



Interagency Coordinating Committee on the Validation of Alternative Methods

What is ICCVAM?

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) is 15 federal research and regulatory agencies working together to advance the acceptance of scientifically valid alternative test methods.

Alternative test methods are those that replace or reduce the use of animals, or refine their use, such as enhancing animal well-being, and lessening or avoiding pain and distress. These test methods are used in regulatory toxicity testing. Reduction, refinement, and replacement are commonly referred to as the 3Rs.

In short, ICCVAM provides a way to bring forward 3R test methods that can accurately detect whether chemicals and products cause harm to people, animals, or the environment.

Why is ICCVAM needed?



Regulatory agencies in the United States are charged with protecting not only human health, but also animal health and the environment. To accomplish this, agencies must have effective ways to

determine possible health hazards from chemicals, consumer products, and other substances.

Remarkable advances in science and technology occurring in the United States and internationally are providing unprecedented opportunities to advance alternatives to animal testing, and offer improved ways to test substances. ICCVAM is poised to take advantage of these opportunities.



ICCVAM members include representatives from the following federal agencies:

- Consumer Product Safety Commission (CPSC)
- Department of Agriculture (USDA)
- Department of Defense (DOD)
- Department of Energy (DOE)
- Department of Health and Human Services (HHS)
 - Centers for Disease Control and Prevention (CDC)
 - Agency for Toxic Substances and Disease Registry (ATSDR)
 - National Institute for Occupational Safety and Health (NIOSH)
 - Food and Drug Administration (FDA)
 - National Institutes of Health (NIH)
 - National Cancer Institute (NCI)
 - National Institute of Environmental Health Sciences (NIEHS)
 - National Library of Medicine (NLM)
- Department of the Interior (DOI)
- Department of Labor (DOL)
- Occupational Safety and Health Administration (OSHA)
- Department of Transportation (DOT)
- Environmental Protection Agency (EPA)

To use the power of science to achieve the 3Rs, ICCVAM provides federal agencies a coordinated way to work together, and to establish productive interactions with others, including test method developers, small businesses, researchers, animal welfare groups, and international validation groups.

Specifically, ICCVAM was established by law (Public Law 106-545) in 2000 as an interagency committee 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.

The law also required the director of the National Institute of Environmental Health Sciences (NIEHS) to establish ICCVAM under the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). NICEATM is an office within NTP at NIEHS.

What are some of the activities ICCVAM has worked on over the years?



Over the past 15 years, ICCVAM has successfully evaluated and recommended numerous alternative test

methods for use. These tests primarily focus on finding alternative ways to identify substances that could be poisonous when taken orally or cause

allergic reactions when absorbed through the skin (acute toxicity and skin sensitization), cause disruption to the endocrine system, or harm the eyes. ICCVAM has also focused on developing alternative ways to test new human or animal vaccines (biologics).

What role does NICEATM play in ICCVAM?



ICCVAM does not have its own laboratory or resources. NICEATM provides administrative and scientific support for ICCVAM activities. NICEATM also provides bioinformatics and

computational toxicology support for Tox21. For example, NICEATM and ICCVAM are helping to evaluate the validity of Tox21 assay data for submission to regulatory agencies. [Tox21](#)¹ is a multiagency collaboration aimed at improving the human hazard characterization of chemicals.

ICCVAM and NICEATM receive external advice on their activities from the Scientific Advisory Committee on Alternative Toxicological Methods ([SACATM](#))²

How does ICCVAM evaluate alternative test methods?

ICCVAM follows a formal process for evaluating new or revised toxicological test methods. It has developed the ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods (NIH Publication No. 03-4508). The guidelines will assist sponsors and nominators in organizing the information needed by ICCVAM to evaluate a new or modified test method.

ICCVAM also convenes 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. More information is available at <http://iccvam.niehs.nih.gov/methods/methods.htm>.

Does ICCVAM work with any international partners?

To reduce the number of animals required for chemical safety testing worldwide, ICCVAM joined with other international organizations to form the International Cooperation on Alternative Test Methods.



International Cooperation on Alternative Test Methods (ICATM)

The five partner organizations include:

- ICCVAM
- European Centre for the Validation of Alternative Methods
- Environmental Health, Science and Research Bureau within Health Canada
- Japanese Center for the Validation of Alternative Methods
- Korean Center for the Validation of Alternative Methods

The International Cooperation on Alternative Test Methods promotes international cooperation that should permit more rapid acceptance of new safety testing methods for evaluating chemicals and products. New testing methods can better protect public health, reduce the number of animals needed for safety testing, and improve animal welfare. More information about ICCVAM's role in international cooperation can be found at <http://iccvam.niehs.nih.gov/about/icatm.htm>.

Through international cooperation, NICEATM and ICCVAM have contributed to the development of new test guidelines and revision of existing test guidelines and guidance documents. For example, ICCVAM recommendations were incorporated into a 2012 update of the Organisation for Economic Co-operation and Development (OECD) [test guideline](#)³ describing animal tests, to identify potential eye irritants.

Moving Forward

As science continues to advance, ICCVAM will work to promote the development, validation, regulatory acceptance, and implementation of test methods that take advantage of novel approaches, while addressing the reduction, refinement, and replacement of animals in toxicity testing.



ICCVAM is working together on strategic directions to better align the alternative test methods validated and the tests required to meet regulatory needs. See [A New Vision and Direction for ICCVAM](#),⁴ for more information.

Story of Success

Improving Endocrine Disruptor Screening

Chemicals that disrupt the body's endocrine system can lead to developmental and reproductive problems, among others. As part of an effort to bring *in vitro*, or non-animal, methods forward, to help identify chemicals that can impact the endocrine system, ICCVAM evaluated test methods that can identify chemicals that mimic estrogen and disrupt the body's natural hormonal balance. These estrogen receptor-based test methods were being evaluated for potential use in the Endocrine Disruptor Screening Program at the U.S. Environmental Protection Agency (EPA).



ICCVAM's evaluation included the BG1Luc estrogen receptor transcriptional activation assay, or *BG1Luc ER TA* test method, a new and potentially improved way to screen for endocrine disruption. This method was developed by Xenobiotic Detection Systems Inc., with support from a Small Business Innovation Research grant from NIEHS.

NICEATM coordinated an international validation study of the *BG1Luc ER TA* agonist and antagonist assays at laboratories in Europe, the United States, and Japan. After the study, ICCVAM recommended that the *BG1Luc ER TA* test method could be used in regulatory safety testing to identify substances that disrupt estrogen receptor activities. EPA adopted ICCVAM's recommendation. Several other regulatory agencies also encourage use of this method as appropriate.

Additionally, the OECD, which houses a collection of the world's most relevant internationally agreed upon test methods for determining the safety of chemicals, developed a new test guideline, [Test No. 457](#),⁵ for the *BG1Luc ER TA* test method. The OECD also used this method to update an existing performance-based test guideline, [Test No. 455](#),⁶ to detect estrogen receptor disruptors.



The *BG1Luc ER TA* test method is also the first validated test method adapted for use in high throughput screening. The *BG1Luc ER TA* test method is being used to screen all compounds in the Tox21 chemical library. Tox21 is a federal collaboration involving the National Institutes of Health (NIH), EPA, and the U.S. Food and Drug Administration to use high throughput screening to better predict toxicity of chemicals.

For more information about ICCVAM and NICEATM, visit <http://iccvam.niehs.nih.gov>.

¹ Tox21: Understanding the potential health risks of chemicals: <http://go.usa.gov/Wjht>

² Scientific Advisory Committee on Alternative Toxicological Methods (SACATM): <http://ntp.niehs.nih.gov/go/167>

³ OECD guideline for the testing of chemicals: <http://go.usa.gov/WjnP>

⁴ A New Vision and Direction for ICCVAM: <http://go.usa.gov/Wjnz>

⁵ Test No. 457: BG1Luc Estrogen Receptor Transactivation Test Method for Identifying Estrogen Receptor Agonists and Antagonists: <http://bit.ly/1aOoB0i>

⁶ Test No. 455: Performance-Based Test Guideline for Stably Transfected Transactivation In Vitro Assays to Detect Estrogen Receptor Agonists: <http://bit.ly/1asue6a>