3.0 PERFORMANCE STANDARDS FOR TEST METHODS

Prior to the acceptance of a proposed test method for regulatory testing applications, validation studies are conducted to assess reliability and accuracy. The purpose of performance standards is to communicate the basis on which a new proprietary (i.e., copyrighted, trademarked, registered) or nonproprietary test method was determined to have sufficient accuracy and reliability for a specific testing purpose. Performance standards may be developed and recommended by ICCVAM as part of its evaluation of the validation status of a proposed test method. Performance standards, based on test methods accepted by regulatory agencies, can be used to evaluate the reliability and accuracy of other proposed test methods that are based on similar scientific principles and measure or predict the same biological or toxic effect.

The three elements of performance standards are:

- **Essential test method components** (previously referred to as "minimum procedural standards" [6]): These consist of essential structural, functional, and procedural elements of a validated test method that should be included in the protocol of a mechanistically and functionally similar proposed test method. These components include unique characteristics of the test method, critical procedural details, and quality control measures. Adherence to essential test method components will help to assure that a proposed test method is based on the same concepts as the corresponding validated test method.

- **Minimum list of reference chemicals:** These are used to assess the accuracy and reliability of a mechanistically and functionally similar proposed test method. These chemicals are a representative subset of those used to demonstrate the reliability and the accuracy of the validated test method. To the extent possible, these reference chemicals should:
  - Be representative of the range of responses that the validated test method is capable of measuring or predicting
  - Have produced consistent results in the validated test method and in the *in vivo* reference test method and/or the species of interest
  - Reflect the accuracy of the validated test method
  - Have well-defined chemical structures
  - Be readily available
  - Not be associated with excessive hazard or prohibitive disposal costs

  These reference chemicals are the minimum number that should be used to evaluate the performance of a proposed, mechanistically and functionally similar test method. The chemicals should not be used to develop the prediction model for the proposed test method. If any of the recommended chemicals are unavailable, other chemicals for which adequate reference data are available could be substituted. To the extent possible, the substituted chemical(s) should be of the same chemical class as the original chemical(s). If desired, additional chemicals representing other chemical or product classes and for which adequate reference data are available can be used to more comprehensively evaluate the accuracy of the proposed test method. However, these additional chemicals should not include any that had been used to develop the proposed test method.

- **Accuracy and reliability values:** These are the comparable performance that should be achieved by the proposed test method when evaluated using the minimum list of reference chemicals.

The ICCVAM process for developing performance standards for new test methods is as follows:

- NICEATM and the appropriate ICCVAM working group develop proposed performance standards for consideration during the ICCVAM evaluation process. If performance standards are proposed by a test method sponsor, these will be considered by ICCVAM during the evaluation process. Generally, the performance standards will be based on the information and data provided in the test method submission or on other available applicable data.

- The ICCVAM/NICEATM Peer Review Panel evaluates the proposed performance standards for completeness and appropriateness during its evaluation of the validation status of the proposed test method. The proposed performance standards will be made available with the test method submission to the public for comment prior to and during the Peer Review Panel meeting.

- The appropriate ICCVAM working group, with the assistance of NICEATM, prepares the final performance standards for ICCVAM approval, taking into consideration the recommendations of the Peer Review Panel and public comments.

Performance standards recommended by ICCVAM would be incorporated into ICCVAM test method evaluation reports, which are provided to Federal agencies and made available to the public. Regulatory authorities may then reference the performance standards in the ICCVAM report when they communicate their acceptance of a new test method. In addition, performance standards adopted by regulatory authorities could be provided in guidelines issued for new test methods. Availability of ICCVAM test method evaluation reports are announced routinely in the *Federal Register*, NTP Newsletters, and ICCVAM/NICEATM e-mail listserve groups.