DRAFT agreed upon at ICCR-2, as slightly revised and agreed on September 25, 2008 by representatives of ICCVAM-NICEATM, ECVAM, and JaCVAM

Framework for International Cooperation on Alternative Test Methods (ICATM)

At the first meeting of the International Cooperation on Cosmetics Regulation (ICCR) on September 26-28, 2007, the ICCR recognized the importance of replacing, reducing, and refining (less pain and distress) animal testing. The group welcomed the efforts of industry and validation centers in developing and validating scientific alternatives to animal testing and recommended that intensive collaboration and communication in the design, execution, and peer review of validation studies should be further strengthened.

To this end, the ICCR invited the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)- National Toxicology Program Interagency Center for the Evaluation of Alternative Methods (NICEATM), European Centre for the Validation of Alternative Methods (ECVAM), Japanese Center for the Validation of Alternative Methods (JaCVAM) and a knowledgeable representative of the Government of Canada to address this issue and to propose options to ensure a collaborative approach to this issue, and noted that such efforts should be supported by scientific experts from the regulatory bodies.

In response, these validation organizations, which coordinate validation studies and test method evaluations in the ICCR member countries, together with a representative from Health Canada, developed a framework to increase international cooperation, collaboration, and communication on alternative test methods. The group met three times and developed a detailed proposal that was discussed with regulators at the ICCR working group meeting held on 9-10 April 2008. This document represents the consensus framework from that meeting.

The group recognized that the above organizations collaborate on an ad hoc informal basis on validation studies, test method peer reviews, and development of test method recommendations for regulatory authorities. Such collaboration has not been consistent, which has led to inadequate consultation and input from the other organizations in these three areas. Additionally, there are currently substantial differences in the processes used by each of the validation organizations to evaluate the validation status of alternative test methods, especially with regard to the procedures in place for involving stakeholders and fulfilling requirements for transparency. The validation organizations agreed that a framework was needed that would provide for enhanced and consistent international cooperation, collaboration, and communication among all four validation organizations in three critical areas:

1) Validation studies
2) Independent peer review of the validation status of test methods
3) The development of formal test method recommendations on alternative testing methods.

DRAFT agreed upon at ICCR-2, as slightly revised and agreed on September 25, 2008 by representatives of ICCVAM-NICEATM, ECVAM, and JaCVAM

Validation Organizations

The initial validation organizations involved in the framework are:

1. **ICCVAM,** which evaluates the validation status of new and alternative test methods, coordinates related activities among the 15 member agencies, and provides recommendations on test method validity to U.S. Federal agencies for regulatory acceptance consideration, and **NICEATM**, which administers ICCVAM and provides scientific support for its activities, including scientific peer review meetings and the conduct of independent international validation studies on alternative test methods.
2. **ECVAM,** within the European Commission**,** which coordinates international validation studies on proposed alternative methods and the independent scientific peer review thereof, by involving its Scientific Advisory Committee (ESAC). ECVAM provides recommendations to EU National Coordinators for regulatory acceptance of the validated methods. Furthermore, ECVAM provides a comprehensive database service on alternative methods and furnishes scientific and technical support to the policy-making Directorate Generals (DG) of the European Commission (EC) and promotes research and development of new alternative methods in close collaboration with the EC Research Directorate General (DG RTD).
3. **The Japanese Center for the Validation of Alternative Methods (JaCVAM)**, within the National Institute of Health Sciences, which coordinates validation studies on proposed alternative methods, coordinates the peer review of test methods, and provides recommendations to regulatory authorities.
4. **Health Canada**, which does not have a formal validation center, but coordinates health related test method validation and acceptance issues.

Goals of this Framework are:

1. To establish international cooperation in the critical areas of validation studies, independent peer review, and development of harmonized recommendations to ensure that alternative methods/strategies are more readily accepted worldwide.
2. To establish international cooperation necessary to ensure that new alternative test methods/strategies adopted for regulatory use will provide equivalent or improved protection for people, animals, and the environment, while replacing, reducing or refining animal use whenever scientifically feasible.

Purpose

The purpose of the framework is to promote consistent and enhanced voluntary international cooperation, collaboration, and communication among national validation organizations in order to:

a. Ensure the optimal design and conduct of validation studies that will support national and international regulatory decisions on the usefulness and limitations of alternative methods proposed for regulatory testing.

b. Ensure high quality independent scientific peer reviews of alternative test methods. and consistency in transparency and stakeholder involvement.

c. Enhance the likelihood of harmonized recommendations by validation organizations on the usefulness and limitations of alternative test methods for regulatory testing purposes. [*Note; ICATM will not develop independent recommendations, rather the ICATM provides the cooperation, collaboration, and communications framework that will facilitate harmonized recommendations by each of the four organizations*].

d. Achieve greater efficiency and effectiveness by avoiding duplication of effort and leveraging limited resources.

e. Support the timely international adoption of alternative methods.

Key Aspects of the Framework

The framework addresses the three critical areas of cooperation:

1) Validation studies
2) Independent peer review of the validation status of test methods, and
3) The development of formal test method recommendations on alternative testing methods.

The framework recognizes that these are three related but independent stages, and that cooperation, collaboration, and communication during all three stages are essential to generate harmonized recommendations that will support faster and more efficient international acceptance of new alternative test methods by regulatory authorities. The goal and key aspects of each critical area of cooperation include the following:

1. Validation Studies:

The goal of cooperation on validation studies is to develop consensus on critical aspects of validation studies before the validation study starts. Key aspects involve information sharing prior to validation studies of the following critical aspects: study objectives, specific regulatory testing purpose, proposed validation study design, detailed study protocols, and substances to be tested and the basis for their selection.

2. **Independent Scientific Peer Review Meetings and Reports**

The goal of this cooperation is to organize and conduct independent scientific peer reviews and meetings in a manner that will meet the needs of all ICATM organizations in order to avoid the need for repetitive peer reviews. Key aspects of this cooperation include:

- Seeking input from the other organizations during preparation of review documents and draft recommendations
- Public availability of review documents and draft recommendations when provided to peer review panels
- Peer Review Panels with international composition, including nominations solicited from ICATM organizations

- Public peer review meetings and/or other opportunities for stakeholder and/or public comment
- Peer Review Panel Reports available to the public and ICATM organizations to consider in developing final recommendations.

3. **Development of Test Method Recommendations for Regulatory Consideration**

   The goal of this cooperation is for each of the validation organizations to develop harmonized recommendations that are forwarded to national regulatory authorities and relevant international organizations. Key aspects of this cooperation include:
   - Lead validation organization includes liaisons from the other ICATM organizations and prepares draft final recommendations, taking into consideration the Peer Panel Report and all relevant documents
   - Draft final recommendations are shared among the validation organizations (i.e., ICCVAM, ECVAM, JaCVAM, and HC), which are considered along with the Peer Panel Report and all other supporting documents. Each organization notifies the lead organization of their draft position.
   - If all organization are in agreement, all ICATM organizations finalize and forward their recommendations to their respective regulatory authorities. If there is any disagreement, this is shared among all organizations and referred to the Lead and liaisons to address/attempt to resolve. Unresolved disagreements are discussed by the ICATM organizations. If no resolution, the scientific rationale for any disagreements is documented and provided by each ICATM member to regulatory authorities with their respective recommendation.

Coordination Meetings

Coordination meetings will be held regularly, in conjunction with travel to advisory committee meetings and national/international scientific meetings. Updates on progress will be made at future ICCR meetings. Organizations will communicate and discuss high and urgent priorities and seek ways to assist each other with such priorities to expedite progress.

Adopted October 2008
International Cooperation on Cosmetics Regulation (ICCR)