Update on International Collaborations/ICATM and Interactions with ECVAM

Anna B. Lowit, Ph.D.
Co-Chair, ICCVAM
Senior Scientist, Health Effects Division
US EPA, Office of Pesticide Programs
lowit.anna@epa.gov
703-308-4135
International Collaboration

- International collaboration, harmonization, and adoption of alternative test methods are high priorities for ICCVAM.

- OECD Test Guidelines program provides a mechanism for the international evaluation and adoption of alternative methods by its 34 member countries.

- The International Cooperation on Alternative Test Methods (ICATM):
  - provides means to coordinate the validation and adoption of alternative test methods among its member countries: United States, Canada, Europe Union, Japan, and Korea.
  - established to promote 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.
  - "Alternative Test Method Validation and Regulatory Acceptance Status Report" includes a comprehensive listing of test method evaluation activities undertaken by ICATM partner organizations.
International Collaboration

• European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM):
  – conducts validation study review and approval processes in a manner that meets the needs of US regulatory agencies.
  – has a dedicated budget and a network of laboratory facilities that can accommodate the requisite level of activity needed to produce a robust pipeline of alternative methods.
• In contrast, to ICCVAM which has no budget & NICEATM which is not budgeted to conduct validation studies.
International Collaboration

• ICCVAM and NICEATM are working with EURL-ECVAM on a process
  – that will enable US scientists to participate actively in the EURL-ECVAM test method evaluation of the usefulness and limitations of relevant test method and
  – that will increase the transparency of the evaluation.

• U.S. designees will participate in each of the various steps of the evaluation from test method submission, to validation study design, to peer review, to final recommendations.
  – The process will also include opportunities for public comment, inform stakeholders of new methods, that are available, and by ICCVAM working together with ECVAM avoid duplicative reviews that can delay test method acceptance.
<table>
<thead>
<tr>
<th>NETVAL laboratories</th>
<th>ICATM cooperation</th>
<th>Stakeholder dialogue</th>
<th>EURL ECVAM Validation Process</th>
<th>Key documents</th>
</tr>
</thead>
</table>
| **ICATM**: Exchange Information on promising submissions. Select mode of collaborative activity. | **Public input** on planned Validation Study. Submission of existing information. | **Relevance assessment:**  
- PARERE: regulatory relevance  
- ESTAF: user relevance | **1. Assessment of test method submission**  
Scientific and regulatory aspects. Stakeholder relevance (priority setting). | **Test Submission**  
**Submission Assessment Report** |
| **ICATM**: Technical aspects of VS. Propose VMG members. Second liaison members (=observers). | **Comments on draft recommendation:**  
- PARERE  
- ESTAF | | **2. Planning and conduct of Validation Study (VS).**  
Test method evaluation. | **Validation Project Plan (VPP)**  
**Validation Report (VR)** |
| **ICATM**: Proposal of experts for the ESAC WG supporting the ESAC peer review. | **Public input** on draft ECVAM recommendations | | **3. ESAC review of (1) VS conduct (2) VS conclusions**  
ESAC opinion on test method’s validity for purpose. | **ESAC Request**  
**ESAC Reports & Opinion** |
| **ICATM**: Harmonised recommendations of validated test methods (if feasible). | | | **4. ECVAM Recommendation on validated test method.**  
4.1. ‘Right to be heard’ process. | **Draft ECVAM Recommendation** |
| | | | **4.2. Public Commenting on EURL ECVAM draft recommendation** | |
ICCVAM Participation on ECVAM Activities (1)
ICCVAM Participation on ECVAM Activities (2)

ICCVAM Statement
- Publish on website and through ICCVAM-All email list
- Relevance of recommendation to US regulations
- Announce any further ICCVAM activities

Additional Validation (Optional)
- Testing of additional substances (expand domain or compare to other methods)
- Additional analysis (e.g., using US categorization)
- Testing at additional laboratories (transferability)

Other Activities (Optional)
- Workshops
- Collect additional data (FR notices)

Formal ICCVAM Recommendation (Optional)
- Recommendation and transmittal to agencies
- Only used when required
- New peer review required if additional data or analysis used in developing recommendation

Negotiate Harmonized Recommendations
- Assess relevance of ECVAM draft recommendation to US regulatory agencies
- Identify additional activities needed for US adoption
- Identify and plan ICCVAM response to ECVAM Recommendation

ICCVAM - NICEATM - Working Groups

Process
4.1 “Right to be heard” process

4.2 Public Commenting
- Public input on draft ECVAM recommendation

4.3 Publication
- Final ECVAM Recommendation
- ESAC Report and Opinion
- Validation Stud Rep
ICCVAM Responses to ECVAM Recommendations

- Recently, ICCVAM, reviewed the recommendations and, has prepared responses that put the recommendations into context relative to their applicability for U.S. regulatory testing.
  - Direct Peptide Reactivity Assay (DPRA)
  - Zebrafish Embryo Toxicity Test (ZFET)
  - Keratinosens
  - Cell Transformation Assay based on the Bhas 42 cell line
  - 3T3 Neutral Red Update (3T3 NRU) Cytotoxicity Assay for the Identification of Substances not Requiring Classification for Acute Oral Toxicity.
International Coordination

• FY 2015 Goals:
  – Nominate ICCVAM agency experts to international expert working groups, validation management teams, and organizing committees
  – Serve as a forum to communicate updates to ICCVAM agencies on international activities relevant to the 3Rs
  – Nominate methods for interlaboratory validation to the EURL ECVAM network of testing laboratories
  – Continue active participation in ICATM
  – Work with ECVAM on a process for test method acceptance
Charge Questions

• Please comment on ICCVAM’s effort toward international evaluation and adoption of alternative methods.
• Please comment on ICCVAM’s statements regarding ECVAM’s recommendations on the alternative test methods.
• Please comment on ICCVAM’s participation on ECVAM Test Methods Evaluations.