PREFACE

Before a new or modified test method is used to generate information to support regulatory decisions, it must a) undergo adequate validation to determine its reliability and accuracy for a specific proposed use, and b) be deemed acceptable by one or more regulatory agencies to fill a specific need. Criteria for validation and regulatory acceptance have been developed by the U.S. Federal government and are described in the report, *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the Ad Hoc Interagency Coordinating Committee on the Validation of Alternative Methods* (1). Prior to the initiation of test method development or validation efforts, sponsors should consider these validation and acceptance criteria.

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) developed this document, *ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods*, to assist test method sponsors and nominators in organizing the information needed by ICCVAM to assess the validation status of a new or modified test method at any stage of the validation process. This document is available online at http://iccvam.niehs.nih.gov/docs/guidelines/subguide.htm; printed copies are available on request from the National Toxicology Center (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) (NIEHS, P.O. Box 12233, MD EC-17, Research Triangle Park, NC 27709; telephone: 919-541-3398, fax: 919-541-0947, e-mail: iccvam@niehs.nih.gov). These guidelines describe:

- The ICCVAM test method nomination and submission process
- 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. These performance standards should be met by proposed test methods that are based on similar scientific principles and that measure or predict the same biological or toxic effect.
- The information that should be provided in test method nominations or submissions so that ICCVAM can evaluate appropriately the extent to which the validation and acceptance criteria have been addressed, or will be addressed in proposed studies

The ICCVAM Authorization Act of 2000 (2) (**Appendix E**) 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.

Test method sponsors are encouraged to consult with NICEATM and ICCVAM throughout the test method development, prevalidation, and validation process, as well as during preparation of submissions. The objective of these interactions is to maximize the likelihood that validation studies and submissions will adequately characterize the usefulness and limitations of the proposed test method. Complete submissions are essential and serve as a basis for assessing the validation status of a proposed test method through an independent ICCVAM peer review process. This interactive process enhances the likelihood that agencies will have sufficient data and information to determine the extent that a test method can generate information that will meet their regulatory needs.

These guidelines now include guidance on the process for submitting nominations to ICCVAM for test methods that are proposed for further consideration, but which may require further compilation of data or even additional validation studies. Test method nominators are encouraged to consult with NICEATM and ICCVAM prior to submitting nominations. The objective of this interaction is to ensure that the nominations contain as much information as possible and to ensure that the proposed test methods have regulatory applicability.

The initial ICCVAM submission guidelines, first released in May 1998, incorporated much of the guidance developed for data submissions for the Second Workshop of the Interagency Regulatory Alternatives Group (3). Revised submission guidelines were published in 1999, based on experience gained with the first two test methods reviewed by ICCVAM – the Local Lymph Node Assay and Corrositex®. This second revision reflects further experience gained with the evaluation of other alternative test methods (Frog Embryo Teratogenesis Assay – *Xenopus*, the Up-and-Down Procedure for Acute Oral Toxicity, EPISKIN™, EpiDerm™, the Rat Skin Transcutaneous Electrical Resistance assay, and *in vitro* estrogen–receptor/androgen–receptor binding and transcriptional activation assays) and incorporates procedures revised in response to the ICCVAM Authorization Act of 2000. ICCVAM continues to welcome suggestions for improving the usefulness of these guidelines.

We gratefully acknowledge the ICCVAM agency representatives, working group members, and peer review panel members who contributed to the preparation of the original document and to subsequent revisions. We also appreciate the constructive suggestions received from scientists who used earlier versions of the guidelines to prepare submissions to ICCVAM.

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