ICCVAM Workgroup Update

PFAS NAMs WG

Shruti V. Kabadi, Ph.D.

CFSAN, US FDA

February 14, 2024

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

ICCVAM Establishment and History

ICCVAM Authorization Act of 2000

PUBLIC LAW 106–545 (42 U.S.C. 285/-3):
ICCVAM Authorization Act of 2000

"To establish, wherever feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness."

ICCVAM Co-chairs

Suzanne Fitzpatrick
US FDA

Natalia Garcia Reyero Vinas
DoD

- 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 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: NCATS, Tox21

Nicole Kleinstreuer
Executive Director, ICCVAM

More information: https://ntp.niehs.nih.gov/go/iccvam

Purposes of ICCVAM

- Increase the efficiency and effectiveness of U.S. Federal agency test method review
- Eliminate unnecessary duplication of effort and share experience among U.S. Federal regulatory agencies
- Optimize utilization of scientific expertise outside the U.S. Federal government
- Ensure that new and revised test methods are validated to meet the needs of U.S. Federal agencies
- Reduce, refine, or replace the use of animals in testing where feasible

More information: https://ntp.niehs.nih.gov/iccvam/docs/about_docs/pl106545.pdf
(ICCVAM Authorization Act)

Key ICCVAM Publications

Casey et al. 2015. A new path forward: the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and National Toxicology Program's Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). J Am Assoc Lab Anim Sci 54(2): 170-173

Kleinstreuer et al. 2016. Adverse Outcome Pathways: From Research to Regulation. Scientific workshop report. Reg Toxicol Pharmacol 76:39-50

Hamm et al. 2017. Alternative approaches for identifying acute systemic toxicity: moving from research to regulatory testing. Toxicology In Vitro 41:245-259

Strickland et al. 2017. Multivariate models for prediction of human skin sensitization hazard. J Appl Toxicol 37(3):347-360

Strickland et al. 2018. Status of acute toxicity testing requirements and data uses by U.S. regulatory agencies. Reg Toxicol Pharmacol 94:183-196

ICCVAM 2018. A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States. Available: https://ntp.niehs.nih.gov/go/natl-strategy.

Casey and Lowit. 2019. USA: ICCVAM and NICEATM. In: Balls M, Combes R, Worth A. 2019. The History of Alternative Test Methods in Toxicology. London: Academic Press. https://doi.org/10.1016/B978-0-12-813697-3.00015-9.

Choksi et al. 2019. United States regulatory requirements for skin and eye irritation testing. Cutan Ocular Toxicol 38(2):141-155

Patlewicz et al. 2019. Exploring current read-across applications and needs among selected U.S. federal agencies. Regul Toxicol Pharmacol 106:197-209

Strickland et al. 2019. Skin sensitization testing needs and data uses by U.S. regulatory and research agencies. Arch Toxicol 92(2):273-291

Bell et al. 2020. An integrated chemical environment with tools for chemical safety testing. Toxicol In Vitro. PMID 32553663.

Mansouri K et al. 2021. CATMoS: Collaborative Acute Toxicity Modeling Suite. Environ Health Perspect 129:47013. PMID 33929906.

Ceger P et al. 2022. Current ecotoxicity testing needs among selected U.S. federal agencies. Reg Toxicol Pharmacol. https://doi.org/10.1016/j.yrtph.2022.105195.

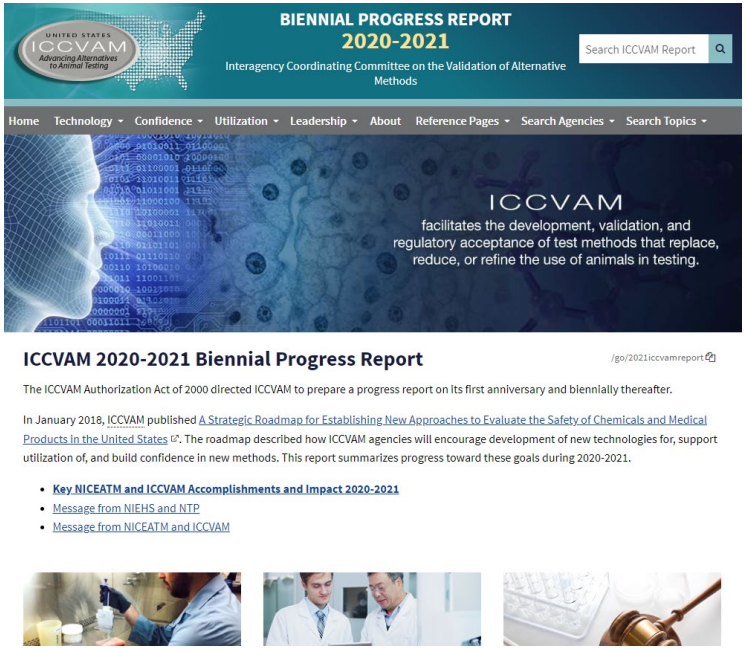
Chang X et al. 2022. IVIVE: facilitating the use of in vitro toxicity data in risk assessment and decision making. Toxics 10(5):232. https://doi.org/10.3390/toxics10050232.

Petersen EJ et al. 2022. U.S. federal agency interests and key considerations for new approach methodologies for nanomaterials. ALTEX 39(2):183-206. https://doi.org/10.14573/altex.2105041.

Existing ICCVAM Workgroups: September 2023

- Acute Toxicity
- Consideration of Alternative Methods
- Ecotoxicology
- In Vitro to In Vivo Extrapolation
- PFAS
- Read Across
- Validation

ICCVAM Biennial Progress Report



- Required by the ICCVAM Authorization Act
- Summarizes agency activities to promote alternatives or reduce animal use
- 2020-2021 report at https://ntp.niehs.nih.gov/go/2021iccvamreport

PFAS Workgroup

ICCVAM Sponsor Agencies: FDA, EPA, DoD

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

Current WG Roster

- Moiz Mumtaz (ATSDR)
- John Gordon (CPSC)
- Adrienne Layton (CPSC)
- Joanna Matheson (CPSC)
- **Natalia Garcia-Reyero Vinas (DoD, Co-Chair)**
- Anna Lowit (EPA/OPPT)
- **Kelly Carstens (EPA/ORD, Co-Chair)**
- Paul South (FDA)
- Jason Aungst (FDA/CFSAN)
- Jacqueline Heilman (FDA/CFSAN)
- Sarvin Moghaddam (FDA/CFSAN)
- Suzanne Fitzpatrick (FDA/CFSAN)
- **Shruti Kabadi (FDA/CFSAN, Co-Chair)**
- Lisa Dzubak (NIOSH)
- Todd Stueckle (NIOSH)
- Warren Casey (NIEHS)
- Stephen Ferguson (NIEHS)
- Dori Germolec (NIEHS)
- Helena Hogberg-Durdock (NIEHS)
- Nicole Kleinstreuer (NIEHS)
- Nigel Walker (NIEHS)
- Penelope Rice (FDA/CFSAN)
- Miao Li (FDA/CFSAN)

NICEATM Support Staff (Inotiv)
- Emily N. Reinke
- David Allen
- Alex Borrel
- Oluwakemi Oyetade

PFAS WG Charges

- Evaluate the state of the science of current PFAS definitions and groupings,
- Assess the utility of NAMs currently being used by national and international regulatory agencies for testing and risk assessment of specific PFAS based on case examples of successful application of certain NAMs
- Identify research challenges and data gaps for the use of specific NAMs for testing and risk assessment of different PFAS
- Identify NAMs that have not been used for PFAS and explore opportunities for expanding their application for their testing and risk assessment

PFAS WG Deliverables

- Interim (timeline: up to a year) – a brief state of knowledge **white paper** or report (up to 10 pages) on definitions and groupings of PFAS, current NAMs used for testing and risk assessment of specific PFAS and the overarching challenges and data gaps for applying NAMs for PFAS.
  - In progress – Draft Outline completed, initial text development ongoing

- Follow up (timeline: 1-1.5 years) – a **workshop or conference session** on application of different NAMs for specific PFAS, specifically broken up into three sections/segments: successes, challenges and opportunities of expanding the utility of NAMs for different PFAS.

- Long term (timeline: 2-3 years) – a **manuscript** to be published in a scientific journal that discusses outcome of the workshop followed by a description of challenges and data gaps for applying NAMs for different PFAS, and ideas to overcome these challenges with specific case examples based on NAMs identified after performing a deeper dive of published literature and regulatory efforts over the years.

Thank you for your time and attention!

Email:

Shruti.Kabadi@fda.hhs.gov