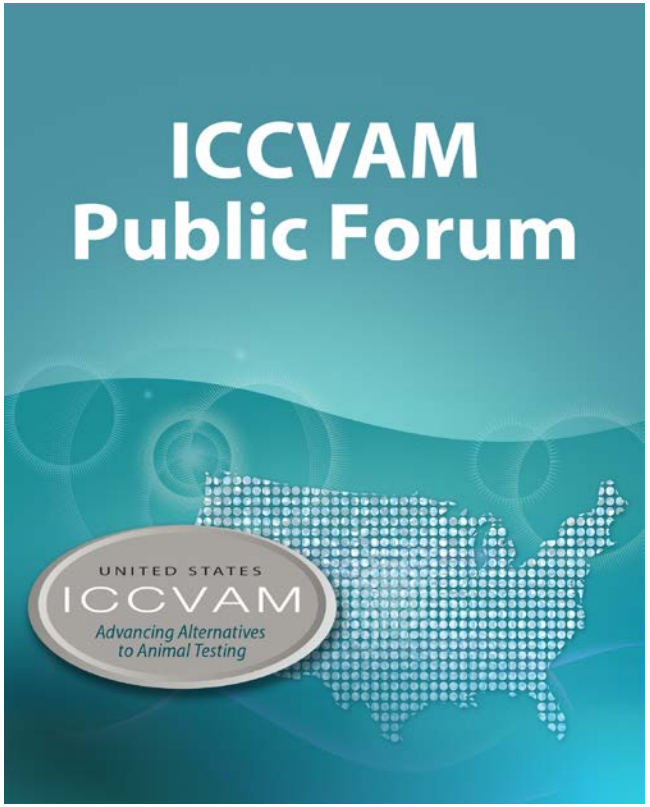
- Fundamentals of Using Quantitative Structure-Activity Relationship Models and Read-across Techniques in Predictive Toxicology, Jan 2016
  - Alex Tropsha, Ph.D., University of North Carolina at Chapel Hill
  - Louis Scarano, Ph.D., Office of Pollution Prevention and Toxics, EPA





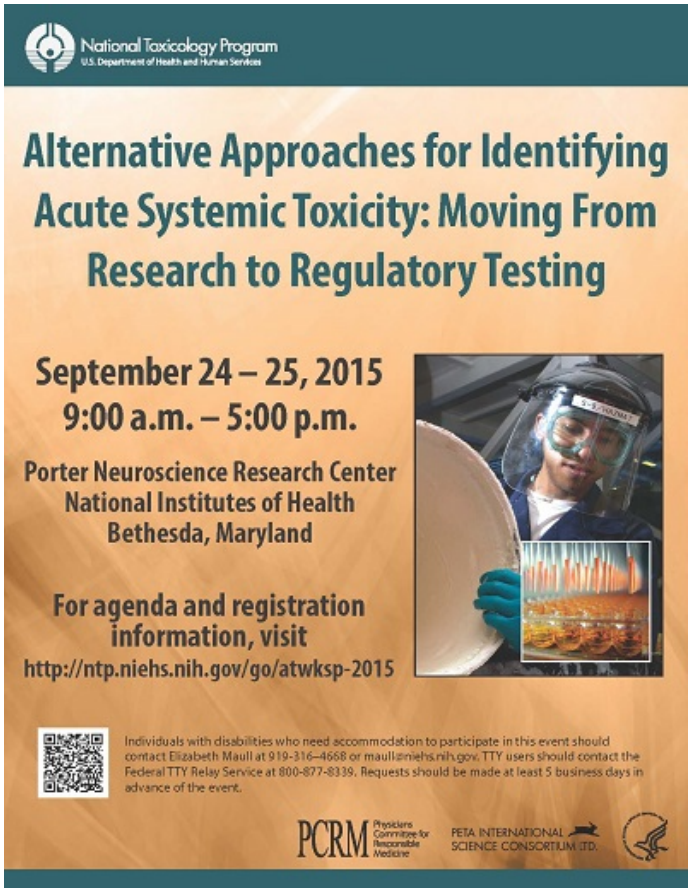
ICCVAM Public Forum

- May 25, 2016
  Natcher Conference Center
  NIH, Bethesda, MD
- Updates by NICEATM and ICCVAM agencies on current activities
- 33 in-person (from 12 ICCVAM agencies) and 160 webcast views
- Opportunities for public comments and questions
- Roadmap concept for replacing animal use for the “6-pack”
- Implementation Plan
- Next ICCVAM Public Forum: May 23, 2017



Alternatives for Acute Toxicity Workshop

- Over 60 participants from industry, academia, NGOs, and regulatory agencies
- Breakout groups charged with identifying key aspects to address in order to replace the in vivo acute systemic toxicity test methods within 3 years
- Recommendations included:
  - Publish a white paper on the regulatory landscape
  - Organize expert groups that will focus on specific tasks (resulted in the Sep 2016 inhalation tox workshop)
  - Work towards global harmonization of testing requirements
  - Provide training and promotion of alternative approaches
  - Collect and collate available data in centralized repositories
- Workshop report submitted (Tox In Vitro)
- See also http://ntp.niehs.nih.gov/go/atwksp-2015



Workshops in 2016: A New Model

- Designed to encourage consistent engagement and maximize productive participation
- Topics driven by ICCVAM agency needs
- Organizing committees with broad stakeholder representation
- Education via pre-workshop webinar series
- Increased emphasis on breakout groups

IVIVE Workshop

- Workshop goals
  - Review state of the science
  - Identify data gaps
  - Describe practices and case study examples
- ~100 attendees from industry, academia, NGOs, and government
- 3 workshop themes
  - Toxicokinetic (TK) model considerations
  - In silico and non-animal methods for obtaining TK parameters
  - Application to prioritization/screening/ risk assessment

Pre-Workshop IVIVE Webinar Series

- Average attendance ~130 participants, ~400 registered
- Provided background in preparation for the in person workshop

October 7: Setting the Stage: Purpose, Definitions, Scope, and Assumptions
Barbara Wetmore, Ph.D., ScitoVation

November 4: Building Fit-for-purpose Pharmacokinetic Models
John Wambaugh, Ph.D., U.S. Environmental Protection Agency

December 3: The Role of Pharmacokinetic Model Evaluation
Lisa Sweeney, Ph.D., Naval Medical Research Unit Dayton

January 6: Framework for Establishing an Internal Threshold of Toxicological Concern
Corie Ellison, Ph.D., The Procter & Gamble Company

IVIVE Workshop Action Items

- Quantitative high throughput TK (HTTK) model review article
- Database for in vitro and in vivo PK/TK data and models
- Best practices for use of IVIVE in a prioritization and risk decision making setting
- Workshop report in prep
  - Case studies highlighting where IVIVE can currently be used
  - Challenges that new data or different models may address

Alternative Approaches for Acute Inhalation Toxicity Testing to Address Global Regulatory and Non-regulatory Data Requirements

September 22-23, 2016
Bethesda, MD

September 22: Bldg. 35 Porter Neuroscience Center, NIH campus
September 23: Hilton Garden Inn Washington DC/Bethesda

- Co-organized with PETA International Science Consortium
- Experts from industry, government, academia, and NGOs
- Compiled an inventory of information on validation status of alternatives
- Identified data gaps
- Outlined a strategy for implementation; action items/responsible parties

Pre-Workshop Inhalation Tox Webinar Series

- Average attendance ~100 participants, >500 registered
- Detailed the state-of-the-science in preparation for the in person workshop

March 29: Current Testing Practices: Regulatory Requirements and Non-regulatory Testing
Jon Hotchkiss, Dow Chemical Co.
Ian Indans, UK Chemicals Regulation Directorate

April 26: State-of-the-science, Practical Application, and Dosimetry Considerations for In Vitro and Ex Vivo Methods
Annie Jarabek, Ph.D., EPA
Marianna Gaca, British American Tobacco

May 26: State-of-the-science and Practical Application of In Silico Methods
Grace Patlewicz, EPA
Dan Wilson, Dow Chemical Co.

June 28: GHS Additivity Approach to Classify Mixtures Based on Ingredient Toxicity
Marco Corvaro, Dow AgroSciences

July 12: Adverse Outcome Pathways
Mathieu Vinken, Free University of Brussels
Barbara Buckley, EPA

September 8: 21st Testing Approaches
Kelly BéruBé, Cardiff University
Dan Huh, University of Pennsylvania

SACATM Liaisons

- **Lauren Black:** ICCVAM Communities of Practice Webinar 2016 - Fundamentals of Using QSAR Models and Read-across Techniques in Predictive Toxicology
- **Pam Spencer:** ICCVAM 2016 Public Forum
- **Kate Willett:** Workshop on Alternative Approaches for Identifying Acute Systemic Toxicity: Moving from Research to Regulatory Testing and Alternative Approaches for Acute Inhalation Toxicity to Address Global Regulatory and Non-regulatory Data Requirements
- **Brian Berridge:** Workshop on In Vitro to In Vivo Extrapolation for High Throughput Prioritization and Decision Making