



Interagency Coordinating Committee on the Validation of Alternative Methods

ICCVAM Workgroup Updates

Emily Reinke, PhD, DABT
ICCVAM Public Forum
July 29-30, 2026

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 Energy
Department of Veterans Affairs Office of Research and Development • Environmental Protection Agency • Food and Drug Administration
National Center for Advancing Translational Sciences • National Institute for Occupational Safety and Health • National Institutes of Health
• National Cancer Institute • National Institute of Environmental Health Sciences • National Institute of Standards and Technology •
National Library of Medicine Occupational Safety and Health Administration

ICCVAM Participating Agencies Update

18 Participating Agencies

- Consumer Product Safety Commission
- Department of Agriculture
- Department of the Interior
- Department of Transportation
- Environmental Protection Agency
- Food and Drug Administration
- Occupational Safety and Health Administration
- National Institute for Occupational Safety and Health
- Agency for Toxic Substances and Disease Registry
- National Cancer Institute
- National Center for Advancing Translational Sciences (since 2024)
- National Inst of Environmental Health Sciences
- National Library of Medicine
- National Institutes of Health
- Department of Defense
- Department of Energy
- National Institute of Standards and Technology (since 2017)
- Dept of Veterans Affairs Office of Research and Development (since 2020)
- Other participants
 - Tox21



Outline

- ICCVAM Update
- ICCVAM Workgroups
 - Acute Toxicity
 - Ecotoxicity
 - PFAS
 - Common Data Elements
 - Neurotoxicity
 - Microphysiological Systems

Biennial Report

- To be released September 2026
 - Covers activities January 2024 to December 2025
 - Draft in preparation includes over 200 articles reporting on activities of every ICCVAM member agency
 - Article topics include machine learning approaches, MPS, data sharing and harmonization, and endpoints including acute toxicity, developmental toxicity, hepatotoxicity, and cardiotoxicity
 - Previous Biennial Report:
 - <https://ntp.niehs.nih.gov/iccvamreport/2023>



Acute Toxicity Testing Work Group (1)

Complete – oral and dermal systemic toxicity

- Evaluate the usefulness of acute oral LD50 data for classifying dermal systemic hazard of potential toxicants such as pesticides, industrial chemicals, chemical warfare agents, and household chemicals
 - Complete – for pesticide formulations and active ingredients; EPA published waiver guidance for formulations in 2016 and for technical chemicals in 2020
- Evaluate in vitro/in silico approaches for predicting acute systemic toxicity
 - Modeling workshop convened – workshop report published (Kleinstreuer et al. 2018; <https://doi.org/10.1016/j.comtox.2018.08.002>)
 - Acute oral toxicity in silico models – CATMoS (Mansouri et al. 2021; <https://doi.org/10.1289/EHP8495>); model predictions for ICCVAM agencies
 - Variability analysis of the in vivo oral test method (manuscript published – Karmaus et al. 2022; <https://doi.org/10.1093/toxsci/kfac042>)



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Research article

Evaluation of Variability Across Rat Acute Oral Systemic Toxicity Studies

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Acute Toxicity Testing Work Group (2)

Complete – oral and dermal systemic toxicity

- GHS additivity formula evaluation for acute systemic toxicity tests
 - Manuscript published – Hamm et al. 2021;
<https://doi.org/10.1016/j.yrtph.2021.105007>
- Publish a scoping document that outlines the current requirements and testing needs for U.S. and international regulatory authorities
 - U.S. published (Strickland et al. 2018;
<https://doi.org/10.1016/j.yrtph.2018.01.022>)
 - International published (Strickland et al., 2023;
<https://doi.org/10.1080/10408444.2023.2240852>)

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Performance of the GHS Mixtures Equation for Predicting Acute Oral Toxicity

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Status of acute systemic toxicity testing requirements and data uses by U.S. regulatory agencies

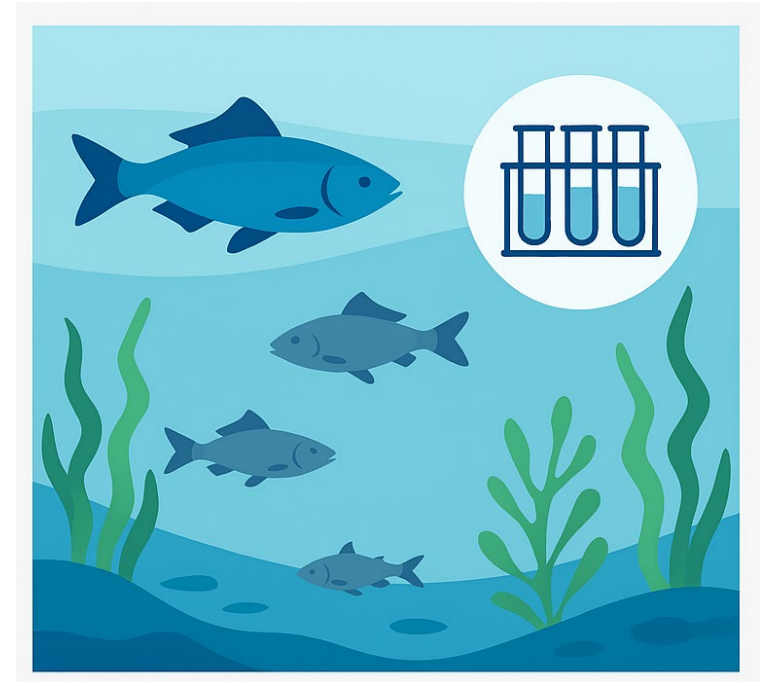
Judy Strickland^a  , Amy J. Clippinger^b , Jeffrey Brown^b , David Allen^a , Abigail Jacobs^{c,1} , Joanna Matheson^d , Anna Lowit^e , Emily N. Reinke^f , Mark S. Johnson^f , Michael J. Quinn Jr.^f , David Mattie^g , Suzanne C. Fitzpatrick^h , Surender Ahirⁱ , Nicole Kleinstreuer^j , Warren Casey^j 

Ongoing: Collaborative Modeling Project for Acute Inhalation Toxicity (CoMPAIT)

- Collaborative effort to build a modeling approach that predicts acute inhalation toxicity
 - Multi-sector collaboration launched March 2024
 - Define, develop, and execute an appropriate approach for predicting an LC50
 - Dataset is relatively small (approximately 760 chemicals)
 - LC50 database finalized, available on NIH Integrated Chemical Environment (NICE; <https://ice.ntp.niehs.nih.gov/>)

Ecotoxicity Testing Work Group (1)

- Revised Scope and Charges
 - Identify one or more New Alternative Methods (NAMs) that can potentially be used alone or in combination to reduce, refine, or replace the acute fish toxicity test
- Criteria & Agency Input
 - Characterize the identified methods
 - Determine criteria that are important to regulatory agencies when considering replacement methods for acute fish toxicity



Ecotoxicity Testing Work Group (2)



- Agency input collected on the use of the acute fish toxicity test and NAMs:
 - What does your agency do with acute fish toxicity data?
 - What is your flexibility to use NAMs?
 - What should the data submitter know about your agency's process?
 - Are there legal or regulatory impediments to the adoption of NAMs, for example, are live animal data specifically called for in your agency's regulations?
- Reference literature is being updated
 - Collecting and extracting manuscripts that employ the acute fish toxicity test and the Fish Embryo Test (OECD TG236) or the Fish Cell Line Acute Toxicity - The RTgill-W1 cell line assay (OECD TG249)

PFAS Testing and Assessment Work Group

- Sponsoring agencies: DoD, EPA, FDA
- Current efforts
 - Assess the current state of the science for PFAS and NAMs – finalizing clearance before publication in August 2026
 - Review of available information for PFAS testing using NAMs and overarching challenges/data gaps for application of NAMs for regulatory assessment.
 - Workshop to address gaps identified in the white paper planned for early Spring 2027
- Future
 - Report the outcome of the workshop/session and future directions



Common Data Elements (CDE) Work Group

- Closed in 2026 – collaboration with other groups underway (e.g. Pistoia Alliance, Complement-ARIE CDE WG, etc).
- CDE – standardized and precisely defined terms and formats used to collect and share data across studies.
- Promote data consistency, interoperability, and integrative analysis – critical for comparing the performance and applicability of different NAMs

Microphysiological Systems Work Group

- FDA and NIST are co-sponsors
- Draft Scope and Charge
 - Recommend cross-cutting criteria for using MPS for Chemical Risk Assessment
 - Context of use and graded scientific confidence in alignment with the ICCVAM validation report criteria
 - Charges
 - Hold a workshop to discuss validation criteria explicit for MPS
 - Publish a manuscript



Neurotoxicity Work Group

- FDA and EPA are co-sponsors
- Scope and Charge still being drafted



Questions?

<https://ntp.niehs.nih.gov/go/iccvam>