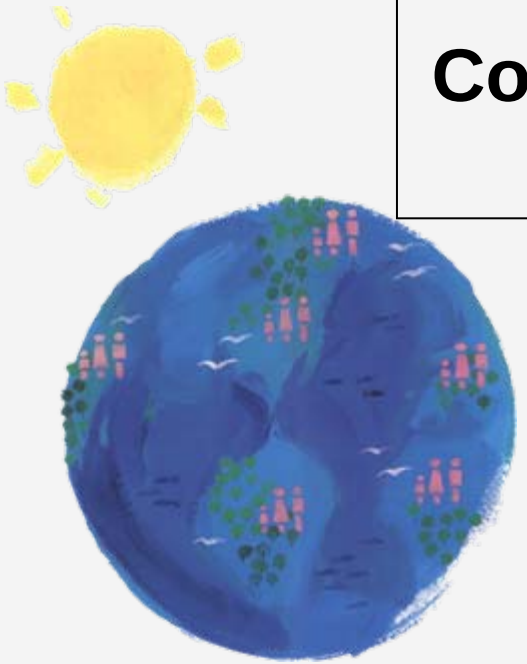
NICEATM ICCVAM

National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods

Interagency Coordinating Committee on the Validation of Alternative Methods

Proposal for International Cooperation on Alternative Testing Methods



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June 19, 2008

Meeting of the Scientific Advisory Committee on Alternative Toxicological Methods

Research Triangle Park, NC

Background: International Cooperation on Cosmetics Regulations (ICCR)

- A *voluntary* international group of cosmetics regulatory authorities; 4 members:
  - U.S. Food and Drug Administration
  - Health Canada
  - European Commission, Directorate General Enterprise
  - Japanese Ministry of Health, Labour and Welfare

- Purpose: to provide a multilateral framework to promote free trade by identifying ways to remove regulatory obstacles among the regions, while maintaining the highest level of global consumer protection

- All decisions and actions by consensus
  - Must be compatible with laws, regulations, policies, rules, and directives of the respective administrations and governments

- First meeting on Sept. 26-28, 2007
  - included discussions on alternatives to animal testing

ICCR Statement and Recommendations: Alternatives to Animal Testing (Sept 07)

- *ICCR recognizes the importance of reducing, refining and replacing animal testing.*
- *The group welcomes the efforts of industry and validation centers in developing and validating scientific alternatives to animal testing.*
- *Intensive collaboration and communication in the design, execution, and peer review of validation studies should be further strengthened.*
- *ICCR invites ICCVAM, ECVAM, 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.*
- *They should be supported by scientific experts from the regulatory bodies.*

Coordination of alternative test method validation and evaluation activities

- Current collaborations among ICCVAM-NICEATM, ECVAM, and JaCVAM
  - Have existed even prior to their respective establishment, and have steadily increased during the past ten years
  - As an example, all ICCVAM-NICEATM peer review panels have included international scientists since the first panel in 1998.
- However, current coordination is on an ad hoc informal basis
  - Level of coordination and communication varies widely for any given test method
  - Requires additional time and resources
  - Additionally, ICCVAM, ECVAM, and JaCVAM have very different processes to evaluate the validation status of alternative methods
- Lack of consistent coordination and different processes has contributed to:
  - Validation studies, peer reviews, and development of formal recommendations by one organization without adequate consultation and input from others
  - Test method recommendations by one organization that often cannot be considered by another organization without extensive additional review efforts
  - Wide variations in transparency and outcomes of peer review processes
  - Differences in recommendations on the usefulness of alternative methods for regulatory purposes

Initial Proposal: Development

- Based on cumulative experience of the validation organizations
  - Lessons *observed* and experience over the last 15 years
- Concept developed over three meetings/ teleconferences by ad hoc ICCR Working Group
  - February 8, 2008
  - March 17, 2008
  - March 19, 2008
- Discussed at ICCR meeting on April 9-10, 2008

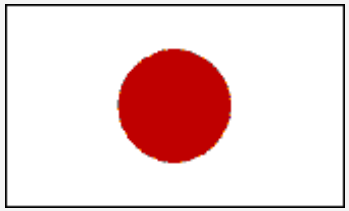
Draft Concept Presented to ICCR on Behalf of "the VAMs", April 2008

- JaCVAM: Japanese Center for the Validation of Alternative Methods:
  - Dr. Hajime Kojima, Director
- ECVAM: European Centre for the Validation of Alternative Methods
  - Dr. Valerie Zuang
  - Dr. Thomas Hartung
- ICCVAM and NICEATM: U.S. Interagency Coordinating Committee on the Validation of Alternative Methods and the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods
  - Dr. Marilyn Wind, Chairman, ICCVAM
  - Dr. William Stokes, Director, NICEATM and Executive Director, ICCVAM
- Health Canada Validation Expert
  - Dr. David Blakey, OECD Test Guidelines National Coordinator for Canada

The Proposal

International Cooperation on Alternative Test Methods (ICATM)






International Cooperation on Alternative Test Methods

GOAL:

- To ensure that new alternative test methods adopted for regulatory use will provide for:
  1. *Equivalent or improved protection of people, animals, and the environment*
  2. *Reduction, refinement (less pain and distress), or replacement of animal use whenever scientifically feasible*

ICATM Purpose

To promote international cooperation, collaboration, and communication among national validation organizations in order to:

- Ensure optimal design and conduct of validation studies
  - That will support national and international regulatory decisions on alternative methods proposed for regulatory testing.
- Ensure high quality independent scientific peer reviews
  - Provide for transparency and the opportunity for stakeholder involvement
- Enhance likelihood of harmonized recommendations by national validation organizations
  - More rapid international adoption of alternative methods
- Avoid duplication of effort and leverage limited resources to achieve greater efficiency and effectiveness

ICATM Proposed Membership

a. ICATM is a *voluntary* international group of validation organizations from the United States, Japan, the European Union, and Canada.
b. The four initial ICATM members are:
    - **NICEATM-ICCVAM**
    - **ECVAM-ESAC**
    - **JaCVAM**
    - **Health Canada**
c. The inclusion of other members and their appropriate status can be decided by consensus by the members.

International Cooperation on Alternative Test Methods

- Provides a framework for enhanced international cooperation, collaboration and communication in **three related but independent critical stages**:
  1. Test method validation studies
  2. Independent peer review of the validation status of test methods
  3. Development of formal test method recommendations

- *Recognizes that consistent and effective cooperation, collaboration, and communication are essential during ALL three stages in order to support and achieve international regulatory acceptance of alternative test methods within the shortest possible timeframe in the most efficient manner*

ICATM Process

a. The heads of each member organization are responsible for ensuring cooperation, communication, and coordination by their respective organization in accordance with this agreement
b. All decisions are by consensus
c. All decisions should respect the laws, policies, rules, regulations, and directives of members

Three Critical Areas of Cooperation

- **Validation Studies**
- **Independent Scientific Peer Review Meetings and Reports**
- **Development of Test Method Recommendations for Regulatory Consideration**

Critical Area #1: Validation Studies

- **Key Aspects of Cooperation**:
  - Information Sharing *Prior to* Validation Effort; Lead Member will provide to other members:
    - Study objectives
    - Specific regulatory testing purpose
    - Proposed validation study design
    - Detailed study protocols
    - Substances to be tested, and the basis for their selection
  - Objective: Develop consensus on critical aspects of validation studies before the validation study starts!

Critical Area #2: Independent Scientific Peer Review Meetings and Reports

- **Key Aspects of Cooperation**
  - Public availability of review documents
    - Available for comments when provided to peer review panels
  - *International* Peer Review Panels
    - Nominees from ICATM members
  - Public peer review meetings
    - Note: this is currently unique to the U.S.evaluation process
    - Need to provide opportunities for public comments
  - Peer Review Panel Report available to public and ICATM members
    - Consider in developing final recommendations
    - Consider public comments on the Report
- **Goal:** conduct peer reviews and meetings in a manner that will meet the needs of all ICATM members
  - Avoid the need to repeat peer reviews

Critical Area #3: Development of Final Test Method Recommendations for Regulatory Acceptance

- **Key Aspects of Cooperation:**
  - Lead Member Working Group considers Peer Panel Report and all relevant documents
    - WG includes liaisons from other ICATM members
    - WG prepares draft final recommendations
  - ICCVAM, ESAC, JaCVAM, and HC
    - Each considers draft final recommendations, peer review report, all supporting documents; notifies Lead of position
    - If agreement, all ICATM members finalize and forward recommendations to regulatory authorities
    - If disagreement, referred to WG to resolve
      - Unresolved disagreements discussed by ICATM members
      - If still not resolved, disagreements documented and scientific rationale provided by each ICATM member to regulatory authorities
- **Goal**: Harmonized ICATM recommendations forwarded to international regulatory authorities (e.g. OECD, ISO, ICH)

ICATM: Responsibilities and Success

- Responsibilities of member organizations: ECVAM-ESAC, NICEATM-ICCVAM, JaCVAM, HC
  - Ensure consistent coordination, cooperation, and communication in order to achieve success
  - Ensure opportunities for stakeholder participation
  - Ensure commitment of time and resources to optimize the processes
- Success will be indicated by:
  - Consensus among ICATM members on the usefulness and limitations of new alternative methods
  - More rapid national and international acceptance of alternative methods

1. Do you have any comments on the proposed approach?
2. Do you consider that the proposed effort for achieving international cooperation on the validation, scientific peer review, and development of harmonized recommendations for regulatory authorities will expedite international regulatory acceptance of alternative methods? If not, please explain why?
3. The proposal emphasizes the importance of transparency and the opportunity for stakeholder participation and public comment throughout the test method validation and evaluation processes, which are incorporated in the NICEATM-ICCVAM process. Do you have suggestions for how to foster international practices of transparency, public meetings of independent peer review panels, and the opportunity for stakeholder and public comment?