

NTP Interagency Center for the Evaluation of Alternative Toxicological Methods

Year 2003

The National Toxicology Program (NTP) established the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) in 1998 to facilitate scientific review, development, and validation of new or revised toxicological test methods. NICEATM provides administrative support for the Interagency Coordinating Committee for the Evaluation of Alternative Methods (ICCVAM), an interagency coordinating committee, and collaborates with the ICCVAM to evaluate new, revised or alternative toxicological test methods of multi-agency interest that predict human health risks better than currently used methods while seeking to reduce, refine, or replace methods using animals. NICEATM also promotes communication and participation by the public and private sectors in ICCVAM activities. Dr. William S. Stokes serves as the NICEATM director. ICCVAM and NICEATM receive external input on their activities from the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM).

The National Institute of Environmental Health Sciences (NIEHS) originally established ICCVAM in 1994 in response to Public Law 103-43 and ICCVAM was designated a permanent NIEHS interagency coordinating committee under the NICEATM in December 2000 by enactment of the ICCVAM Authorization Act of 2000 (P.L.106-545). The purposes of ICCVAM as defined in the law are to

- increase the efficiency and effectiveness of Federal agency test method review,
- eliminate unnecessary duplicative efforts and share experiences between Federal regulatory agencies,
- optimize utilization of scientific expertise outside the Federal government,
- ensure that new and revised test methods are validated to meet the needs of Federal agencies, and
- reduce, refine, or replace the use of animals in testing, where feasible.

ICCVAM is composed of representatives from 15 federal regulatory and research agencies that generate, use, or provide information from toxicology test methods for risk assessment purposes.

ICCVAM Member Agencies

Agency for Toxic Substances and Disease Registry	Food and Drug Administration
Consumer Product Safety Commission	National Cancer Institute
Department of Agriculture	National Institute of Environmental Health Sciences
Department of Defense	National Institutes of Health, Office of the Director
Department of Energy	National Institute of Occupational Safety and Health
Department of Interior	National Library of Medicine
Department of Transportation	Occupational Safety and Health Administration
Environmental Protection Agency	

What is SACATM?

The SACATM is a federally chartered scientific advisory committee established January 9, 2002, to provide advice to the NIEHS Director, the ICCVAM, and the NICEATM concerning the duties of ICCVAM mandated by statute and the activities of the NICEATM. Specifically, the SACATM advises on priorities and directives related to the development, validation, scientific review, and regulatory acceptance of new or revised toxicological test methods and on ways to foster partnerships and communication with interested groups. The SACATM meets 2-3 times annually and has 15 members who serve rotating terms of up to 4 years. Additional information about the SACATM, including the membership roster, charter and summary minutes from its meetings, is available on the NICEATM/ICCVAM web site.

How Does the ICCVAM Evaluate Alternative Test Methods?

The ICCVAM follows a formal process for evaluating new or revised toxicological test methods and has developed specific guidelines *Validation and Regulatory Acceptance of Toxicological Test Methods, a Report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods* (NIH Publication No. 97-3981) to aid in their evaluation.

When adequate information is available for a new revised test method, the NICEATM with the ICCVAM convenes an independent scientific peer review panel. Expert scientists from industry, academia, government, and the international community serve on these panels. The panel is charged with developing recommendations about the validation status of proposed test methods, including their usefulness and limitations for generating information for specific human health and/or ecological risk assessment purposes. The NICEATM and ICCVAM also convene workshops and expert panel meetings to assess research, development, and validation efforts needed to advance promising new or revised toxicological test methods.

- The deliberations of all panels are conducted in public session with opportunities for public participation.
- Final reports are published, posted on the NICEATM/ICCVAM web site, and available for public comment.
- The final reports and any public comments are forwarded by NICEATM to the ICCVAM.

The ICCVAM makes recommendations as to scientific validity and acceptability of the proposed test method, and these recommendations, along with the panel reports and public comments, are forwarded to appropriate federal regulatory agencies for consideration. Each agency determines the acceptability of a method according to its own mandated statutes.

Test Method Evaluations

- An assessment of the Murine Local Lymph Node Assay (LLNA), a method for assessing the allergic contact dermatitis of chemicals, was completed in 1998. In 1999, EPA, FDA, and OSHA announced their acceptance of this assay, which can now be used as a substitute for traditional guinea pig tests. The LLNA was adopted as an international test guideline by the 30-member country Organization for Economic Cooperation and Development (OECD) in 2002.
- The review of Corrositex[®], an *in vitro* method for assessing the dermal corrosivity potential of chemicals, was completed in 1999 and has been accepted by regulatory agencies.
- The NICEATM completed an expert panel evaluation of the Frog Embryo Teratogenesis Assay in *Xenopus* (FETAX).
- A peer review panel was convened in July 2000 and August 2001 to evaluate the validation status of a revised Up-and-Down Procedure (revised UDP) for acute oral toxicity. The panel recommended the revised UDP as a substitute for the conventional LD50 test for hazard classification testing. The ICCVAM concurred with this recommendation and has forwarded test recommendations for transmittal to federal agencies.
- An expert panel meeting was held in May 2002 to evaluate *in vitro* test methods, including estrogen receptor and androgen receptor binding and transcriptional activation assays, for use in the EPA's Endocrine Disruptor Screening Program. The panel could not recommend any specific assay noting additional validation studies were needed for all assays. The panel recommended a proposed list of substances for validation of the assays.

NICEATM Workshops

- In October 2000 an international workshop was held to review and evaluate *in vitro* methods for assessing acute systemic toxicity. The workshop experts recommended *in vitro* cytotoxicity methods as one approach that could be used to estimate starting doses for *in vivo* acute toxicity studies. The goal was to reduce the number of animals needed for a study thus reducing the number of animals that receive highly toxic doses. The ICCVAM concurred with this recommendation and has forwarded test recommendations for transmittal to the appropriate federal agencies.
- NICEATM and ICCVAM in partnership with the EPA and the International Life Sciences Institute held a training workshop on alternative *in vitro* and *in vivo* acute toxicity testing methods in February 2002.
- NICEATM is currently conducting a multi-laboratory validation study on two *in vitro* methods for acute toxicity in collaboration with the European Center for the Validation of Alternative Methods (ECVAM).

**For additional information or specific questions about the NICEATM visit the NICEATM/ICCVAM web site at <http://iccvam.niehs.nih.gov> or contact: Dr. William S. Stokes, Director, NTP Interagency Center for the Evaluation of Alternative Toxicological Methods, NIEHS, P.O. Box 12233, MD EC-17, Research Triangle Park, NC, 27709
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