NATIONAL TOXICOLOGY PROGRAM

FACT SHEET

Headquartered at the National Institute of Environmental Health Sciences • NIH • DHHS

NTP INTERAGENCY CENTER FOR THE EVALUATION OF ALTERNATIVE TOXICOLOGICAL METHODS

Year 2005

The **N**ational **T**oxicology Program (NTP) established the **N**TP **I**nteragency **C**enter for the **E**valuation of **A**lternative **T**oxicological **M**ethods (NICEATM) in 1998 to facilitate scientific review, development, and validation of new, revised, and alternative toxicological test methods. NICEATM and provides administrative and scientific support for the **I**nteragency **C**oordinating **C**ommittee for the **E**valuation of **A**lternative **M**ethods (ICCVAM). It collaborates with the ICCVAM to evaluate new, revised, and alternative toxicological test methods that protect human and animal health and the environment while reducing, refining (less pain and distress), or replacing 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 advice on their activities from the **S**cientific **A**dvisory **C**ommittee on **A**lternative **T**oxicological **M**ethods (SACATM) (http://ntp.niehs.nih.gov, *select* Advisory Board & Committees).

The National Institute of Environmental Health Sciences (NIEHS) originally established ICCVAM in 1994 in response to Public Law 103-43. 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.L106-545). 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.
- 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
Consumer Product Safety Commission
Department of Agriculture
Department of Defense
Department of Energy
Department of Interior
Department of Transportation
Environmental Protection Agency
Food and Drug Administration
National Cancer Institute
National Institute of Environmental Health Sciences
National Institutes of Health, Office of the Director
National Institute of Occupational Safety and Health
National Library of Medicine
Occupational Safety and Health Administration

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 *ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods* (NIH Publication No. 03-4508) to aid in their evaluation.

When adequate information is available for a new revised test method, the NICEATM in collaboration with the ICCVAM convenes an independent scientific peer review panel. Scientists from industry, academia, government, and the international community serve on these panels. A 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. NICEATM and ICCVAM also convene workshops and expert panel meetings to

assess research, development, and validation efforts needed to further characterize the usefulness and limitations of proposed new, revised, or alternative toxicological test methods.

ICCVAM develops recommendations on the scientific validity of the proposed test method that are forwarded with panel reports and public comments to appropriate federal regulatory agencies. 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 as a substitute for traditional guinea pig tests. The LLNA was adopted as an international test guideline by the Organization for Economic Cooperation and Development (OECD) in 2002 as Test Guideline 429. The LLNA provides for **refinement** by avoiding pain and distress encountered with the traditional test.
- The review of Corrositex®, an *in vitro* method for assessing the dermal corrosivity potential of chemicals, was completed in 1999 and, based on ICCVAM recommendations, is now accepted by regulatory agencies. An OECD Test Guideline is under consideration. This test method can **replace** the use of animals when positive results are obtained.
- The NICEATM completed an expert panel evaluation of the Frog Embryo Teratogenesis Assay in *Xenopus.* Recommendations for improving the test's accuracy and reproducibility were developed.
- 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. Based on ICCVAM recommendations, the revised UDP was subsequently adopted by US agencies and the OECD (TG425) as a substitute for the conventional LD50 test for hazard classification testing. This test **reduces** the number of animals needed by over 70%.
- 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 concluded that additional validation studies were needed for all assays. Based on this review, ICCVAM recommended a standardized list of substances to validate the assays, and identified essential components that should be included in each of the four types of assays.
- An expert panel meeting was held in January 2005 to evaluate the validation status of *in vitro* test methods for determining the potential ocular irritancy of chemicals and other substances. The test methods include the Bovine Corneal Opacity and Permeability [BCOP] assay, the Hen's Egg Test—Chorioallantoic Membrane [HET-CAM] assay, the Isolated Chicken Eye [ICE] assay, and the Isolated Rabbit Eye [IRE] assay. The panel recommended additional investigations and improvements for all of the methods to enhance their relevance and reliability.

Other NICEATM-ICCVAM Activities

- Two scientific symposia are planned for May 10-12, 2005, to review the current understanding and knowledge gaps regarding cellular and molecular mechanisms of chemically induced ocular injury and reversibility and to examine approaches for avoiding or alleviating potential pain and distress in ocular safety testing.
- 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. Preliminary findings indicate that using *in vitro* data from these methods to set starting doses for acute toxicity studies can further reduce the number of animals needed.

For additional information visit the NICEATM/ICCVAM web site at http://iccvam.niehs.nih.gov or contact:
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