The ICCVAM Process for Nomination and Submission of New, Revised and Alternative Test Methods

LM Schechtman[1], WS Stokes[2], ML Wind[3], BC Blackard[4], RR Tice[4]

[1]U.S. Food and Drug Administration, NCTR, Rockville, MD; [2]NTP Interagency Center for the Evaluation of Toxicological Methods (NICEATM), NIEHS, RTP, NC; [3]U.S. Consumer Product Safety Commission, Washington, DC; [4]Integrated Laboratory Systems, Inc., RTP, NC.

Abstract

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) coordinates (a) the technical evaluation of new, revised and alternative test methods of Federal agency interest, and (b) cross-agency issues relating to the validation, acceptance and national and international harmonization of toxicological test methods. ICCVAM recently developed and adopted a process by which test method nominations and submissions are considered and prioritized for review and evaluation. Prioritization of proposed test methods is based on several criteria, including: the applicability of the method to regulatory testing needs; the extent of anticipated use by one or more agencies; the level of multi-agency interest; the potential for the method to reduce, refine or replace animal use; the prospect of the test method to provide improved prediction of adverse health or environmental effects compared to current test methods accepted by regulatory agencies; and the extent to which the test method affords other advantages, such as reduced time or cost. The newly revised "ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods" describe: 1) the ICCVAM nomination and submission process, 2) the information that should be provided in a test method submission or nomination and an outline for organizing the necessary information; and 3) the ICCVAM process for developing performance standards, which communicate the basis on which a validated and accepted test method has been determined to have sufficient accuracy and reliability for a specific testing purpose. Test method submitters/ nominators are encouraged to utilize these Guidelines and communicate with NICEATM and ICCVAM during the preparation of test method submissions and nominations. These Guidelines are expected to facilitate the preparation of test method submissions and nominations and their consideration by ICCVAM. ILS staff supported by NIEHS contract NO1-ES-35504.The views expressed above do not necessarily represent the official positions of any federal agency.

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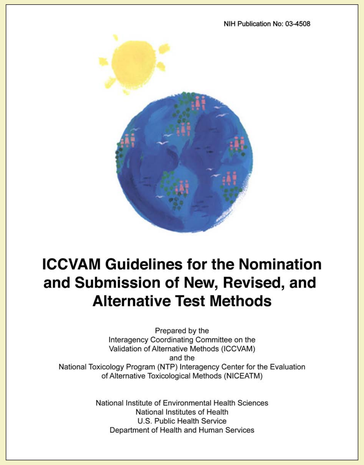
NIH Publication No: 03-4508

ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods

Prepared by the
Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)
and the
National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

National Institute of Environmental Health Sciences
National Institutes of Health
U.S. Public Health Service
Department of Health and Human Services

ICCVAM Authorization Act of 2000[1] directs ICCVAM to:

- Review and evaluate new, modified, or alternative test methods, including batteries of tests and test screens, that may be acceptable for specific regulatory uses
- Coordinate technical reviews of test methods of interagency interest
- Review and evaluate petitions received from the public that:
  - Identify a specific regulation, recommendation, or guideline regarding a regulatory mandate
  - Recommend new or modified test methods and provide valid scientific evidence of the potential of the recommended test method to improve prediction of adverse human or animal health or ecological effects, and to reduce, refine, or replace animal use in existing regulatory test methods.

[1]Public Law 106-545

The recently revised "ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods" [NIH Publication No. 03-4508] describes:

- The ICCVAM test method nomination and submission process
- The information that should be provided in test method submissions or nominations
- The ICCVAM process for developing Performance standards, which communicate the basis on which a validated and accepted proprietary (i.e., copyrighted, trademarked, registered) or nonproprietary test method has been determined to have sufficient accuracy and reliability for a specific testing purpose.

ICCVAM Nomination and Submission Process

Test method nomination: A test method proposed to ICCVAM for review and evaluation for which a complete test method submission is not available. Four examples are:

(1) test methods for which adequate validation studies presumably have been completed but lack a complete submission package
(2) test methods that appear promising based on limited prevalidation or validation data and are proposed for additional validation studies
(3) test methods that have been developed and are proposed for prevalidation or validation studies
(4) test methods that are recommended for a workshop or other activity

Test method submission: A test method proposed to ICCVAM for review and evaluation for which adequate validation studies have been completed to characterize the usefulness and limitations of the test method for a specific proposed regulatory testing requirement or application, and adequate documentation of the scientific validity has been prepared in accordance with ICCVAM test method submission guidelines.

Test method nominations and test method submissions to ICCVAM are considered and prioritized for review and evaluation. Submissions should be accompanied by all requested information. Although there is no mandatory minimum requirement for information to provide with nominations, ICCVAM consideration of the proposed test method will be expedited by providing as much information as possible.

Test Method Nominations or Submissions are Prioritized by ICCVAM According to the following Criteria:

- The extent to which the proposed test method is:
  - Applicable to regulatory testing needs
  - Applicable to multiple agencies/programs
  - Warranted, based on the extent of expected use or application and impact on human, animal, or ecological health
- The potential for the proposed test method, compared to current test methods accepted by regulatory agencies, to:
  - Refine animal use (decreases or eliminates pain and distress)
  - Reduce animal use
  - Replace animal use
- The potential for the proposed test method to provide improved prediction of adverse health or environmental effects, compared to current test methods accepted by regulatory agencies
- The extent to which the test method provides other advantages (e.g., reduced cost and time to perform) compared to current methods
- The completeness of the nomination or submission with regard to ICCVAM test method submission guidelines

ICCVAM Nomination And Submission Process

NICEATM
- Solicits, receives, and tracks nominations and submissions
- Conducts preliminary evaluation of each nomination or submission
  - determines completeness of each nomination or submission
  - summarizes findings
  - proposes appropriate future efforts (e.g., workshop, expert panel meeting, peer review meeting, expedited review, validation study)

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ICCVAM Working Group
- Reviews NICEATM preliminary evaluation report
- Develops draft recommendations on priority for future efforts
- Seeks comment from the public on the nominated or submitted test method (via NICEATM)

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SACATM
- Considers public comments on the nominated or submitted test method
- Comments on NICEATM and ICCVAM draft recommendations

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ICCVAM
- Considers SACATM and public comments
- Finalizes recommendations and priorities
- NICEATM estimates resource requirements

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Director, ETP/NIEHS
- Responds to NICEATM resource requests for proposed test method activities

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Director, NICEATM
- Informs ICCVAM of availability of resources for activities recommended for nominated or submitted test methods
- If appropriate, ICCVAM Working Group established
- If appropriate, test method evaluations or validation studies organized in conjunction with ICCVAM Working Group

Information that Nominations and Submissions Should Include

- An introduction, including the scientific and regulatory rationale for the proposed test method
- Information on the development of the proposed test method protocol and its key components
- Characterization of the substances used for validation studies on the proposed test method
- The reference data used to assess the accuracy and reliability of the proposed test method
- Proposed test method data and results
- An assessment of the accuracy of the proposed test method
- An assessment of the reliability (repeatability/reproducibility) of the proposed test method
- An assessment of test method data quality
- Other scientific reports and reviews pertinent to the proposed test method
- An assessment of animal welfare considerations (refinement, reduction, and replacement)
- Practical considerations (e.g., test method study costs, time needed to perform a study, ease of transferability of the test method among laboratories)
- A comprehensive and complete list of references cited
- Supporting materials (e.g., the proposed standardized test method protocol) in appendices

Outline for Nominations and Submissions to Iccvam

1.0 Introduction and Rationale for the Proposed Test Method

2.0 Test Method Protocol Components
Note: A complete, detailed protocol should be included as an appendix to the submission or nomination

3.0 Substances Used to Evaluate the Validation Status of a Proposed Test Method

4.0 *In Vivo* Reference Data Used to Assess the Accuracy of the Proposed Test Method

5.0 Test Method Data and Results

6.0 Test Method Accuracy

7.0 Test Method Reliability (Repeatability/Reproducibility)

8.0 Test Method Data Quality

9.0 Other Scientific Reports and Reviews

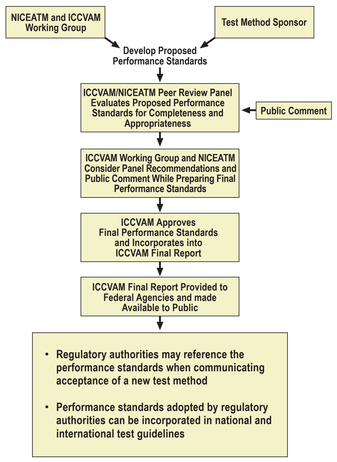
10.0 Animal Welfare Considerations (Refinement, Reduction, and Replacement)

11.0 Practical Considerations

12.0 References

13.0 Supporting Materials (Appendices)

ICCVAM/NICEATM Process for Developing Test Method Performance Standards



- Regulatory authorities may reference the performance standards when communicating acceptance of a new test method
- Performance standards adopted by regulatory authorities can be incorporated in national and international test guidelines

PLEASE ALSO SEE SOT POSTER #1812 - THE ICCVAM/NICEATM PROCESS FOR DEVELOPING TEST METHOD PERFORMANCE STANDARDS

References

(1) ICCVAM. 2003. ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods. NIH Publication No. 03-4508. Research Triangle Park, NC: National Institute of Environmental Health Sciences. Available: http://iccvam.niehs.nih.gov/docs/guidelines/subguide.htm

(2) NIEHS. 1997. 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. Research Triangle Park, North Carolina: National Institute of Environmental Health Sciences. Available: http://iccvam.niehs.nih.gov/docs/guidelines/validate.pdf

More information on ICCVAM and NICEATM can be accessed at: http://iccvam.niehs.nih.gov