



Health
Canada

Santé
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Your health and safety...our priority

Votre santé et votre sécurité... notre priorité

Helping the people
of Canada maintain and
improve their health

Aider les Canadiens et
les Canadiennes à maintenir
et à améliorer leur santé

Challenges to Implementation of Risk Assessment and Testing Guidelines



Challenges

- Validation
- Interpretation
- Regulatory Instruments



Validation



Development of Alternative Tests

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.***



Key Elements of Validation

- Prediction Model – Validated for what purpose
- Intra-laboratory repeatability and reproducibility
- Inter-laboratory transferability
- Inter-laboratory reproducibility
- Predictive capacity (accuracy – sensitivity and specificity)



From Test Concept to Regulatory Acceptance

1. Prevalidation
industry/academia/government/validation centre
2. Validation Study Design
3. Validation study
4. Peer Review
5. Background Review Document
6. Statement of Validation
7. Recommendation for regulatory acceptance
8. National regulatory acceptance
9. International guideline (OECD, ICH)

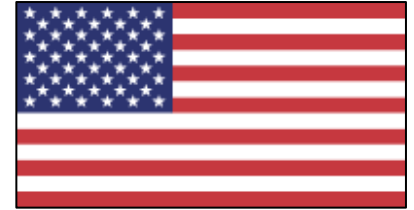
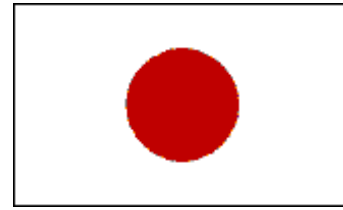


Current coordination of alternative test method validation and evaluation activities

- Currently on an ad hoc informal basis, but:
 - Level of coordination and communication varies widely for any given test method
 - ICCVAM, ECVAM, and JaCVAM have very different processes to evaluate the validation status of alternative methods
- This lack of consistent cooperation has led to:
 - **The conduct of validation studies, peer reviews, and development of formal recommendations by one organization without adequate consultation and input from the other validation organizations**
 - **Test method recommendations by one validation organization that often cannot be considered by another organization without extensive additional efforts**
 - **Wide variations in transparency and outcomes of peer review processes**
 - **Differences in recommendations on the usefulness of alternative methods for regulatory purposes**



International Cooperation on Alternative Test Methods (ICATM)



Working Group Members

ICCVAM

US Interagency Coordinating Committee on Validation of Alternative Methods

ECVAM

European Centre for Validation of Alternative Methods

JaCVAM

Japanese Centre for the Validation of Alternative Methods

Health Canada (BVam)

no specific agency or dedicated resources



International Cooperation on Alternative Test Methods

- Developed in response to ICCR recommendation (International Coordination on Cosmetics Regulation)
- 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**



Role of ICATM

To promote 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 that incorporate transparency and the opportunity for stakeholder involvement.
- c. Enhance the likelihood of **harmonized recommendations** by national validation organizations on the usefulness and limitations of alternative test methods for regulatory testing purposes.
- d. **Avoid duplication** of effort and leverage limited resources to achieve greater efficiency and effectiveness.



Interpretation

- In future, will methods be more sensitive?
- When is a response a toxicological effect?
- At what level of response would you expect manifestation as an adverse effect?



Regulatory Instruments

- Can be inflexible
- Can take significant time to change
- Need a nimble regulatory system

