
DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Toxicology Program (NTP); NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM); Workshop on Acute Chemical Safety Testing: Advancing In Vitro Approaches and Humane Endpoints for Systemic Toxicity Evaluations

AGENCY: National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH).

ACTION: Workshop announcement.

SUMMARY: The Interagency Committee on the Validation of Alternative Methods (ICCVAM) and NICEATM announce the upcoming ''Scientific Workshop on Acute Chemical Safety Testing: Advancing *In Vitro* Approaches and Humane Endpoints for Systemic Toxicity Evaluations.'' The goals of the workshop are to:

(1) Review the state-of-the-science and identify knowledge gaps regarding the key pathways involved in acute systemic toxicity.

(2) Recommend how these knowledge gaps can be addressed by collecting mechanistic biomarker data during currently required *in vivo* safety testing.

(3) Recommend how key *in vivo* pathway information can be used to develop more predictive mechanism-based *in vitro* test systems and earlier, more humane endpoints for *in vivo* test methods.

(4) Recommend how mechanism-based *in vitro* test systems and earlier, more humane endpoints can be used to further reduce, refine, and eventually replace animal use for acute systemic toxicity testing while ensuring the protection of human and animal health.

This workshop is open to the public with attendance limited only by the space available.

DATES: The workshop will be held on February 6–7, 2008.

ADDRESSES: The workshop will be held at the NIH, Natcher Conference Center, 45 Center Drive, Bethesda, MD 20892. A draft agenda and other information are available on the ICCVAM workshop Web site (*http://iccvam.niehs.nih.gov/meetings/AcuteToxWksp08/AcuteToxWksp08.htm*) and can be obtained from NICEATM (see **FOR FURTHER INFORMATION CONTACT** below).

FOR FURTHER INFORMATION CONTACT: Dr. William S. Stokes, NICEATM Director, NIEHS, P.O. Box 12233, MD EC–17, Research Triangle Park, NC 27709, (telephone) 919–541–2384, (fax) 919–541–0947, (e-mail) *niceatm@niehs.nih.gov.*

SUPPLEMENTARY INFORMATION:

Background

NICEATM and ICCVAM convened a peer review panel meeting in 2006. The panel was charged to determine the

usefulness and limitations of two *in vitro* cytotoxicity test methods for determining starting doses for two acute oral toxicity test methods, the Up-and-Down Procedure and the Acute Toxic Class method, in order to reduce the number of animals used in each of these *in vivo* tests. The panel's conclusions and recommendations are described in the *Peer Review Panel Report: The Use of In Vitro Basal Cytotoxicity Test Methods for Estimating Starting Doses for Acute Oral Systemic Toxicity Testing* (available at *http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_scpeerrev.htm*). The panel recommended that ICCVAM consider convening a working group to explore mechanisms of action for acute toxicity and to identify approaches for acquiring additional information on acute toxicity mechanisms when conducting required *in vivo* acute toxicity testing. The Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) met by teleconference on August 3, 2006, and expressed support for the panel's recommendations (minutes of that meeting are available at *http://ntp.niehs.nih.gov/files/SACATMAug06MinutesVF081506.pdf*).

NICEATM and ICCVAM included activities in their draft Five-Year Plan (2008–2012) (*http://iccvam.niehs.nih.gov/docs/5yearplan.htm*) to further reduce animal use and potential pain and distress associated with acute toxicity testing. These included organizing an international workshop to (1) identify predictive and more humane endpoints that may be used to terminate studies earlier in order to further reduce the severity and duration of pain and distress and (2) identify and standardize procedures for collecting mechanistic information from *in vivo* acute oral toxicity testing that will aid in developing batteries of predictive *in vitro* test methods that can further reduce and eventually replace animals for acute toxicity testing.

The ICCVAM Acute Toxicity Working Group subsequently organized this workshop in coordination with NICEATM, the European Centre for the Validation of Alternative Methods, and the Japanese Center for the Validation of Alternative Methods. The goals of the workshop are to:

(1) Review the state-of-the-science and identify knowledge gaps regarding the key pathways involved in acute systemic toxicity.

(2) Recommend how these knowledge gaps can be addressed by collecting mechanistic biomarker data during currently required *in vivo* safety testing.

(3) Recommend how key *in vivo* pathway information can be used to develop more predictive mechanism-based *in vitro* test systems and earlier more humane endpoints for *in vivo* test methods.

(4) Recommend how mechanism-based *in vitro* test systems and earlier, more humane endpoints can be used to further reduce, refine, and replace animal use for acute systemic toxicity testing while ensuring the protection of human health.

Workshop Attendance and Registration

The workshop will be held on February 6–7, 2008, at the NIH Natcher Conference Center, 45 Center Drive, Bethesda, MD 20892. Sessions will begin at 8 a.m. and end at approximately 5 p.m. on both days. Persons needing special assistance in order to attend, such as sign language interpretation or other reasonable accommodation, should contact 919–541–2475 voice, 919–541–4644 TTY (text telephone, through the Federal TTY Relay System at 800–877–8339), or e-mail *niehsoeeo@niehs.nih.gov*. Requests should be made at least seven days in advance of the event. This workshop is open to the public with attendance being limited only by the space available. Individuals who plan to attend are encouraged to register in advance with NICEATM. Registration information, an agenda, and additional information are available on the workshop Web site (*http://iccvam.niehs.nih.gov/meetings/AcuteToxWksp08/AcuteToxWksp08.htm*) and upon request to NICEATM (see **FOR FURTHER INFORMATION CONTACT** above).

Preliminary Workshop Agenda

Day 1—Wednesday, February 6, 2008

- Opening Plenary Session—Welcome and Overview of Workshop Objectives.
- Session 1—Current Acute Systemic Toxicity Injury and Toxicity Assessments.
- Session 2—Key Pathways and Biomarkers for Acute Systemic Toxicity.
- Concurrent Breakout Group (BG) Discussions:

—BG 1: Acute Systemic Toxicity Injury and Toxicity Assessments.

—BG 2: Key Pathways and Biomarkers for Acute Systemic Toxicity.

- Adjournment.

Day 2—Thursday, February 7, 2008

- Plenary Session—Discussion of Conclusions and Recommendations from Breakout Groups 1 and 2.
- Session 3—Developing Earlier Humane Endpoints for Acute Systemic Toxicity.
- Session 4—State of the Science: Using *In Vitro* Methods to Predict Acute Systemic Toxicity.
- Concurrent BG Discussions:

—BG 3: Developing Earlier Humane Endpoints for Acute Systemic Toxicity Testing.

—BG 4: Applying *In Vivo* Mechanistic Pathway Information to the Development and Validation of *In Vitro* Methods for Assessing Acute Systemic Toxicity.

—BG 5: Partnering with Industry to Advance Acute Toxicity Alternative Test Method Development, Validation, and Use.

- Plenary Session—Discussion of Conclusions and Recommendations from Breakout Groups 3, 4, and 5.
- Workshop Adjournment.

Background Information on ICCVAM, NICEATM, and SACATM

ICCVAM is an interagency committee composed of representatives from 15 Federal regulatory and research agencies that use, generate, or disseminate toxicological information. ICCVAM conducts technical evaluations of new, revised, and alternative methods with regulatory applicability and promotes the scientific validation and regulatory acceptance of toxicological test methods that more accurately assess the safety and hazards of chemicals and products and that refine, reduce, and replace animal use. The ICCVAM Authorization Act of 2000 (42 U.S.C. 285*l*–3) established ICCVAM as a permanent interagency committee of the NIEHS under NICEATM. NICEATM administers ICCVAM and provides scientific and operational support for ICCVAM-related activities. NICEATM and ICCVAM work collaboratively to evaluate new and improved test methods applicable to the needs of Federal agencies. Additional information about ICCVAM and NICEATM can be found on their Web site (*http://iccvam.niehs.nih.gov*).

SACATM was established January 9, 2002, and is composed of scientists from the public and private sectors (**Federal Register**, Vol. 67, No. 49, page 11358, March 13, 2002). SACATM provides advice to the Director of the NIEHS, ICCVAM, and NICEATM regarding the statutorily mandated duties of ICCVAM and activities of NICEATM. Additional information about SACATM, including the charter, roster, and records of past meetings, can be found at *http://ntp.niehs.nih.gov/go/167*.

Dated: December 19, 2007.

Samuel H. Wilson,

Acting Director, National Institute of Environmental Health Sciences and National Toxicology Program.

[FR Doc. E7–25536 Filed 1–2–08; 8:45 am]

BILLING CODE 4140–01–P