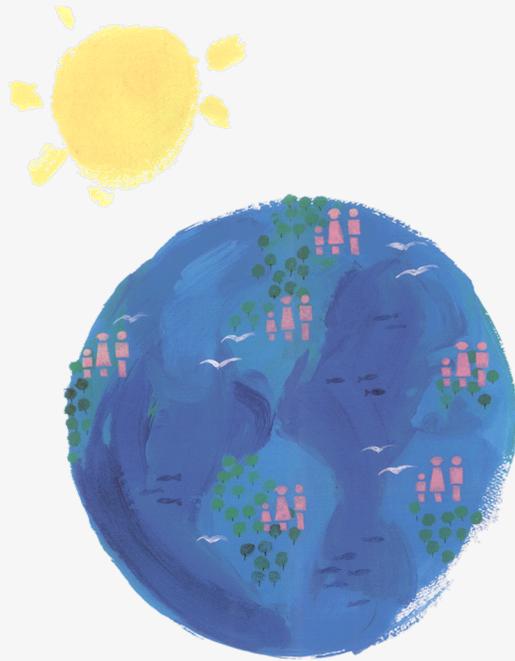


NICEATM

*National Toxicology Program
Interagency Center for the Evaluation of
Alternative Toxicological Methods*

ICCVAM

*Interagency Coordinating Committee on
the Validation of Alternative Methods*



ICCVAM and NICEATM: The First Ten Years

**William S. Stokes, D.V.M., D.A.C.L.A.M
RADM, U.S. Public Health Service
Director, NICEATM**

**ICCVAM Ten-Year Anniversary Symposium
February 5, 2008
U.S. Consumer Product Safety Commission
Bethesda, MD**



National
Toxicology
Program



NIEHS



Acknowledgements: The First Ten Years

- ICCVAM members
- ICCVAM Test Method Working Groups
- NICEATM staff and support contract
- Workshop participants
- Advisory Committee members
- Expert Panel and Peer Review Panel members
- Stakeholder Participants: Industry, government, academe, animal protection and public interest groups, public citizens
- Test method developers
- ECVAM
- JaCVAM



Pre-ICCVAM History: 1993-1997

- 1993 NIH Reauthorization Act (P.L. 103-43)
- 1994 *ad hoc* ICCVAM established in response to NIEHS directives:
- *Develop criteria for validation and regulatory acceptance of test methods*
 - *Develop a process to achieve regulatory acceptance of scientifically validated methods*
- 1995 International Workshop: *Validation and Regulatory Acceptance of Toxicological Test Methods*
- 1997 Final report of the *ad hoc* ICCVAM
ICCVAM established
- Replaced *ad hoc* ICCVAM
 - Implemented NIEHS directives: P.L. 103-43



The ad hoc ICCVAM: 15 Agencies

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

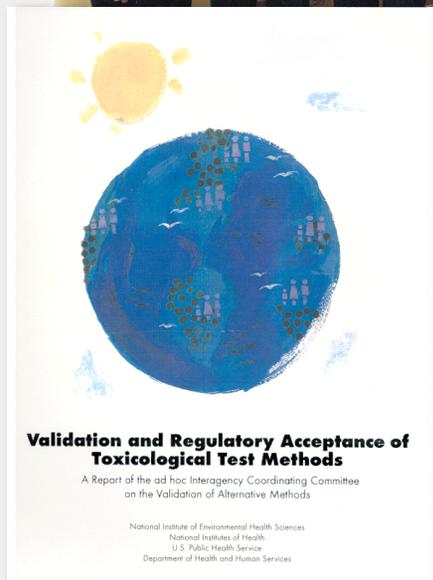


Research Agencies

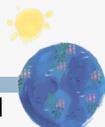
- Agency for Toxic Substances and Disease Registry
- National Institute for Occupational Safety and Health
- National Cancer Institute
- National Institute of Environmental Health Sciences
- National Library of Medicine
- National Institutes of Health
- Department of Defense
- Department of Energy



Workshop on Validation and Regulatory Acceptance of Toxicological Test Methods



- December, 1995
- Open public meeting
- Scientists and stakeholders from international community
- Recommendations
 - Criteria for validation and regulatory acceptance
 - Process to achieve regulatory acceptance



ICCVAM's Mission¹

- To *facilitate* development, validation and regulatory acceptance of new and revised regulatory test methods that
 - Reduce, refine, and replace the use of animals in testing
 - Maintain and promote scientific quality and the protection of human health, animal health, and the environment



¹Adopted by ICCVAM February 2004

All of ICCVAM's activities are grounded in the U.S. Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training

<http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples>



Alternative Methods for Allergic Contact Dermatitis: The LLNA



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Methods

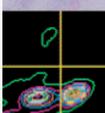
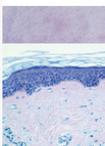
**Independent Scientific Peer Review:
Validation Status of the Murine Local
Lymph Node Assay for the Assessment
of the Contact Dermatitis Potential of
Chemicals and Products**

March 4-6, 2008
U.S. Consumer Product Safety Commission Headquarters
Bethesda, MD

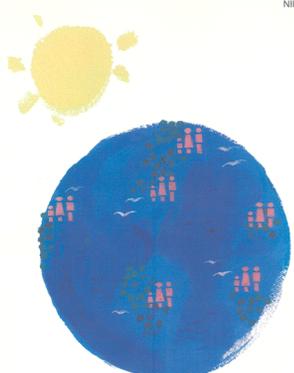
The public is invited to
submit comments on
information and to register
<http://iccvam.niceatm.gov>

ICCVAM Agencies:

- Agency for Toxic Substances and Disease Registry
- Consumer Product Safety Commission
- Department of Agriculture
- Department of Defense
- Department of Energy
- Food and Drug Administration
- National Cancer Institute
- Department of Transportation



NIH Publication No: 99-4494



The Murine Local Lymph Node Assay:
A Test Method for Assessing the Allergic Contact Dermatitis Potential of Chemicals/Compounds

Results of an Independent Peer Review Evaluation Coordinated by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

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

- Murine Local Lymph Node Assay-1998
 - Avoids pain and distress
 - Valid substitute for traditional guinea pig tests
- A reduction and refinement success
- 2008-- ICCVAM Evaluation
 - Non-radioactive methods

Alternative Methods for Acute Oral Toxicity Testing

Scientific Workshop on Acute Chemical Safety Testing: Advancing *In Vitro* Approaches and Humane Endpoints for Systemic Toxicity Evaluations

NICEATM
National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods

ECVAM - European Centre for the Validation of Alternative Methods

ICCVAM
Interagency Coordinating Committee on the Validation of Alternative Methods

JaCVAM - Japanese Center for the Validation of Alternative Methods



This workshop will explore how to improve our understanding of key pathways involved in acute systemic toxicity and application of this knowledge to develop new *in vitro* methods and humane endpoints that will further reduce, refine, and eventually replace animal use for chemical safety testing.

February 6-7, 2008 | NIH - Natcher Conference Center | Bethesda, MD

For more information and to register, please contact NICEATM:
http://iccvam.niehs.nih.gov
910.541.2354
nicvatm@niehs.nih.gov

ICCVAM Agencies:
• Agency for Toxic Substances • National Institute for Occupational Safety and Health

Putting Acute Oral Toxicity Testing Guidelines into Practice:

A Training Workshop

February 19-21, 2002

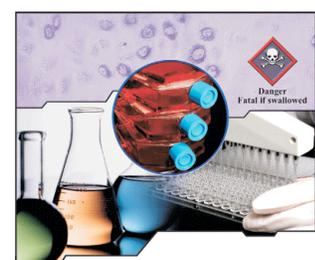
Natcher Conference Center
National Institutes of Health
Bethesda, Maryland USA

Organized by:

- ILSI Risk Science Institute (ILSI RSI)
- U.S. Environmental Protection Agency (USEPA)
- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)



NIH Publication No: 07-4519



ICCVAM TEST METHOD EVALUATION REPORT

***In Vitro* Cytotoxicity Test Methods for Estimating Starting Doses for Acute Oral Systemic Toxicity Tests**

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

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

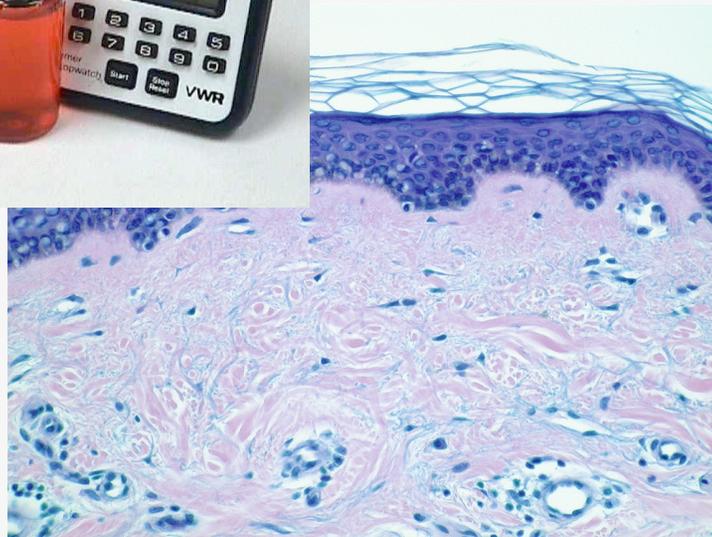
National Institute of Environmental Health Sciences
National Institutes of Health
U. S. Public Health Service
Department of Health and Human Services

- Revised Up-and-Down Procedure, 2001
 - Reduces animal use by 70%
- *In vitro* methods recommended to further reduce animal use up to 50% per test
- February 6-7, 2008 Workshop:
 - *Advancing In Vitro Approaches and Humane Endpoints for Systemic Toxicity Evaluations*

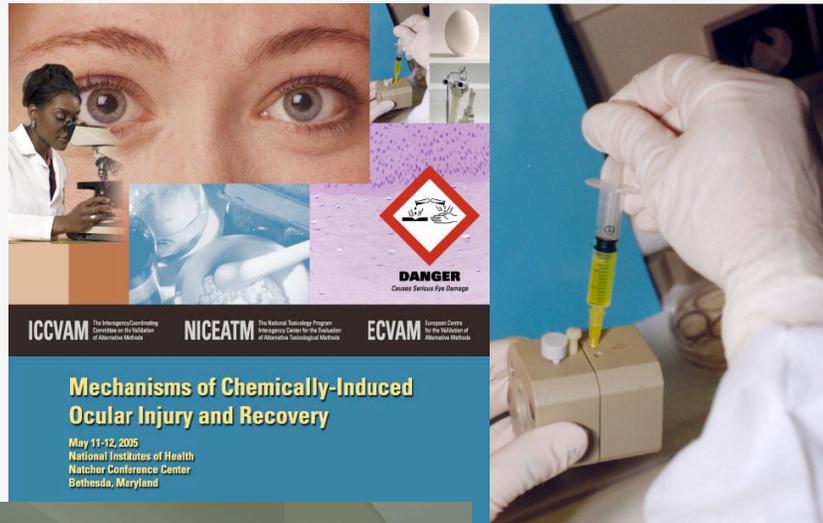
ICCVAM Evaluation of *In Vitro* Methods for Skin Corrosivity



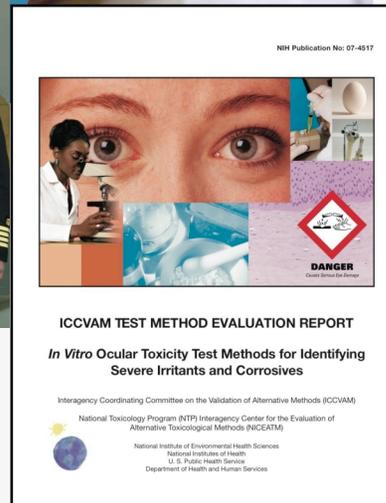
- Corrositex, 1999
- Epiderm, Episkin, Rat skin TER, 2002
- Performance Standards, 2004



Alternative Methods for Ocular Safety Testing

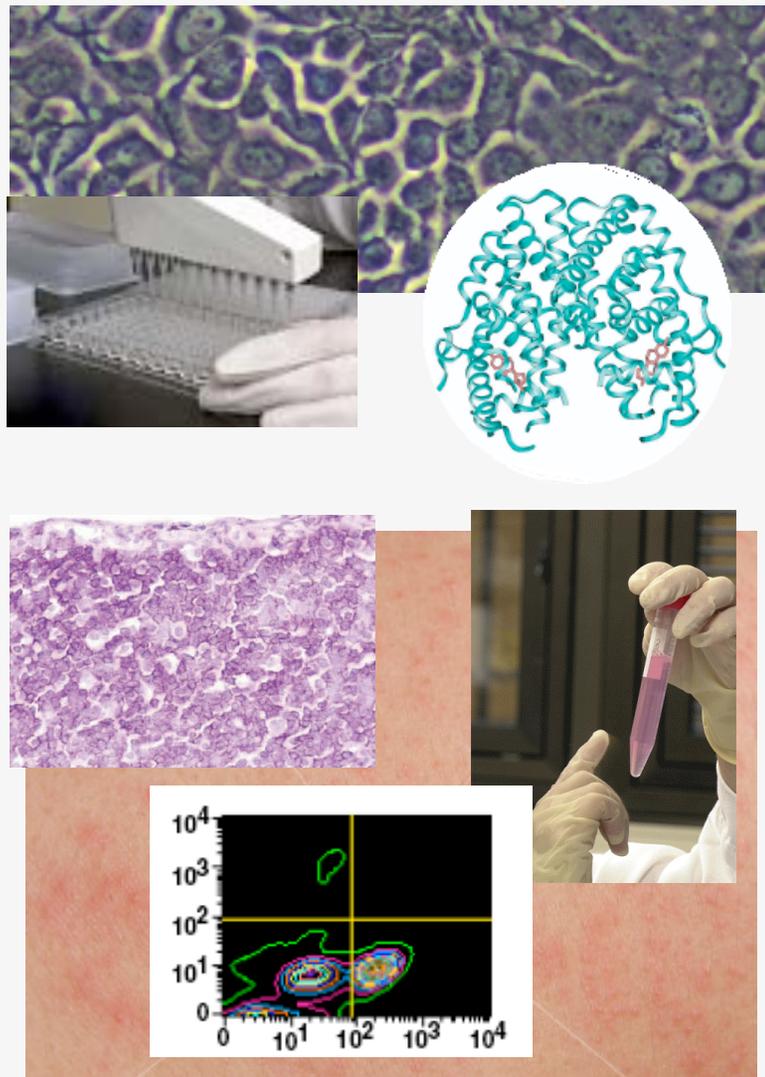


- ICCVAM Scientific Symposia
 - Mechanisms of Chemically-Induced Ocular Injury and Recovery
 - Minimizing Pain and Distress
 - Recommendations for R&D, validation, and data collection



- In Vitro test methods for identifying severe and irreversible eye damage
 - Forwarded to agencies, 2007

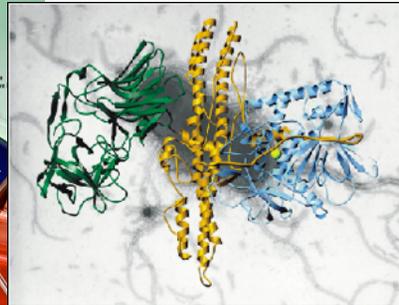
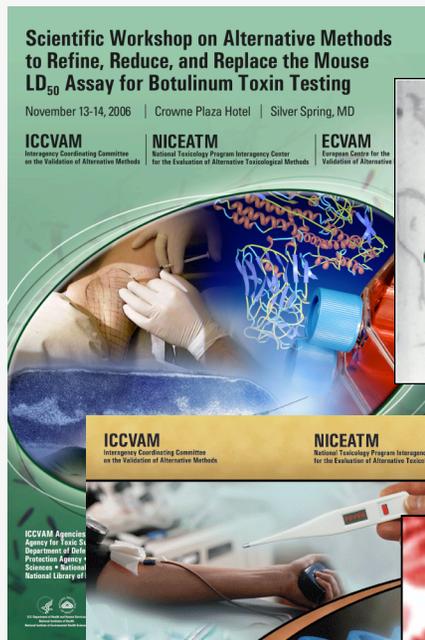
Addressing Other Agency Test Method Priorities



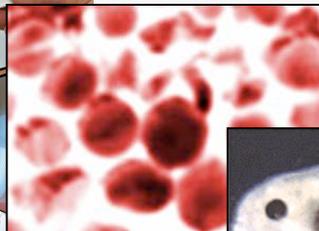
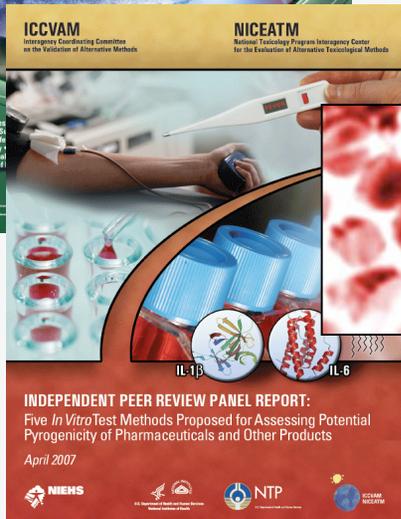
- In Vitro Methods for EPA's Endocrine Disruptor Screening Program - EPA
 - Guidance for validation
 - International validation study underway: NICEATM-ICCVAM, ECVAM and JaCVAM
 - Performance Standards



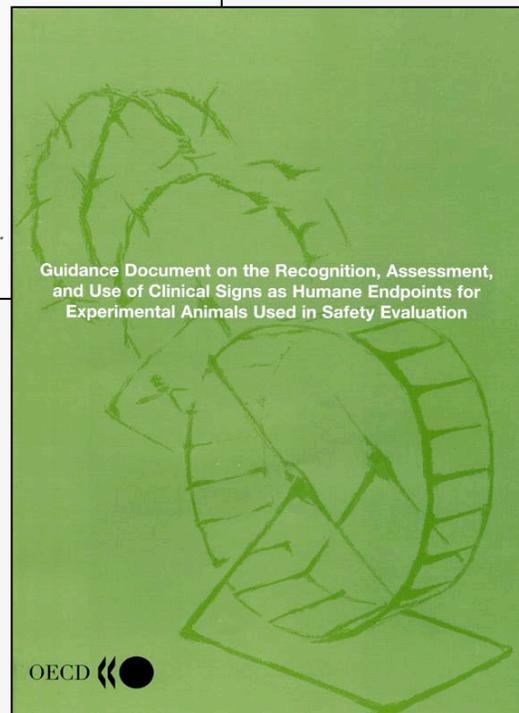
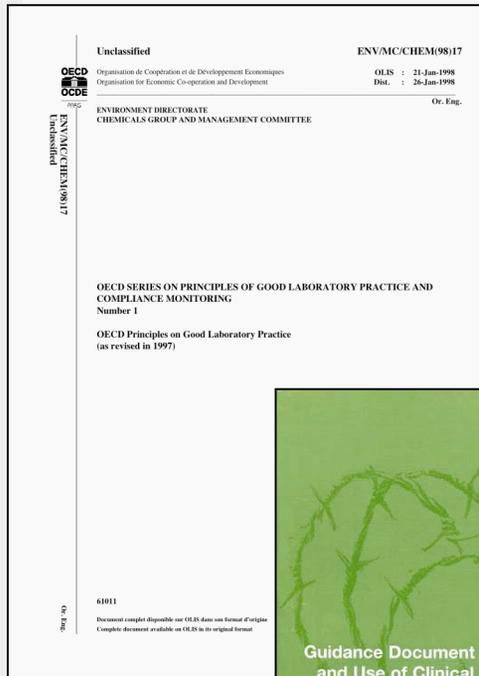
Other Nominations for Workshops and Test Method Evaluations



- Workshop on Alternatives for Botulinum Toxin Testing - HSUS
- Evaluation of 5 *In vitro* Pyrogenicity Methods - ECVAM
- Evaluation of FETAX -- EPA



International Guidance for Alternative Test Methods: ICCVAM Contributions



- OECD Guidance Document on Humane Endpoints, 2000
- OECD Guidance Document on Validation and Acceptance, 2005
- OECD Guidance on Application of Good Laboratory Practices to *In Vitro* Test Methods, 2005



ICCVAM: The First Ten Years

- Over 185 test methods evaluated since 1997
- Alternative methods recommended for the four most common product safety tests
 - Regulatory acceptance as national and international test guidelines
- Recommended R&D, translation, and validation activities to advance alternative methods for many testing areas
- Performance standards to expedite validation studies and regulatory acceptance
- International guidance documents
- International partnerships: ECVAM & JaCVAM



Thank you for your attention!



***ICCVAM-NICEATM:
Advancing Public Health and Animal Welfare***