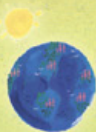


Nominations and Submissions to ICCVAM

A Guide for Test Method Developers and Sponsors



National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods
Interagency Coordinating Committee on the Validation of Alternative Methods
National Institute of Environmental Health Sciences
Research Triangle Park, NC

NICEATM and ICCVAM carry out a wide range of activities, including test method validation studies and comprehensive evaluations, to promote the development, scientific validation, and regulatory acceptance of new, revised, and alternative safety testing methods and testing strategies. Accordingly, NICEATM and ICCVAM seek **nominations** and **submissions** of new or revised safety testing methods and integrated testing strategies for validation studies or formal evaluations. Methods and testing strategies are especially sought that have the potential to:

- Reduce, refine, and/or replace the use of animals in testing
- Maintain and promote scientific quality and improve the protection of human health, animal health, and the environment

On behalf of the National Toxicology Program, NICEATM also invites the nomination of pathway-based *in vitro* assays that can be considered for incorporation into the Tox21 high-throughput screening initiative.

- A test method **submission** consists of a proposal to ICCVAM for review and evaluation of a test method or testing strategy for which there are completed validation studies. After review, ICCVAM forwards test method recommendations to Federal agencies. Agencies use this information to determine the acceptability of the test method or testing strategy for their needs.
- A test method **nomination** consists of a proposal to ICCVAM for activities relevant to the review or validation of specific test methods or testing strategies, or to address relevant testing or validation issues. Nominations might consist of proposals for validation studies, workshops, peer reviews, or other appropriate activities.



The NICEATM-ICCVAM graphic symbolizes the important role of new and alternative toxicological and safety testing methods in protecting and advancing the health of people, animals, and the environment.



What are NICEATM and ICCVAM?

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) is an interagency committee of the U.S. Government established by the ICCVAM Authorization Act of 2000 (42 U.S.C. 285f-3). ICCVAM's members include 15 Federal regulatory and research agencies that require, use, generate, or distribute safety testing information. Such information is used to protect workers and consumers from injuries or diseases that may result from exposure to hazardous chemicals and products.

ICCVAM coordinates interagency technical reviews of new and revised safety testing methods. The National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) administers ICCVAM, provides support for ICCVAM-related activities, and conducts independent validation studies.

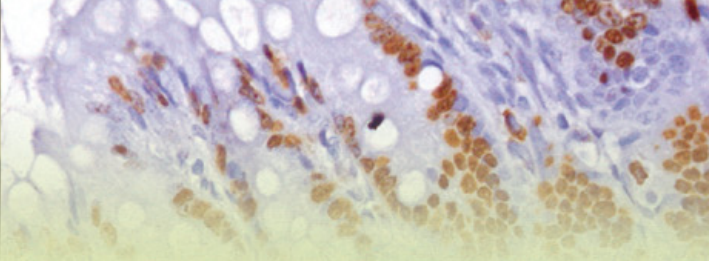
What kinds of test methods are eligible for ICCVAM evaluation?

Any new, revised, or alternative safety testing method or integrated testing strategy with regulatory applicability is eligible for evaluation by ICCVAM.

ICCVAM prioritizes test methods for evaluation using criteria that include:

- The potential for the proposed test method or testing strategy to improve the prediction of adverse health or environmental effects
- The potential for the alternative test method or testing strategy to reduce, refine (enhance animal well-being and lessen or avoid pain or distress), or replace animal use
- The potential for the proposed test method or testing strategy to apply to regulations across multiple agencies

NICEATM and ICCVAM conduct test method evaluation activities in a number of areas. Currently, the four highest priority areas are biologics, acute systemic toxicity, ocular toxicity, and dermal toxicity. Other areas of interest include dermal sensitization, endocrine disruption, pyrogen testing, reproductive/developmental toxicity, and chronic toxicity/carcinogenicity.



How do we prepare a nomination or submission to ICCVAM?

The *ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods* (NIH Publication No. 03-4508; available on the NICEATM-ICCVAM website) provides detailed guidance on preparing nominations and submissions of test methods for consideration by ICCVAM. Elements of a complete submission package include:

- Rationale for the proposed test method
- Test method protocol
- Substances used for validation of the proposed test method
- Reference data used to assess the accuracy of the proposed test method
- Test method data and results
- Characterization of test method accuracy and reliability
- Assessment of test method data quality
- Animal welfare considerations (reduction, refinement, and replacement)

Complete submissions serve as a basis for assessing the validation status of a proposed test method through an independent ICCVAM peer review process.

Sponsors may nominate test methods and testing strategies for which a complete submission package is not available for evaluation by ICCVAM. These test methods may be evaluated in an expert workshop or become the basis for an international validation study sponsored by NICEATM.

NICEATM evaluates nominations or submissions to assess the relevance of the nomination or the adequacy and completeness of the submission. ICCVAM then determines the priority the proposed test method will have for technical evaluation and, in conjunction with NICEATM, develops recommendations and priorities for further efforts. These might include an expert workshop, an evaluation with independent scientific peer review, or a validation study.

Can we get assistance in preparing our nomination or submission?

Yes. Sponsors are encouraged to consult with NICEATM and ICCVAM throughout the test method development and validation process, as well as during preparation of submissions. This will increase the likelihood that validation studies and submissions will adequately characterize the usefulness and limitations of the proposed test method. An adequate characterization will give agencies the information necessary to determine whether a test method can generate information that will meet their regulatory needs.

Are NICEATM and ICCVAM supporting development of Tox21 assays?

Yes. As we move towards the Tox21 goal of pathway-based *in vitro* screens, the ability of test methods to be run on a high-throughput screening (HTS) platform is an important aspect of their potential utility. NICEATM will support the Tox21 Pathways Group by actively soliciting assay nominations from Federal agencies, international partners, and the general public. Nominated assays will be collated and forward to the Tox21 Pathways Group for consideration.

Does NICEATM sponsor validation studies?

Yes. NICEATM conducts and coordinates international validation studies to evaluate promising new alternative test methods that may reduce, refine, or replace animal use for toxicity testing and that may improve safety assessment for people, animals, and the environment. These studies are conducted in cooperation with NICEATM's international counterparts through an International Cooperation on Alternative Test Methods.

Are grants available for development of test methods?

Yes. NIEHS supports research and training focused on the identification, assessment and mechanism of action of agents in the environment and how they contribute to disease. This includes development, standardization, and validation of new and novel tests or batteries of tests that will provide faster and less expensive alternatives to the use of standard laboratory animal tests. Information about the NIEHS Small Business Innovation Research/ Small Business Technology Transfer grants program is available on the NIEHS website at <http://www.niehs.nih.gov/research/supported/programs/sbir/>

ICCVAM Member Agencies

(Member agencies are indicated in boldface)

- **Consumer Product Safety Commission**
- **Department of Agriculture**
- **Department of Defense**
- **Department of Energy**
- Department of Health and Human Services
 - Centers for Disease Control and Prevention
 - **Agency for Toxic Substances and Disease Registry**
 - **National Institute for Occupational Safety and Health**
 - **Food and Drug Administration**
 - **National Institutes of Health**
 - **National Cancer Institute**
 - **National Institute of Environmental Health Sciences**
 - **National Library of Medicine**
- **Department of the Interior**
- Department of Labor
 - **Occupational Safety and Health Administration**
- **Department of Transportation**
- **Environmental Protection Agency**

More information about NICEATM and ICCVAM can be found on the NICEATM-ICCVAM website:

<http://iccvam.niehs.nih.gov>

NICEATM encourages companies and organizations that wish to propose nominations or submissions of promising test methods to contact us for information and guidance on preparing proposals. Please contact us at:

Telephone: [919] 541-2384

E-mail: niceatm@niehs.nih.gov



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

