

ICCVAM PROCEDURES FOR TEST METHODS THAT HAVE BEEN ENDORSED BY ECVAM

There may be opportunities for harmonization between the United States (US) and European Union (EU) with respect to the validation of certain toxicological test methods. The question is how should the US address test methods that have been reviewed and approved by the EU? In both geographical areas, the status of validation of new and revised toxicological test methods is assessed prior to their being considered for acceptance by regulatory agencies. In the US, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) often serves the role of validation assessment for methods of common interest among federal agencies, while in the EU, alternative test method activities are coordinated by the European Centre for the Validation of Alternative Methods (ECVAM).

ICCVAM must carefully set priorities given its limited resources. It is staffed by scientists from various federal agencies who donate their time and by the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) which is a support function for the National Toxicology Program (NTP). ICCVAM is unable to conduct in depth peer reviews for every ECVAM-approved test method. Once more, it is inappropriate for ICCVAM to conduct such reviews for methods where there is no **substantive** disagreement with the ECVAM assessment. In addition, some methods after being approved by ECVAM quickly move to the Organisation for Economic Cooperation and Development (OECD) for consideration and acceptance. Whenever appropriate, ICCVAM will employ an abbreviated process for test methods endorsed by ECVAM.

ICCVAM will use the following evaluation steps for ECVAM approved products:

1. **If the test method will not be immediately sent to OECD, ICCVAM will determine whether it is of sufficient priority to commence a review. In those cases, the method, the prevalidation and validation studies, the peer review report and any other received material supporting the case will be assessed for completeness by the NICEATM.** The assessment will utilize the ICCVAM principles for evaluating the adequacy of information supporting the validity of test methods¹ and the established ICCVAM criteria for assessment of test method validation status². ICCVAM will make determinations as to whether there are or are not major issues with the data supporting the

¹ *Evaluation of the Validation Status of Toxicological Methods: General Guidelines for Submissions to ICCVAM* (1999; <http://iccvam.niehs.nih.gov/docs/guidelines/subguide.htm>)

² *Validation and Regulatory Acceptance of Toxicological Test Methods* (1997 <http://iccvam.niehs.nih.gov/docs/guidelines/validate.pdf>)

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)

method or with the peer review report. Major issues would include such things as absence of adequate data to assess the validity of the method.

2. If NO MAJOR issues are noted:
 - a. ICCVAM will develop a draft position on the test method.
 - b. The position will be published in the *Federal Register* for public comment.
 - c. Comments will be addressed.
 - d. If no major problems are found in the comments, ICCVAM will revise its position.
 - e. ICCVAM will make recommendations concerning the method and send it to federal agencies for determination of acceptability.
3. If MAJOR problems are noted
 - a. ICCVAM will assess all **accessible and appropriate** information on the test method.
 - b. The established ICCVAM peer review process and criteria² will be used to evaluate the validity of the method for a given use. The ICCVAM review may also result in recommendations for research or for further validation.
 - c. ICCVAM will make recommendations concerning the method and send it to federal agencies for determination of acceptability.
4. The results of ICCVAM and regulatory agency decisions will be communicated to ECVAM and the public **for comment**.

These procedures may need revision as experience is gained with its implementation.

Adopted by ICCVAM
April 23, 2001