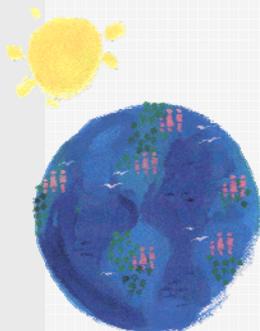


NICEATM

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

ICCVAM

Interagency Coordinating Committee on
the Validation of Alternative Methods



ICCVAM/NICEATM 5-Year Plan

Leonard M. Schechtman, Ph.D.
Chair, ICCVAM
Deputy Director, Washington Operations
National Center for Toxicological Research
US Food and Drug Administration

Scientific Advisory Committee on Alternative Toxicological Methods
(SACATM)

November 30, 2006
NIEHS, Research Triangle Park, NC



ICCVAM Authorization Act of 2000

(P.L. 106-545)*

→ *an Act 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*

***Congressional passage: December 19, 2000**

ICCVAM's Mission*

- ➔ 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 while maintaining and promoting scientific quality and the protection of human health, animal health, and the environment

* Adopted 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
[\[http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples\]](http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples)

3



ICCVAM's Vision* (1)

- To be recognized as a leading authority on test method development and validation both within the federal government and internationally

* Adopted by ICCVAM February 2004

4



ICCVAM's Vision* (2)

■ To play a leading role in:

- Promoting high quality science as the basis of national & international regulatory policy
- Setting and harmonizing international standards for scientific validation of test methods
- Promoting and facilitating the development of priority alternative test methods
- Identifying key alternative test methods and strategies and facilitating their validation and acceptance
- Fostering humane and ethical approaches to testing that replace, reduce, and refine the use of animals
- Promoting awareness and adoption of scientifically validated test methods by regulatory agencies both nationally & internationally

*Adopted by ICCVAM February 2004

5



ICCVAM's Vision* (3)

■ To develop the internal and collaborative capacity to:

- Ensure the scientific quality and integrity of its work
- Implement reliable processes and operating procedures that are credible, effective & efficient
- Build national and international partnerships with governmental and nongovernmental groups, including academia, industry, advocacy groups, and other key stakeholders
- Secure the necessary human and financial resources to effectively carry out its mission

*Adopted by ICCVAM February 2004

6



FY07 Senate Appropriations Report (1)

- Acknowledges completion of the NTP Roadmap, *Roadmap to Achieve the NTP Vision, A Toxicology Program for the 21st Century*
 - NTP commits to “develop and validate improved testing methods and, where feasible, ensure that they reduce, refine or replace the use of animals.”
- Requests NICEATM/ICCVAM to build on the NTP Roadmap

7



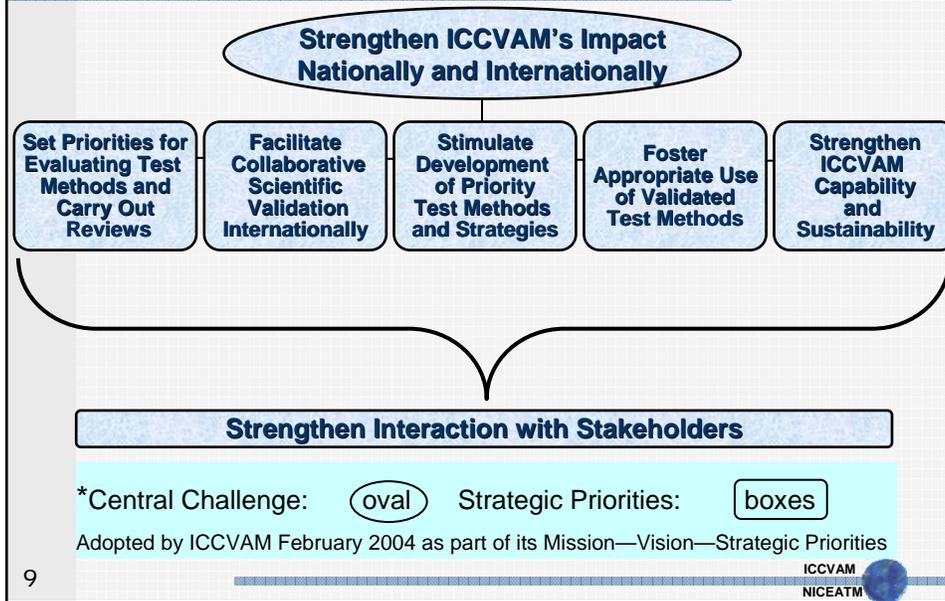
FY07 Senate Appropriations Report (2)

- Requests NICEATM/ICCVAM to create 5-year plan to:
 - **Research, Develop, Translate, and Validate**
 - new and revised non-animal and other alternative assays for integration of relevant and reliable methods into the Federal agency testing programs
- Expectations of Federal agency program offices:
 - **Identify areas of high priority** for new and revised non-animal and alternative assays or batteries of those assays to create a path forward for the 3Rs, when this is scientifically valid and appropriate
- Requests submission of the plan by November 15, 2007

8



ICCVAM Strategic Map*



9

Key Considerations for Plan Development

- **Provide opportunity for Federal agency input**
 - During the draft plan preparation phase
 - On the draft plan itself
 - Through the drafting activities by the ICCVAM 5-Year Plan Subcommittee
 - Through active solicitation (email, listserv) for input
 - Through review and commenting on draft plan
 - Through discussion during ICCVAM meetings and telecons
- **Provide opportunity for public input**
 - During the draft plan preparation phase
 - During the draft plan commenting period
 - Through FR notice request
 - Through comments voiced at SACATM public meeting (November 30, 2006)
- **Provide opportunity for SACATM input**
 - During the draft plan preparation phase
 - During the draft plan commenting period
 - Through active solicitation (emailing of questions and request for comments)
 - Through SACATM public meeting (November 30, 2006)
- **Complete the Plan by September 24, 2007**

10

ICCVAM
NICEATM

ICCVAM August 26, 2006 Meeting

- **Reviewed Senate/House Language**
- **Endorsed formation of ICCVAM Work Group to develop the requested 5-Year Plan**
- **Work Group Members:**
 - Dr. Allan Poland (NCI), Subcommittee Chair
 - Dr. Dave Hattan (FDA)
 - Dr. Abigail Jacobs (FDA)
 - Dr. Amy Rispin (EPA)
 - Dr. Leonard Schechtman (FDA), ICCVAM Chair
 - Dr. Margaret Snyder (NIH)
 - Dr. William Stokes (NIEHS)
 - Dr. Marilyn Wind (CPSC), ICCVAM Vice-Chair

11



ICCVAM October 25, 2006 Meeting

- **Endorsed Revised Timeline**
 - Developed to meet NIEHS constraint to send Final Report up Budget channels by September 24, 2007
- **Endorsed Revised SACATM/Public Questions**
 - Also developed in concert with NIEHS
- **Endorsed FR notice and memorandum to Agencies for information**

12



Information Requested from Agencies

- Agency (1) activities and (2) priorities relevant to new or revised test methods or strategies that will provide for the refinement (less pain and distress), reduction, and replacement of animal use in federal agency testing programs

13



Agency Activity Information Sought

1. Information regarding research, development, translation, and validation activities currently in progress or planned during the next five years
 - Title of activity
 - Type of activity (i.e., research, development, translation, validation)
 - Brief description of the activity
 - The federal agency testing requirement for which the activity is relevant (e.g., ocular irritation, reproductive toxicity, acute oral toxicity)
 - Brief description of how the activity is expected to potentially contribute to reduced animal use, replacement of animal use, or refinement (reduced pain and distress)
 - Organizational unit and staff contact for the activity
 - Any relevant supplemental information that might be helpful (publications, reports, etc.)

14



Agency Priority Information Sought

2. Information regarding areas of high priority for new and revised non-animal and alternative assays or batteries of those assays to create a path forward for the replacement, reduction, and refinement (less pain and distress) of animal tests, when this is scientifically valid and appropriate
 - A rank-ordered list of the priority areas
 - A description of the endpoints or specific testing requirements
 - A brief description as to the priority for the activity, i.e. refinement (less pain and distress), reduction, and/or replacement
 - Activities from the above list relevant to the priority area

15



5-Year Plan Timeline (2006)

Phase 1: Obtain Initial Comments

- Aug 23 Work Group established by ICCVAM
- Oct 25 Work Group recommendations presented to ICCVAM
- Oct 26 Questions sent to SACATM for comments and response
- Oct 30 Request sent to agencies for input
- Nov 9 FR notice requesting public comments
- Nov 30 SACATM public meeting: SACATM/Public comments
- Dec 31 Deadline for public and SACATM comments

16



5-Year Plan Timeline (2007)

Phase 2: Prepare Draft Plan

- Jan 5 SACATM and Public comments forwarded to ICCVAM
- Feb 5 Deadline for Agency responses
- Feb 5 ICCVAM Work Group/NICEATM prepare draft
- Mar 20 Draft submitted to ICCVAM for agency review and comment
- Apr 4 Initial ICCVAM comments due back
- Apr 11 ICCVAM Work Group/NICEATM submits revised draft plan to ICCVAM
- Apr 25 ICCVAM Meeting: ICCVAM discussion and approval of Draft Plan for release to public/SACATM for comments

17



5-Year Plan Timeline (2007 cont'd.)

Phase 3: Prepare Final Plan

- May 12 FR notice announcing Draft ICCVAM Plan
 - Also provided to SACATM for comment
- Jun 12 SACATM Public Meeting: discussion of public comments and Draft ICCVAM Plan
- Jun 12 Deadline for public/SACATM comments on draft Plan
- Jun 13 ICCVAM Work Group/NICEATM begin preparation of draft Final Plan
- Jul 2 ICCVAM Work Group/NICEATM forward draft Final Plan to ICCVAM for agency review and comment
- Jul 25 ICCVAM Work Group/NICEATM submits revised Final Plan to ICCVAM

18



5-Year Plan Timeline (2007 cont'd.)

Phase 4: Approve & Distribute Final Plan

- Aug 8 ICCVAM Meeting: ICCVAM discussion and approval of Final Plan
- Aug 15 Final ICCVAM Plan sent to agencies for concurrence by September 15
- Sep 24 Final ICCVAM/NICEATM Plan sent to NIH Budget Office
- Nov 15 Final ICCVAM Plan forwarded to House and Senate Appropriations
- Nov 15 Public availability of the ICCVAM Final Plan announced
- Nov 29 SACATM Meeting: ICCVAM/NICEATM presents Final ICCVAM/NICEATM 5-Year Plan

19



ICCVAM 3Rs Test Method Priorities

- Areas identified and ranked by ICCVAM considered to be of highest priority for the development of alternative test methods for regulatory safety testing:
 1. Acute eye irritation/corrosion
 2. Biologics/Vaccines
 3. Acute skin toxicity (including irritation/corrosion, sensitization, absorption)
 4. Acute systemic toxicity (oral/dermal/inhalation)
 5. Chronic toxicity/carcinogenicity
 6. Reproductive/developmental toxicity
 7. Endocrine disruptors
 8. Neurotoxicity
 9. Immunotoxicity

20



Discussion Question for SACATM

(Lead Discussants: Drs. Marsman and Fox)

- 1. Considering available science and technology, what development, translation, and validation activities are most likely to have the greatest impact within the next five years on refining, reducing, or replacing animal use?**

21



Discussion Question for SACATM

(Lead Discussants: Drs. Cunningham and Charles)

- 2. What research and development activities hold the greatest promise in the long-term for refining, reducing, or replacing animal use?**

22



Discussion Question for SACATM
(Lead Discussants: Drs. Stephens and McClellan)

3. What are appropriate measures for evaluating progress in enhancing the development and use of alternative test methods?