

MEMORANDUM OF COOPERATION

Between the
Japanese Center for the Validation of Alternative Methods
National Institute of Health Sciences
Ministry of Health, Labour, and Welfare of Japan

and the
National Toxicology Program Interagency Center for the Evaluation of Alternative
Toxicological Methods
National Institute of Environmental Health Sciences
National Institutes of Health
Department of Health and Human Services
The United States of America

and the
European Centre for the Validation of Alternative Methods
Institute for Health and Consumer Protection
Joint Research Centre, European Commission of the European Union

and the
Environmental Health Science and Research Bureau
Safe Environments Programme
Healthy Environments and Consumer Safety Branch
Health Canada of Canada

Regarding

International Cooperation on Alternative Test Methods (ICATM)

The participants to this Memorandum of Cooperation (“ICATM Validation Organizations”) seek to establish an International Cooperation on Alternative Test Methods (ICATM) in order to expand and strengthen cooperation, collaboration, and communications among national validation organizations on the scientific validation and evaluation of new alternative testing methods proposed for regulatory health and safety assessments.

I. Participants / ICATM Validation Organizations

The Japanese Center for the Validation of Alternative Methods (JaCVAM), within the National Institute of Health Sciences, coordinates validation studies on proposed alternative methods and peer review of test methods, and provides recommendations to regulatory authorities.

Memorandum of Cooperation

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), a component of the National Institute of Environmental Health Sciences, administers the U.S. Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). ICCVAM evaluates the validation status of new, revised, and alternative test methods, provides recommendations on test method validity to U.S. federal agencies for regulatory acceptance consideration, and coordinates cross agency issues on test method development, validation, and national and international harmonization. NICEATM also coordinates validation studies and independent scientific peer review of proposed alternative test methods.

The European Centre for the Validation of Alternative Methods (ECVAM), within the Institute for Health and Consumer Protection, Joint Research Centre, European Commission, coordinates validation studies on proposed alternative methods and evaluates the results by peer review and provides recommendations to the European Union National Coordinators for regulatory acceptance of the methods validated.

The Environmental Health Science and Research Bureau within Health Canada coordinates activities relevant to health-related test method validation and acceptance issues.

II. Purpose

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

1. Further the optimal design and conduct of validation studies to support national and international regulatory decisions on the usefulness and limitations of alternative methods.
2. Further high quality independent scientific peer reviews of alternative test methods that incorporate transparency and the opportunity for stakeholder involvement.
3. Enhance the likelihood of harmonized recommendations by validation organizations on the usefulness and limitations of alternative test methods for regulatory testing purposes.
4. Achieve greater efficiency and effectiveness by avoiding duplication of effort and leveraging limited resources.
5. Support the timely international adoption of alternative methods.

III. Objectives and Key Aspects

This Memorandum of Cooperation addresses the following objectives and key aspects for three critical areas:

Memorandum of Cooperation

1. Validation studies. The objective is to share information and develop consensus when feasible on critical aspects, prior to the conduct of validation studies, regarding:
 - Study objectives
 - Specific regulatory testing purpose
 - Proposed validation study design
 - Detailed study protocols
 - Substances to be tested
 - The basis for the selection of test substances
 - Participating laboratories

2. Independent scientific peer review meetings and reports. The objective is to organize and conduct when feasible independent scientific peer review meetings and develop reports that meet the needs of all ICATM Validation Organizations. Key aspects include, when feasible:
 - Seeking input from the other ICATM Validation Organizations during preparation of review documents and draft recommendations.
 - Providing public availability of review documents and draft recommendations when provided to peer review panel(s).
 - Developing peer review panels with international composition, including nominations solicited from ICATM Validation Organizations.
 - Holding public peer review meetings and/or providing other opportunities for stakeholder and/or public comment.
 - Making peer review panel reports available to the public and to ICATM Validation Organizations to consider in developing final recommendations.

3. Development of test method recommendations for regulatory consideration. The objective is development when feasible of harmonized test method recommendations by each of the ICATM Validation Organizations that can then be forwarded to other national and international organizations for regulatory consideration. Key aspects include, when feasible:
 - Efforts by ICATM Validation Organizations to cooperate in the preparation of draft final recommendations, taking into consideration peer review panel report(s) and other relevant documents and information.
 - Sharing of draft final recommendations among the ICATM Validation Organizations to be considered along with the peer review panel report(s) and other supporting documents.
 - Notifying the other ICATM organizations of each ICATM Validation Organization's draft position. In cases where all of the ICATM Validation Organizations mutually consent, each organization may finalize and forward their recommendations to their respective regulatory authorities to the extent authorized by applicable law.
 - Discussing unresolved disagreements to reach resolution among all of the ICATM Validation Organizations. If no resolution is reached within a reasonable timeframe, the scientific rationale for any disagreements may be documented and provided by the ICATM Validation Organizations to

regulatory authorities with their respective recommendations, to the extent authorized by applicable law.

IV. Meetings

Coordination meetings among the ICATM Validation Organizations should be held regularly as frequently as necessary to promote effective cooperation. ICATM Validation Organizations should communicate and discuss high and urgent priorities and seek ways to assist each other on expediting progress in these areas.

V. Involvement in ICATM by Non-member Validation Organizations

Non-member governmental organizations that perform validation activities and seek limited involvement with ICATM (*e.g.*, observing meetings, sharing information) may do so when feasible upon application to ICATM and unanimous consent of the ICATM Validation Organizations. Non-member governmental organizations that perform validation activities and seek full membership in ICATM may do so upon application to ICATM, unanimous consent of the ICATM Validation Organizations, and execution and adoption of this Memorandum of Cooperation.

VI. Representatives

The participants intend for the responsible Directors of the ICATM Validation Organizations, or their authorized designees at the Institutions that are signatory to this Memorandum of Cooperation, to serve as the organizational representatives on the ICATM and represent their signing institutions in all activities related to ICATM.

VII. Information, Specific Plans, and Participants' Understanding

Any exchange of information or other activity under this Memorandum of Cooperation are to be performed in accordance with applicable laws and regulations. As the need arises with regard to the objectives and key aspects described in Section III, the participants may when feasible develop specific plans of cooperation which may be incorporated in written arrangements and procedures.

Participants understand that this Memorandum of Cooperation does not establish legally binding obligations on the part of any of its participants. All cooperative activities undertaken by the participants are subject to the availability of appropriated funds, personnel, and other resources. The participants are signing this Memorandum of Cooperation with the express understanding that the Memorandum of Cooperation itself does not give rise to a claim for compensation for services against any of the respective participants.

Memorandum of Cooperation

Signed in the English and French languages.

Signed this 23rd day of April, 2009.

/ Masahiro Nishijima/

Masahiro Nishijima, Ph.D.
Director General

For the National Institute of Health Sciences
Ministry of Health, Labour, and Welfare of Japan

Signed this 27th day of April, 2009.

/ Linda S. Birnbaum/

Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S.
Director

For the National Toxicology Program and the National Institute of
Environmental Health Sciences, National Institutes of Health,
Department of Health and Human Services

Signed this 27th day of April, 2009.

/ Elke Anklam/

Elke Anklam, Ph.D.
Director

For the Institute for Health and Consumer Protection
Joint Research Centre, European Commission of the European Union

Signed this 27th day of April, 2009.

/David H. Blakey/

David H. Blakey, D.Phil.
Director

For the Environmental Health Science and Research Bureau
Safe Environments Programme
Healthy Environments and Consumer Safety Branch
Health Canada

Proper signatures
Treat as signed, § 1.4(d)(2)