NICEATM and ICCVAM: Recent ICATM Contributions and Future Plans

Marilyn Wind, Ph.D.
ICCVAM Chair, 2007-2010
U.S. Consumer Product Safety Commission (Retired)

ICATM: Translating Science to Provide Improved Public Health Safety Assessment Tools

Society of Toxicology
50th Anniversary Annual Meeting
March 7, 2011
Washington, DC
What is ICCVAM?

- The Interagency Coordinating Committee on the Validation of Alternative Methods was established by the NIEHS in 1997.
- Members represent the heads of 15 U.S. Federal regulatory and research agencies.
- Duties include:
  - Advising on test method development and validation
  - Conducting technical reviews of new safety testing methods
  - Transmitting formal recommendations to Federal agencies
  - Promoting regulatory acceptance of valid methods
  - Fostering national and international harmonization
- Began as ad hoc committee, 1994
- Standing committee, 1997
  - Permanent committee under NICEATM
What is NICEATM?

- The **National Toxicology Program (NTP)** **Interagency Center for the Evaluation of Alternative Toxicological Methods**
- A Center of the U.S. NTP, headquartered at the National Institute of Environmental Health Sciences, NIH, DHHS
  - NIEHS is one of the 27 NIH Institutes and Centers
  - NTP coordinates toxicology testing programs across the federal government
  - Located in Research Triangle Park, North Carolina
- Administers and provides scientific support for the **Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)**
- Conducts international validation studies
The 15 ICCVAM Member Agencies

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<td>- Consumer Product Safety Commission</td>
<td>- Agency for Toxic Substances and Disease Registry</td>
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<td>- Department of Agriculture(^1)</td>
<td>- National Institute for Occupational Safety and Health-CDC</td>
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\(^1\) Also has research component
NICEATM and ICCVAM Progress

- 40 alternative safety testing methods accepted/endorsed by U.S. and international agencies since 1999
  - Can significantly reduce, refine, and replace animal use
  - International test guidelines and guidances

- Recommendations for R&D, translation, and validation activities to further advance methods
NICEATM Coordination: International Validation Studies

Consultation Sponsors
- Industry
- Others
- NIEHS

Study Management Team
- NICEATM Staff
- ICATM Liaisons
- Sponsor Representatives

Consultation
- ICCVAM Working Group
- Developers
- Other Stakeholders

International Study Sites
- Laboratory #1 (Lead)
- Laboratory #2
- Laboratory #3

NTP Coded Chemical Distribution
ICCVAM Test Method Evaluations: Coordination with ICATM Partners

**Interagency Test Method Working Group (WG)**
- ICATM partners designate a liaison to WG
- ICATM input to draft Background Review Documents, draft test method recommendations

**Independent Scientific Peer Review**
- ICATM and public: nominations for international Peer Review Panel members
- ICATM partners help solicit public comments on draft BRDs/recommendations
- ICATM attendance at public Panel meeting
- ICATM and public availability of Final Panel report

**Harmonized Test Method Recommendations**
- WG & ICATM liaisons consider PRP Report, SACATM and public comments
  - Propose final recommendations
  - Seek ICATM consensus on recommendations (or document basis for differences)
- ICCVAM Final Reports
  - Forwarded to regulatory authorities for acceptance decisions
  - Provided to ICATM partners to send to their regulatory authorities
  - Forwarded for international test guideline adoption (OECD, etc.)
Recently Adopted Alternatives: Isolated Chicken Eye (ICE) Test Method

- **Whole eyes isolated from chickens:**
  - Easy to collect
  - Similar to human
  - Bowman’s layer present
  - Very uniform

- **3 primary endpoints** – combined for an *in vitro* hazard category

- **ICE is now accepted internationally (OECD TG 438) as a screen for identifying ocular corrosives and severe irritants**
Recently Adopted Alternatives: Bovine Corneal Opacity and Permeability (BCOP)

- Viable corneas maintained in organ culture
- Test substance exposure on the corneal surface
- Scores combined to calculate an in vitro irritancy score
- **BCOP is now accepted internationally (OECD TG 438) as a screen for identifying ocular corrosives and severe irritants**

**Quantitative** change in light passage (opacity)

Photos from MB Research Laboratories (http://www.mbresearch.com/bcop.htm)

**Quantitative** change in the epithelial barrier (fluorescein penetration)
Recent International Adoption: Reduced LLNA (rLLNA)

- Reduces animal use by 40% for each test vs. multi-dose LLNA
  - Modification of the murine local lymph node assay (LLNA) to test for allergic contact dermatitis hazards
  - Applicable to most testing situations

- OECD LLNA test guideline (TG 429) updated to include rLLNA in 2010

Abbreviations: GPMT/BT = guinea pig maximization test/Buehler test
Recent International Adoption: Nonradioactive “Green” LLNA Test Methods

- **LLNA: BrdU-ELISA**
  - Measures BrdU incorporation as a correlate to lymph node cell proliferation
  - ELISA detects peroxidase-labeled BrdU antibody

- **LLNA: DA**
  - Measures ATP content as a correlate to lymph node cell proliferation
  - ATP content assessed by a luciferin-luciferase assay to measure ATP bioluminescence

**OECD Test Guidelines for each adopted in 2010**
- TG 442A - LLNA: DA
- TG 442B - LLNA: BrdU-ELISA
International Validation Study: BG1 Luc ER TA (LumiCell®) Assay

- Human ovarian carcinoma cells (BG1)
- NIEHS SBIR-funded development (XDS, Inc)
- NICEATM (lead), ECVAM and JaCVAM sponsored validation labs
- Completed 2010
- Independent international peer review
  - March 29-30, 2011 public meeting
  - NIH, Bethesda, MD
International Validation Study: MCF-7 Cell Proliferation Assay

- Human breast carcinoma cells (MCF-7)
- Cell proliferation – DNA content
- NIEHS SBIR-funded development (Certichem, Inc.)
- NICEATM (lead), KoCVAM and JaCVAM sponsored validation labs
- Scheduled completion – Spring 2011
Nominations and Submissions to ICCVAM

- Advances in science and technology are expected to yield new methods applicable to regulatory safety testing
  - Tox 21, ToxCast, etc.
- NICEATM and ICCVAM seek nominations and submissions for:
  - Validation studies
  - Formal evaluations
  - Other activities
- Of particular interest are methods with potential to:
  - Provide improved safety or hazard assessment
  - Reduce, refine, and replace the use of animals
- Contact NICEATM for more information
Thank you for your attention.

NICEATM-ICCVAM

http://iccvam.niehs.nih.gov/

Email: niceatm@niehs.nih.gov

This presentation may not necessarily reflect the official position of any U.S. Agency.