Session EB4: Status report on ICATM

The International Cooperation on Alternative Test Methods (ICATM)

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Summary

On April 27, 2009, Canada, the European Union, Japan, and the United States signed a Memorandum of Cooperation (MOC) on International Cooperation on Alternative Test Methods (ICATM). The agreement provides for enhanced cooperation and collaboration between four national validation organizations: the U.S. National Toxicology Program Interagency Center for the Evaluation of Alternative Methods and its Interagency Coordinating Committee on the Validation of Alternative Methods, the Japanese Centre for Validation of Alternative Methods, the European Centre for the Validation of Alternative Methods, and the Environmental Health Science and Research Bureau within Health Canada. The validation organizations developed a framework to promote harmonization of scientific recommendations on alternative toxicity testing methods in response to a 2007 charge from the International Cooperation on Cosmetics Regulation (ICCR). The MOC, which implements the framework adopted by ICCR in 2008, provides for enhanced cooperation in three critical areas: validation studies, independent scientific peer review, and development of harmonized test method recommendations for regulatory consideration. By communicating and working together, the ICATM validation organizations will identify and embrace scientifically sound and robust test methods that will protect human and animal health and the environment and that will also reduce, refine, and replace the use of animals in testing.

Keywords: ICATM, validation, regulation, international harmonization, alternative test methods

1 Introduction

On April 27, 2009, representatives from four international agencies signed a Memorandum of Cooperation (MOC) establishing the International Cooperation on Alternative Test Methods (ICATM). The agreement promotes enhanced international cooperation and coordination on the scientific validation of non- and reduced-animal toxicity testing methods. The test methods evaluated under this agreement are expected to be more readily accepted by regulatory agencies by assuring international agreement on the scientific information demonstrating that the methods are reproducible and able to accurately identify product related health hazards. This paper describes the development of the MOC and the three major areas of cooperation covered by the agreement.

2 ICATM validation organizations

ICATM is a voluntary international cooperation of four validation organizations from the United States, Japan, the European Union, and Canada. The four initial ICATM Validation Organizations are:

- Japanese Center for the Validation of Alternative Methods (JaCVAM)
- European Centre for the Validation of Alternative Methods (ECVAM)
- U.S. Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)
- Environmental Health Science and Research Bureau, Canada

The inclusion of other participants and their appropriate status will be decided by consensus by the participating validation organizations.

3 ICATM development

The impetus for the development of ICATM occurred during the first meeting of the ICCR in September 2007. The ICCR recognized the importance of reducing, refining, and replacing animal use in toxicity testing and recommended the strengthening of international collaboration and communication. In response to the ICCR recommendation, ICCVAM, ECVAM, JaCVAM, and Health Canada developed a framework to ensure a collaborative approach to this issue. ICCR noted that such efforts should be supported by scientific experts from the regulatory bodies. Figure 1 shows a timeline of the development and adoption of the ICATM framework leading to the signing of the MOC in April of 2009. The ICATM Memorandum of Cooperation was signed at the National Institutes of Health on April 27, 2009. Signers included Masahiro Nishijima, Ph.D., Director General, National Institute of Health Sciences, Ministry of Health, Labour, and Welfare of Japan; Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S., Director, National Toxicology Program and the National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services of the United States; Elke Anklam, Ph.D., Director, Institute for Health and Consumer Protection, Joint Research Centre, European Commission of the European Union; and David H. Blakey, D.Phil., Director, Environmental Health Science and Research Bureau, Safe Environments Programme, Healthy Environments and Consumer Safety Branch, Health Canada.

4 Coordination of alternative test method validation and evaluation activities

Collaborations between ICCVAM, ECVAM, and JaCVAM have existed and have steadily increased during the past ten years. However, coordination of interactions had been on an ad hoc informal basis. The lack of consistent coordination and the different processes used by the different validation organizations sometimes resulted in validation studies, peer reviews, and development of formal recommendations by one organization without adequate consultation and input from the others. This often led to test method recommendations by one organization that could not be considered by another organization without extensive additional review efforts, and wide variations in transparency and outcomes of peer review processes.

5 ICATM Memorandum of Cooperation

The purpose of the MOC is to promote consistent and enhanced voluntary international cooperation, collaboration, and communication among national validation organizations in order to:
- Further the optimal design and conduct of validation studies to support national and international regulatory decisions on the usefulness and limitations of alternative methods
- Further high quality independent scientific peer reviews of alternative test methods that incorporate transparency and opportunity for stakeholder involvement
- Enhance the likelihood of harmonized recommendations by validation organizations on the usefulness and limitations of alternative test methods for regulatory testing purposes
- Achieve greater efficiency and effectiveness by avoiding duplication of effort and leveraging limited resources
- Support the timely international adoption of alternative methods

The Memorandum of Cooperation (MOC) was signed at the National Institutes of Health on April 27, 2009 (ICATM, 2009; U.S. NIH, 2009). The goals of the MOC are 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; and
- 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 (causing less pain and distress) animal use whenever scientifically feasible.

Development of ICATM Framework and Memorandum of Cooperation	
Sep 2007	• ICCR Initial Meeting – Brussels
Feb/Mar 2008	• Validation Organizations Develop Draft Framework
Apr 2008	• Validation Organizations Present Draft Framework to ICCR Working Group
Jul 2008	• Revised Draft Discussed at Second ICCR Meeting – Rockville, Maryland, U.S.A.
Oct 2008	• ICATM Framework Adopted by ICCR
Apr 2009	• ICATM Memorandum of Cooperation Signed by Canada, European Union, Japan, and the United States.

Fig. 1: The development of the ICATM Framework was an interactive process involving consensus development among all four validation organizations.

The MOC addresses three critical areas of cooperation: validation studies, independent peer review of the validation status of test methods, and the development of formal test method recommendations on alternative testing methods. By coordinating the validation, peer review, and development of recommendations, ICATM will reduce differences between the organizations in recommendations on the usefulness of alternative methods for regulatory purposes. This should accelerate international adoption of scientifically valid alternative test methods.

Critical area #1 – Test method validation studies
The objective of ICATM cooperation on test method validation studies is to share information and develop consensus on critical scientific aspects of validation studies prior to their initiation. Participants will collaborate and seek consensus on the proposed validation study design, study protocol, and selection of reference substances to be tested. Data developed in such studies are more likely to be usable by all members and meet the needs of their regulatory authorities, reducing the cost and time wasted in duplication of efforts. (Fig. 2)

Critical area #2 – Independent Scientific Peer Review Meetings and Reports
The organization and conduct of Independent Scientific Peer Review Meetings is a critical, but timely and costly component of evaluating alternative test methods. ICATM members have agreed to consider the needs of all ICATM Validation Organizations when organizing and conducting such meetings.

Specifically, member organizations have agreed to share and seek input from each other during the preparation of background review documents and draft recommendations and to make these publically available when provided to peer review panel(s). Peer review panels will have international representation including solicitation of nominations from other ICATM Validation Organizations.

ICATM is also committed to making the review process as open and transparent as possible by holding public peer review meetings or providing other opportunities for stakeholder and public comment and by making peer review panel reports available to the public and to ICATM Validation Organizations to consider in developing final recommendations.

Critical area #3 – Development of harmonized test method recommendations
The last critical area of ICATM cooperation is the development of harmonized test method recommendations to forward to regulatory authorities for acceptance decisions. Ultimately, the most expeditious international adoption of new alternative test methods can be accomplished when there is agreement on test method recommendations by all of the national validation organizations. In order to achieve such harmonization, the ICATM framework provides for the cooperation between ICATM Validation Organizations in the preparation of both draft and final recommendations. Draft final recommendations will be shared within ICATM and will be considered along with the peer review panel report(s) and other supporting documents. Members will notify each other of their respective draft position. In cases where all of the ICATM Validation Organizations mutually agree, each organization will finalize and forward their recommendations to their respective regulatory authorities as authorized by applicable law. If there are unresolved disagreements among the ICATM Validation Organizations, the scientific rationale for these disagreements will be documented and provided by each validation organization with recommendations.

Harmonization of recommendations prior to regulatory consideration is expected to reduce differences in test methods adopted by various countries. This in turn will reduce issues created by differing regulatory guidelines, thereby facilitating more rapid adoption of new alternative test methods internationally.

6 Conclusions

The development of the ICATM framework and signing of the MOC has set the stage for a high level of transparency and the opportunity for broad stakeholder involvement during validation, peer review meetings, and preparation of final recommendations. ICATM participants are committed to consist-

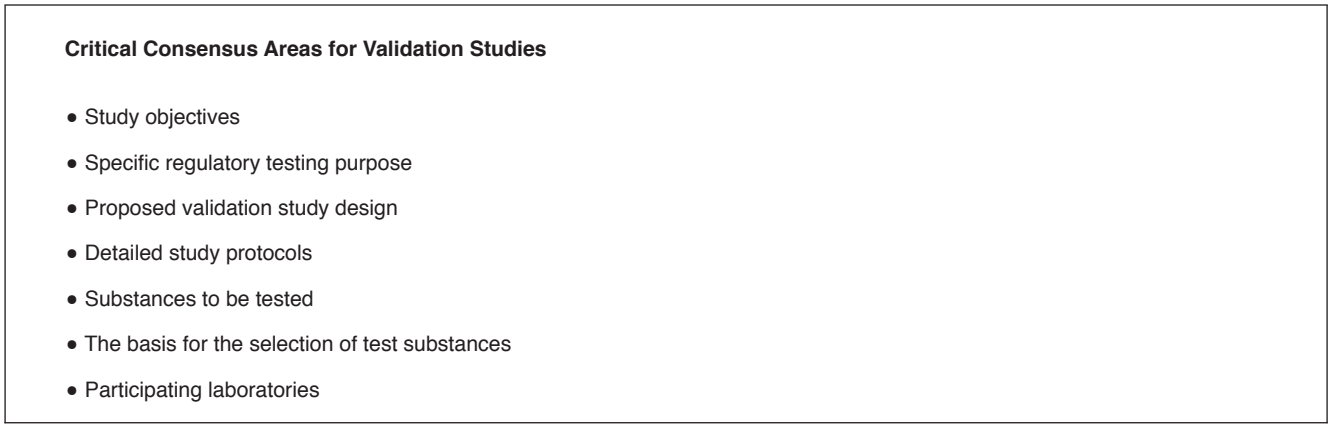

Fig. 2: Critical areas for ICATM Validation Organizations to reach consensus prior to initiation of validation studies.

ent coordination, cooperation, and communication to achieve success in the adoption of scientifically valid alternative test methods. Success will be indicated by consensus on the usefulness and limitations of new alternative methods, followed by rapid national and international acceptance.

We are encouraged that the new level of cooperation and coordination outlined in the ICATM agreement will ensure that new test methods provide for equivalent or better protection of people, animals, and the environment, and the reduction, refinement, and replacement of animals where scientifically feasible.

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