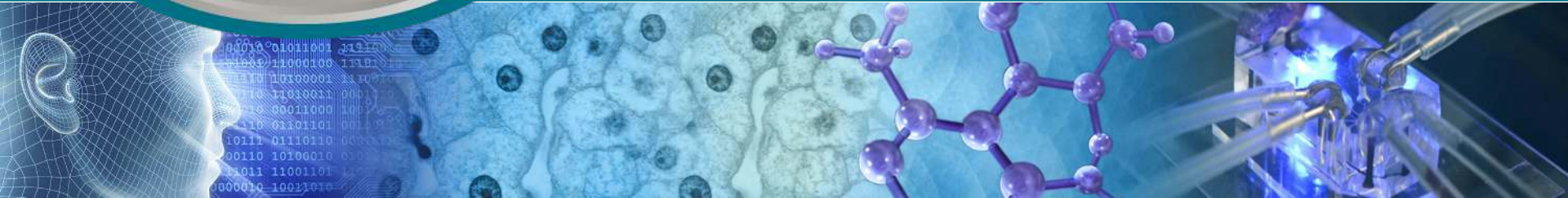




Interagency Coordinating Committee on the Validation of Alternative Methods



US Interagency Strategic Plans

Warren Casey, PhD, DABT
Director, NICEATM

May 30, 2019

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 Institute of Standards and Technology • National Institutes of Health • National Cancer Institute • National Library of Medicine
National Institute of Environmental Health Sciences • Occupational Safety and Health Administration



NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

NICEATM

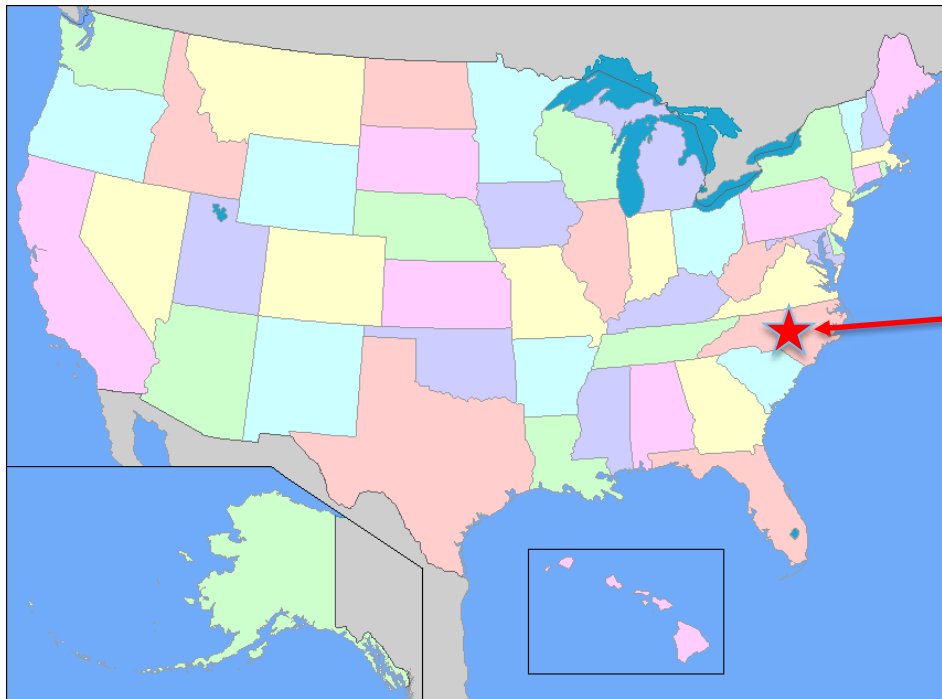


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Interagency Coordinating Committee on the Validation of Alternative Methods



ICCVAM

- [Agency for Toxic Substances and Disease Registry](#)
- [Consumer Product Safety Commission](#)
 - [Recommended Procedures Regarding the CPSC's Policy on Animal Testing](#)
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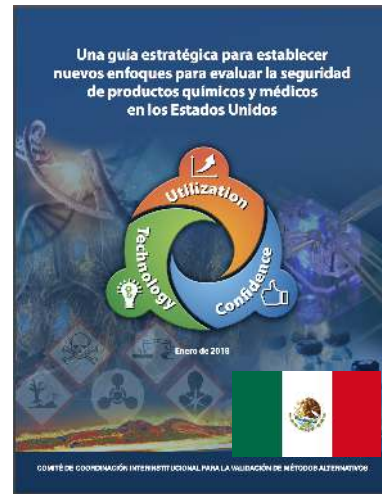
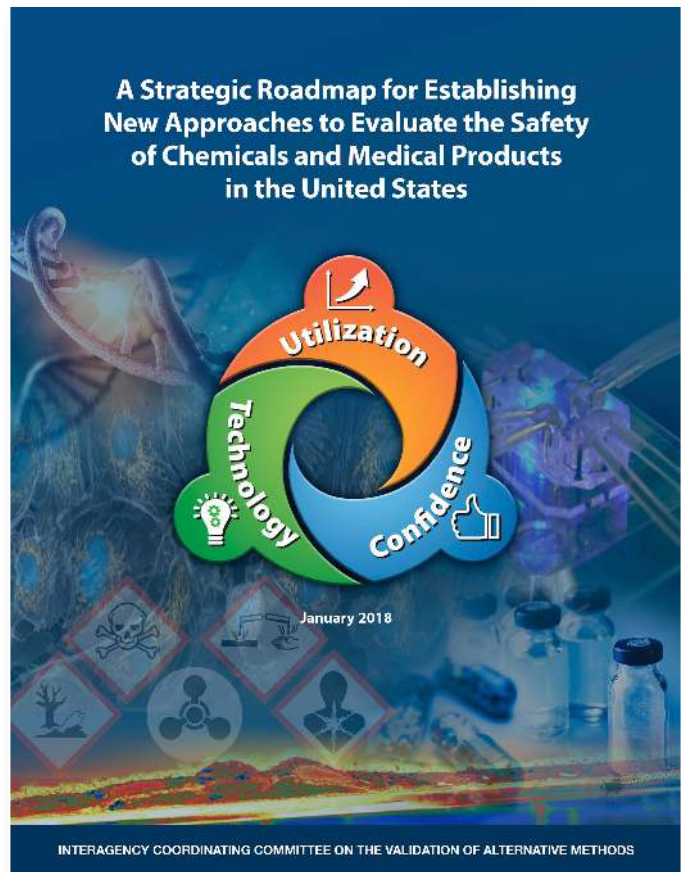
ICCVAM



NICEATM



NICEATM supports ICCVAM





Encourage the adoption of new methods

Help end-users guide the
development of the new methods

Use efficient and flexible approaches to establish
confidence in new methods



US Agencies must:

- **Identify** testing requirements



Identifying Testing Requirements



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 Kleinstreuerⁱ, Warren Casey^j



International regulatory requirements for skin sensitization testing

Amber B. Daniel^a, Judy Strickland^{a,*}, David Allen^a, Silvia Casati^b, Valérie Zuang^b, João Barroso^b, Maurice Whelan^b, M.J. Régimbald-Knel^c, Hajime Kojima^d, Akiyoshi Nishikawa^d, Hye-Kyung Park^e, Jong Kwon Lee^e, Tae Sung Kim^e, Isabella Delgado^f, Ludmila Rios^g, Ying Yang^h, Gangli Wangⁱ, Nicole Kleinstreuerⁱ



Alternative approaches for acute inhalation toxicity testing to address global regulatory and non-regulatory data requirements: An international workshop report

Amy J. Clippinger^{a,*}, David Allen^b, Annie M. Jarabek^c, Marco Corvaro^d, Marianna Gaça^a, Sean Gehen^a, Jon A. Hotchkiss^a, Grace Patlewicz^b, Jodie Melbourne^a, Paul Hinderliter^a, Miyoung Yoon^a, Dongeun Huh^a, Anna Lowit^a, Barbara Buckley^c, Michael Bartels^m, Kelly Bérubé^o, Daniel M. Wilson^a, Ian Indans^a, Mathieu Vinken^a



- Each paper identifies requirements, needs, and decision contexts
- To date: acute systemic toxicity, skin sensitization, and skin/eye irritation published or in press
- ICCVAM is actively compiling the regulations and guidance used by federal agencies in the assessment of DART

US Agencies must:

- **Identify** testing requirements
- Provide clear language regarding the **validation** and **acceptance** of NAMs



Related Topics: [Pesticide Science and Assessing Pesticide Risks](#) | [Risk Assessment](#)

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Strategic Vision for Adopting 21st Century Science Methodologies

Related Topics: [Pesticide Science and Assessing Pesticide Risks](#)

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Process for Establishing & Implementing Alternative Approaches to Traditional in Vivo Acute Toxicity Studies

Assessing and Managing Chemicals under TSCA

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How EPA Evaluates the Safety
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Prioritizing Existing
Chemicals for Risk Evaluation

Alternative Test Methods and Strategies to Reduce Vertebrate Animal Testing



U.S. FOOD & DRUG
ADMINISTRATION

FDA'S PREDICTIVE TOXICOLOGY ROADMAP

Dec 2017

Qualification of Medical Device Development Tools

Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

Document issued on: August 10, 2017

US EPA Office of Pesticides and US EPA Office of Toxics (Chemicals) are now accepting waivers using in vitro methods in place of LLNA

“Given the substantial scientific evidence and international activities supporting the new methodologies for skin sensitization testing, EPA will begin accepting these approaches immediately under the conditions described in the draft policy document.”





US EPA Office of Pesticides now accepts waivers for dermal LD50 testing

Pesticides

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[Biopesticides](#)

[Freedom of Information Act Requests](#)

New EPA Guidance for Testing Pesticides Will Reduce Animal Testing

For Release: November 29, 2016

US Agencies must:

- **Identify** testing requirements
- Provide clear language regarding the **validation** and **acceptance** of NAMs
- Promote **International Harmonization**



The International Cooperation on Alternative Test Methods (ICATM)



- Promote international cooperation in the areas of:
 - validation studies,
 - independent peer review, and
 - development of harmonized test methods and recommendations.

6 Most Common Toxicity Test

- Acute oral
- Acute dermal
- Acute inhalation
- Eye irritation
- Skin irritation
- Skin sensitization

U.S. Strategic Roadmap

Introduction

Implementation

Acute Systemic Toxicity

Skin and Eye Irritation

Skin Sensitization

Development

Contributors

References

Strategic Roadmap: Implementation

View details of ongoing and planned activities for implementation of the Strategic Roadmap in the following areas:

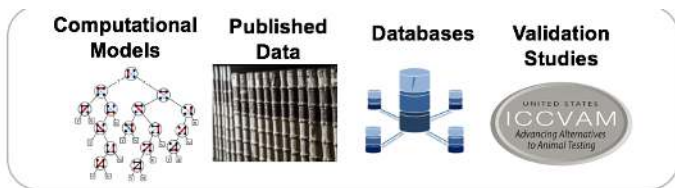
- [Acute Systemic Toxicity](#)
- [Eye and Skin Irritation](#)
- [Skin Sensitization](#)

ICCVAM establishes temporary ad hoc workgroups to perform specific tasks identified by the committee as being important for the development or validation of new approach methodologies, and it is envisioned that ICCVAM workgroups will play a key role in implementing the goals of the strategic roadmap. The workgroups are chaired by representatives from agencies that use or require data from the topic of interest. The chairs are responsible for developing the group's scope and charge, which is then reviewed and approved by ICCVAM. ICCVAM member agencies and partners in the [International Cooperation on Alternative Test Methods](#) (EURL ECVAM, JaCVAM, KoCVAM, and Health Canada) are then invited to participate in the workgroup.

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<https://ntp.niehs.nih.gov/go/838279>





National Toxicology Program
U.S. Department of Health and Human Services

Integrated Chemical Environment

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Search:

Selected Reference Lists: ICCVAM Chemicals Data 2019: ICCVAM Chemicals Data 2019

Substance Name	CASRN	Chemical Structure
Organotin	20539-75-5	<chem>CC(C)(Cl)C(=O)Nc1ccc(Cl)cc1</chem>
Hydroquinone	106-66-6	<chem>Oc1ccc(O)cc1</chem>
Trifluoromethane	75-91-9	<chem>FC(F)(F)C</chem>
Isobutyl alcohol	108-10-1	<chem>CC(C)CO</chem>

Chemical Breakdown

Number of Unique Chemicals

Acute Oral Toxicity: 100
Skin Sensitization: 100
Skin Irritation: 100
Eye Irritation: 100
Endocrine: 100
In vitro (all): 100
In vitro: 100

Chemicals

3 chemical reference lists loaded

Enter one CASRN per line



**Integrated
Chemical
Environment**

Making Data and Tools Available



**Download
reference lists**



Export queries



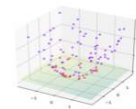
**Link to other
resources**



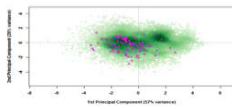
Run workflows



**In vitro to in vivo
extrapolation**



Machine learning



**Chemical space
characterization**

And more coming spring 2019...





Questions?

warren.casey@nih.gov

nicole.kleinstreuer@nih.gov