The comments in this presentation are those of the Validation Workgroup. They have not been reviewed or approved by, and may not necessarily reflect the views of any federal agency.

Validation Workgroup

SACATM

September 21, 2023

The comments in this presentation are those of ICCVAM. They have not been reviewed or approved by, and may not necessarily reflect the views of any federal agency.

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 Authorization Act of 2000: To establish, wherever feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new and revised toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing (3Rs) animal tests and ensuring human safety and product effectiveness.

7 Regulatory 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

*Other participants include:
NCATS, Tox21 Representatives, and NICEATM

10 Research Agencies

Agency for Toxic Substances and Disease Registry
National Institute for Occupational Safety and Health
National Cancer Institute
National Institute of Environmental Health Sciences
National Library of Medicine
National Institutes of Health
Department of Defense
Department of Energy
National Institute of Standards and Technology
Veterans Affairs Office of Research and Development

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

Validation Workgroup Roster

ATSDR	Moiz Mumtaz, PhD
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EPA/ORD	Nisha Sipes, PhD
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FDA/CFSAN	Suzanne Fitzpatrick, PhD, DABT (Co-chair)
FDA/CFSAN	Anneliese Striz, PhD
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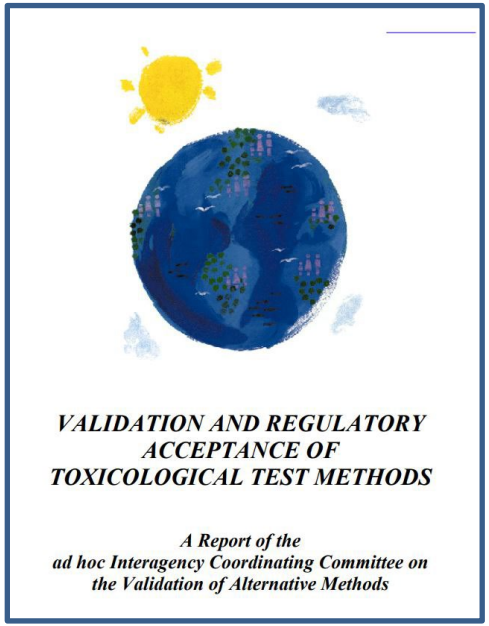
NIEHS	Warren Casey, PhD, DABT
NIEHS	Nicole Kleinstreuer, PhD
NIST	Elijah Petersen, PhD (Co-chair)
OSHA	Janet Carter, MS, MPH

NICEATM Support Staff:

Inotiv	Amber Daniel, MTox
Inotiv	David Allen, PhD
Inotiv	Michaela Blaylock

ICCVAM: Validation Workgroup

Updating the ICCVAM Report



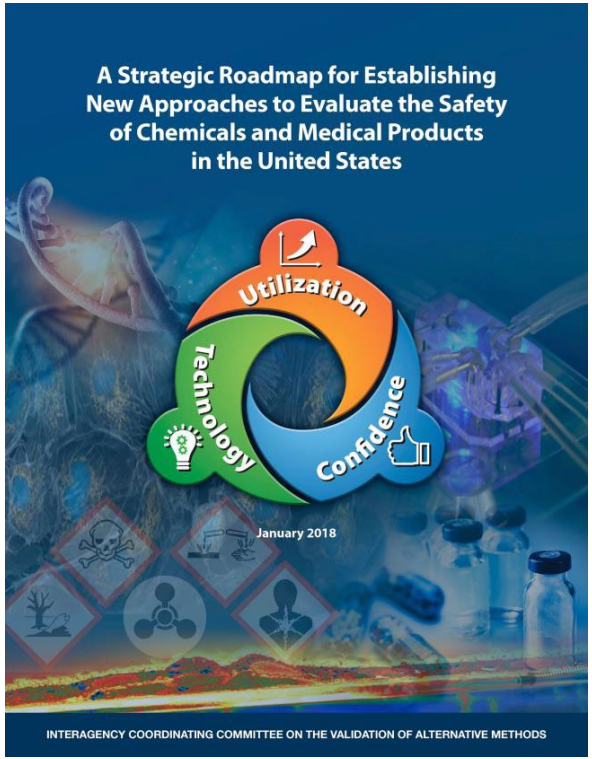
NIH PUBLICATION NO: 97-3981

National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina 27709

National Institutes of Health
U.S. Public Health Service
Department of Health and Human Services

March 1997

"Advances in science and technology have not been effectively leveraged to predict adverse human health effects"

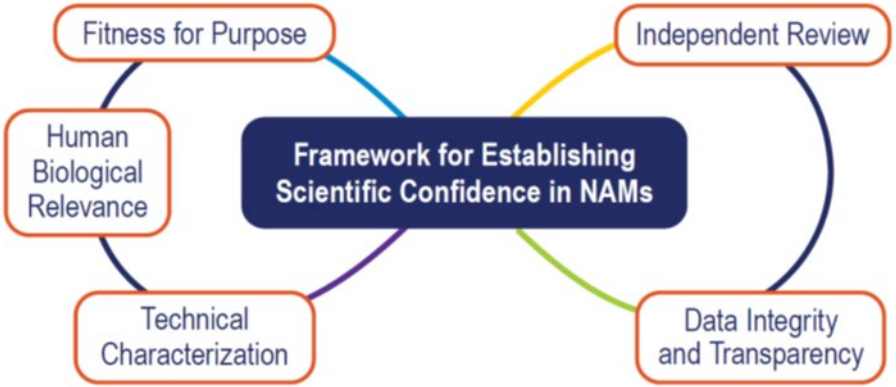


Help end users guide the development of the new meth

Use effi nt and ible appr ches to establish confidence in new m hods

Encourage the adoption of new methods by federal Agencies and regulated industries

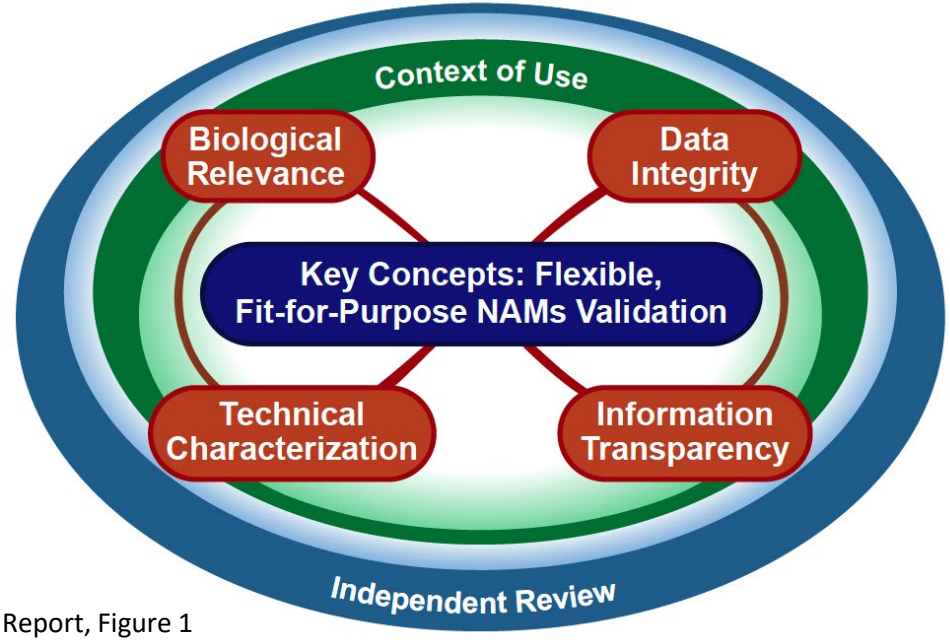
ICCVAM Roadmap: Inspiring papers on how to increase confidence:



van der Zalm et al. 2022 Arch Tox

A. Harrill , EPA NAMs Conference, Oct 2022

Key Concepts to Consider During Development and Implementation of Flexible, Fit for Purpose NAMs Validation Strategies



Final Draft ICCVAM Validation Report, Figure 1
(adapted from van der Zalm et al. 2022 Arch Tox)

Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies

A Report of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Validation Workgroup

Topics of Consideration

1. Foster the use of efficient, flexible, and robust practices to establish confidence in new methods

2. Developing and evaluating flexible practices that consider context of use to build confidence in new methods

3. Recommendations to facilitate regulatory acceptance

4. Determine how new principles of validation can fit into a globally harmonized approach to allow for continued mutual acceptance of data

Topics of Consideration

5. Reference existing and well-vetted documents (e.g., GIVIMP, OECD GD34, GD69 on QSAR Validation, FDA Guidance for Industry, etc.)

6. Outlining best laboratory practices

7. Examining best practices for quality and quality systems development

Validation Work Group

- Scope and Charges were developed in March of 2021.
- Completed the draft version of the document in August 2023
- The document was cleared by all participating federal agencies.
- The Federal Registry notice was published on August 10th, 2023.
- The document went out for Public Comments August 10th, 2023.
- Public comment period ended September 5th, 2023.

Public Comments: Terminology

- NAM definition
- “predictive” vs. “protective”
- “validation” vs. “qualification”
- Use of flexible vs prescriptive language
  - i.e. some commenters asking for use of the term “required”
- “as good as or better” concept

Public Comments: Role of ICCVAM

- Communication amongst stakeholders
- Ensuring clear and up-to-date communication from agencies
- 5 Cs (confidence, collaboration, clarity, communication, commitment…)
- Clarify in executive summary the role of this guidance to support diverse needs across agencies and the importance of communicating directly with individual agencies

Public Comments: Context of Use (COU)

- How to expand COU?

- What information and evaluation are needed to expand an existing COU?

Public Comments: Additional Topics for Discussion

- Transferability and/or interlaboratory evaluation: when is it needed?
- Biological relevance
  - How to integrate diverse evidence streams?
  - Necessity for AOPs?
- How to transparently describe animal reference data to set expectations for assessing the performance of NAMs?
- Comments around need for standards or use of “good practices”.

Thank You.