

Workshop on Acute Chemical Safety Testing: Advancing *In Vitro* Approaches and Humane Endpoints for Systemic Toxicity Evaluations

National Institutes of Health (NIH) Natcher Conference Center

February 6 – 7, 2008

Workshop Agenda and Topics

Day 1 Wednesday, February 6, 2008

0800 Registration

0830 Opening Session - Welcoming Remarks

William Stokes, D.V.M., DACLAM, Director NICEATM, Executive Director, ICCVAM

Marilyn Wind, Ph.D., CPSC, Chair, ICCVAM

Thomas Hartung, M.D., Ph.D., Director, ECVAM

Hajime Kojima, Ph.D., Director, JaCVAM

Workshop Objectives

William Stokes, D.V.M., DACLAM

Session 1 Acute Systemic Toxicity: Public Health Significance and Regulatory Testing Needs

*Co-chairs: William Stokes, D.V.M., DACLAM (NIEHS)
 Marilyn Wind, Ph.D. (CPSC)*

0900 Public Health Perspective of Acute Poisoning

Daniel Cobaugh, PharmD., DABAT, Director of Research and Program Development, American Society of Health-System Pharmacists (ASHP) Research and Education Foundation, Silver Spring, MD

0930 Regulatory Needs and Uses for Acute Systemic Toxicity Data

Amy Rispin, Ph.D., Senior Scientist, Field and External Affairs Division, Office of Pesticide Programs, EPA

Session 2 Acute Systemic Toxicity: Human and Animal Assessments, Biomarkers, and Key Pathways

*Co-Chairs: Debbie McCall (EPA)
 Thomas Hartung, M.D., Ph.D. (ECVAM)*

0950 Data Currently Collected During Acute Systemic Toxicity Tests

Gary Wnorowski, B.A., M.B.A., LAT, President, Eurofins Product Safety Laboratories

1010 Break

- 1030 Quantifying Evident Toxicity for the Fixed Dose Procedure**
Robert Guest, B.Sc., Head of Alternative and Acute Toxicology, Safepharma Laboratories
- 1050 Clinical Biomarkers Used to Diagnose and Treat Acute Poisoning in Humans**
Frank Paloucek, Pharm.D. DABAT, FASHP, Director of Residency Programs, College of Pharmacy, University of Illinois at Chicago
- 1120 Clinical Biomarkers Used to Diagnose and Treat Acute Poisoning in Animals**
Steven Hansen, D.V.M., DABT, DABVT, Senior Vice President, ASPCA Animal Poison Control Center, University of Illinois at Urbana-Champaign
- 1150 Lunch**
- 1250 Methodologies for Collecting Clinical Biomarker Data in Laboratory Animals**
Karen Steinmetz, Ph.D., DABT, Director, Mammalian Toxicology Dept., Biosciences Division, SRI International
- 1310 Non-Invasive and Minimally Invasive Techniques for Measuring Physiological Parameters in Laboratory Rodents**
Kathleen Murray, D.V.M., M.S., DACLAM, Senior Director, Animal Program Management, Charles River Laboratories
- 1335 Break**
- 1350 Concurrent Breakout Group Discussions**
- a. Breakout Group 1: Key Pathways for Acute Systemic Toxicity**
Co-chairs: Daniel Acosta, Ph.D., Dean, College of Pharmacy, University of Cincinnati
Frank Paloucek, PharmD., DABAT, FASHP, Director of Residency Programs, College of Pharmacy, University of Illinois at Chicago
Recorders: David Allen, Ph.D., Integrated Laboratory Systems, Inc.
Raymond Tice, Ph.D., Deputy Director, NICEATM, NIEHS
- b. Breakout Group 2: Current Acute Systemic Toxicity Injury and Toxicity Assessments**
Co-chairs: A. Wallace Hayes, Ph.D., DABT, FATS, Flbiol, Science Advisor and Visiting Scientist, Harvard School of Public Health
Daniel Marsman, D.V.M., Ph.D., DABT, Section Head, Animal Welfare and Alternatives, Procter & Gamble
Recorders: Michael Paris, Integrated Laboratory Systems, Inc.
Judy Strickland, Ph.D., DABT, Integrated Laboratory Systems, Inc

1520 Break

1535 Concurrent Breakout Group Discussions (continued)

1700 Breakout Groups Adjourn

1715 Breakout Group Co-chairs meet with Organizing Committee

Close of Day 1

- Day 2** **Thursday, February 7, 2008**
- 0800** **Registration**
- 0830** **Plenary Session - Discussion of Conclusions and Recommendations Reached by Breakout Groups 1 & 2**
Co-Chairs: William Stokes, D.V.M., DACLAM, NIEHS/NICEATM
Marilyn Wind, Ph.D., CPSC
- 0830** **a. Breakout Group 1: Key Pathways for Acute Systemic Toxicity**
Co-chairs: Daniel Acosta, Ph.D.
Frank Paloucek, PharmD. DABAT, FASHP
- 0850** **b. Breakout Group 2: Current Acute Systemic Toxicity Injury and Toxicity Assessments**
Co-chairs: A. Wallace Hayes, Ph.D., DABT, FATS, Flbiol
Daniel Marsman, D.V.M., Ph.D., DABT
- Session 3** **Humane Endpoints**
Co-Chairs: Masih Hashim, Ph.D. (EPA)
Cassandra Prioleau, Ph.D. (CPSC)
- 0910** **The Concept of Humane Endpoints and Their Identification: Application for Acute Systemic Toxicity Testing**
 William Stokes, D.V.M., DACLAM, NIEHS, Director, NICEATM
- 0930** **Opportunities for Detecting Pain and Distress Associated with Acute Systemic Toxicity**
 Steven Niemi, D.V.M., DACLAM, Director, Center for Comparative Medicine, Massachusetts General Hospital
- 1000** **Break**
- Session 4** **State of the Science: Using *In Vitro* Methods to Predict Acute Systemic Toxicity**
Co-Chairs: Steven Reynolds, Ph.D. (NIOSH)
Hajime Kojima, Ph.D. (JaCVAM)
- 1015** **The Future of Toxicology as a Predictive Science**
 Melvin Andersen, Ph.D., DABT, Director, Division of Computational Biology, The Hamner Institutes for Health Sciences
- 1045** **Recommendations from the ICCVAM-NICEATM International Workshop on *In Vitro* Methods for Assessing Acute Systemic Toxicity**
 A. Wallace Hayes, Ph.D., DABT, FATS, Flbiol, Science Advisor and Visiting Scientist, Harvard School of Public Health

1105 **Current ICCVAM Recommendations for the Use of *In Vitro* Test Methods to Estimate Acute Systemic Toxicity**
Marilyn Wind, Ph.D., CPSC

1125 **The ACuteTox Project: Optimization and Prevalidation of an *In Vitro* Test Strategy for Predicting Human Toxicity**
Thomas Hartung, M.D., Ph.D., Director, ECVAM

1145 **Using High Throughput Screening (HTS) to Identify Predictive *In Vitro* Biomarkers for Acute Systemic Toxicity**
Raymond Tice, Ph.D., Deputy Director, NICEATM, NIEHS

1205 **Lunch**

1300 **Concurrent Breakout Group Discussions**

a. **Breakout Group 3: Identifying Earlier Humane Endpoints for Acute Systemic Toxicity Testing**

Co-chairs: Helen Diggs, D.V.M., M.Ed., SACATM member; Director, Office of Laboratory Animal Care, University of California, Berkeley

Steven Niemi, D.V.M., DACLAM, Director, Center for Comparative Medicine, Massachusetts General Hospital

Recorder: David Allen, Ph.D., Integrated Laboratory Systems, Inc.

b. **Breakout Group 4: Application of *In Vivo* Mode of Action and Mechanistic Information to the Development and Validation of *In Vitro* Methods for Assessing Acute Systemic Toxicity**

Co-chairs: Melvin Anderson, Ph.D., DABT, Director of the Division of Computational Biology, The Hamner Institutes for Health Sciences

Eugene Elmore, Ph.D., Project Scientist, Department of Radiation Oncology, University of California, Irvine

Recorder: Michael Paris, Integrated Laboratory Systems, Inc.

c. **Breakout Group 5: Industry Involvement in Test Method Development, Validation, and Use**

Co-chairs: Robert Scala, Ph.D., DABT, DATS, Consultant

William Stott, Ph.D., DABT, Senior Scientist, Toxicology and Environmental Research and Consulting, The Dow Chemical Company

Recorder: Judy Strickland, Ph.D., DABT, Integrated Laboratory Systems, Inc.

- 1420 **Break**
- 1435 **Concurrent Breakout Group Discussions (continued)**
- 1535 **Break**
- 1550 **Plenary Session - Discussion of Conclusions and Recommendations Reached
by the Breakout Groups**
*Co-Chairs: William Stokes, D.V.M., DACLAM, NIEHS/NICEATM
Marilyn Wind, Ph.D., CPSC*
- 1550 a. **Breakout Group 3: Humane Endpoints for Acute Systemic Toxicity
Testing**
*Co-chairs: Helen Diggs, D.V.M., M.Ed.
Steven Niemi, D.V.M., DACLAM*
- 1610 b. **Breakout Group 4: Application of *In Vivo* Mode of Action and
Mechanistic Information to the Development and Validation of *In Vitro*
Methods for Assessing Acute Systemic Toxicity**
*Co-chairs: Melvin Andersen, Ph.D., DABT
Eugene Elmore, Ph.D.*
- 1630 c. **Breakout Group 5: Industry Involvement in Test Method Development,
Validation, and Use**
*Co-chairs: Robert Scala, Ph.D., DABT, DATS
William Stott, Ph.D., DABT*
- 1650 **Closing Comments**
Marilyn Wind, Ph.D., CPSC, Chair, ICCVAM
William Stokes, D.V.M., DACLAM, Director NICEATM, Executive
Director, ICCVAM
- 1700 **End of Meeting**