

International Workshop on Alternative Methods for Leptospira Vaccine Potency Testing: State of the Science and the Way Forward

Welcoming Remarks and Introduction

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Director, NICEATM

September 19, 2012

National Centers for Animal Health
Ames, Iowa



What is NICEATM?

- The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods: “*Nigh’ see tum*”
- A Center of the NIEHS and NTP
 - NIEHS: one of 27 NIH Institutes and Centers
 - NTP headquartered at the National Institute of Environmental Health Sciences, NIH, DHHS
 - conducts and coordinates toxicology testing programs across the federal government
 - Research Triangle Park, North Carolina, USA
- NICEATM functions:
 - Conduct international validation studies
 - Administer and provide scientific support for the **Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)**
 - Evaluate proposed new, revised, and alternative test methods



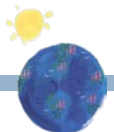
ICCVAM
NICEATM



What is ICCVAM?

The Interagency Coordinating Committee on the Validation of Alternative Methods

- Established by NIEHS in 1997
 - In response to Public Law 103-43
- ICCVAM Authorization Act of 2000
 - ICCVAM becomes permanent committee under NICEATM
- Members: 15 U.S. Federal regulatory and research agencies
- **Purposes and duties include:**
 - Reduce, replace, and refine animal use in testing
 - Share experiences between agencies, avoid duplication of effort
 - Advise on test method development and validation
 - Ensure test methods are validated to meet agency needs
 - Conduct technical reviews of new testing methods
 - Transmit recommendations to Federal agencies for adoption decisions
 - Foster national and international harmonization



The 15 ICCVAM Member Agencies

Regulatory Agencies (7)

- Consumer Product Safety Commission
- Department of Agriculture¹
- Department of the Interior¹
- Department of Transportation
- Environmental Protection Agency¹
- Food and Drug Administration¹
- Occupational Safety and Health Administration

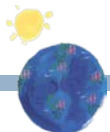
Research Agencies (8)

- Agency for Toxic Substances and Disease Registry-CDC
- National Institute for Occupational Safety and Health-CDC
- National Cancer Institute
- National Institute of Environmental Health Sciences
- National Library of Medicine
- **National Institutes of Health**
- Department of Defense
- Department of Energy



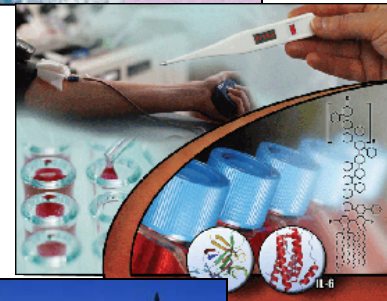
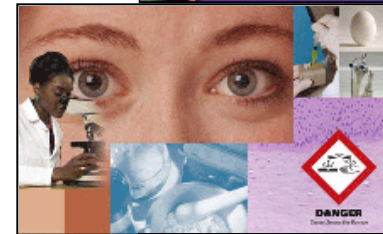
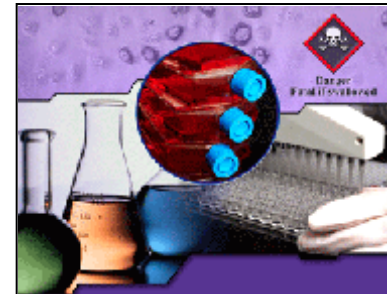
Other agencies as appropriate

¹ Also has research component



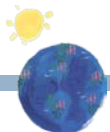
NICEATM and ICCVAM Progress

- 58 alternative safety testing methods accepted/endorsed by U.S. and international authorities since 1999¹
- Recommendations for R&D, translation, and validation activities to further advance methods
- International test guidelines and guidances
- International Cooperation on Alternative Methods (ICATM):
 - Japan: JaCVAM, NIHS
 - Europe: EURL ECVAM, IHCP
 - Canada: Health Canada
 - Korea: KoCVAM, KFDA

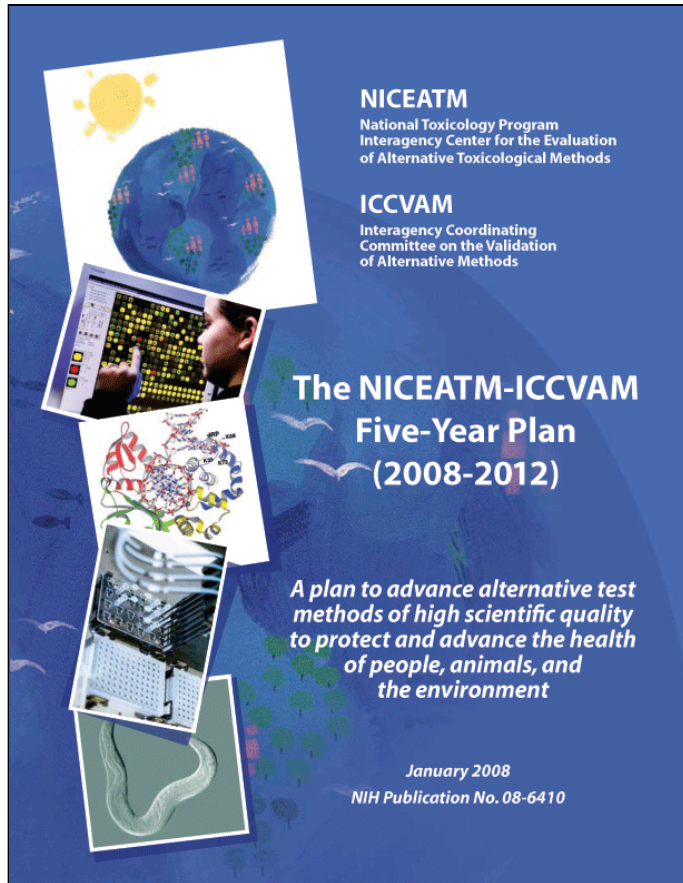


¹ U.S. and international acceptance of alternative methods, 1998-2012.

Website: <http://iccvam.niehs.nih.gov/about/accept.htm>



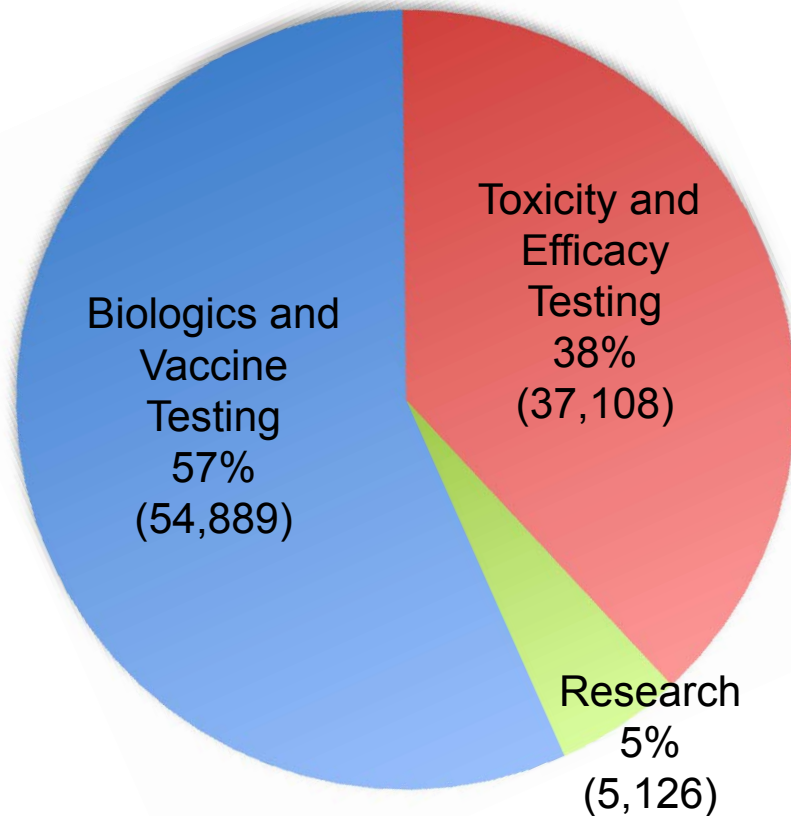
NICEATM-ICCVAM Five-Year Plan: 2008-2012



- **Vaccine Potency and Safety Testing**
 - One of ICCVAM's four highest priorities:
 - Large numbers of animals required
 - Involves significant unrelieved pain and distress
 - Multiple agencies involved
- "NICEATM and ICCVAM will:
 - Evaluate alternative test methods and testing strategies for vaccine potency testing
 - Facilitate acceptance of adequately validated test methods and humane endpoints found to be sufficiently accurate and reliable."

Use of Animals for Testing that Involves Unrelieved Pain and Distress (No Pain Relievers Used)

Animals by Testing Type
Reported to USDA (2010):



- 57% (54,889) of the animals reported to USDA that experience unrelieved pain and distress are used for testing Biologics and Vaccines
- Including rats, mice, and birds (not reported to USDA):
 - Est. 2 million animals used for testing that involves unrelieved pain and distress (in the U.S.)

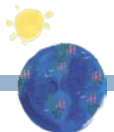
Data for all states with all animal data for Column E of APHIS Form 7023; USDA. 2010. Annual Report - Animal Usage by Fiscal Year. United States Department of Agriculture. Animal and Plant Health Inspection Service. Available at: http://www.aphis.usda.gov/animal_welfare/efoia/7023.shtml

NICEATM-ICCVAM International Workshop: Human and Veterinary Vaccine Potency and Safety Testing



- September 14-16, 2010 – Co-organizers included:
 - ECVAM, JaCVAM, Health Canada
 - Nearly 200 scientists, 13 countries
- Workshop Output:
 - *Procedia in Vaccinology 5: 1-266 (2011)*
 - Recommendations for implementation and use of alternative methods
 - Priorities for future work needed to advance alternatives
 - Enhanced International harmonization
 - Vaccine-specific workshops for priority areas:
 - Rabies (2011)
 - Leptospirosis (2012)
 - Pertussis vaccines-HIST (2012)
 - Clostridials and diphtheria (2013)

<http://www.sciencedirect.com/science/article/pii/S1877282X11000245>



International Workshop on Alternative Methods for Human and Veterinary Rabies Vaccine Testing



International Workshop on Alternative Methods for Human and Veterinary Rabies Vaccine Testing: State of the Science and Planning the Way Forward

October 11-13, 2011
U.S. Department of Agriculture
Center for Veterinary Biologics
National Centers for Animal Health
Ames, Iowa, USA

Organized by:
National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)
Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)
European Centre for the Validation of Alternative Methods (ECVAM)
Japanese Center for the Validation of Alternative Methods (JaCVAM)
Health Canada

ICCVAM Agencies:

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- Consumer Product Safety Commission
- Department of Agriculture
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- National Institutes of Health
- National Library of Medicine
- Department of the Interior
- Occupational Safety and Health Administration
- Environmental Protection Agency

Photomicrograph courtesy of F.A. Murphy, School of Veterinary Medicine, University of California, Davis



- October 2011: Organized by NICEATM-ICCVAM with ICATM partners
 - National Centers for Animal Health, Ames, Iowa
 - Sponsors: NICEATM, USDA, ECVAM
- 80 participants, 12 countries
- Workshop addressed:
 - Refinement (less pain and distress)
 - Reduction
 - Replacement
- Report published in *Biologicals*
 - Vol 40, No 5, pp 369-381
 - Summary of workshop presentations, discussions, and recommendations



NICEATM-ICCVAM Workshop on Alternative Methods for *Leptospira* Vaccine Potency Testing



International Workshop on Alternative Methods for *Leptospira* Vaccine Potency Testing: State of the Science and the Way Forward

September 19–21, 2012
U.S. Department of Agriculture Center for Veterinary Biologics
National Centers for Animal Health
Ames, Iowa, USA

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NICEATM - National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods
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EURL ECVAM - European Union Reference Laboratory for Alternatives to Animal Testing
JaCVAM - Japanese Center for the Validation of Alternative Methods
KoCVAM - Korean Center for the Validation of Alternative Methods
Health Canada

For more information and to register, please contact NICEATM:
<http://iccvam.niehs.nih.gov/> — (919) 541-2384 — niceatm@niehs.nih.gov

Individuals with disabilities who need accommodation to participate in this event should contact Debbie McCarley at 919-541-2384 or mccarley@niehs.nih.gov. TTY users should contact the Federal TTY Relay Service at 800-877-8339. Requests should be made at least 5 days in advance of the event.

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		• Environmental Protection Agency



- September 19-21, 2012
- USDA Centers for Animal Health Ames, Iowa, USA
- Co-organized with ICATM partners
- Will address:
 - ✉ How to further implement replacement methods for potency testing
 - ✉ How to further reduce and refine testing until complete replacement
- Experts from government, academia and industry
- Plenary and Breakout Sessions
- Poster Session
- Workshop proceedings to be published in *Biologicals*

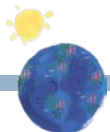


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Why a Leptospirosis Vaccine Workshop?

- Potency testing still involves large numbers of animals
 - In vitro methods have been approved for some serovars pending product specific validation
 - What are the obstacles to further implementation?
- Where animals are still used, many experience significant unrelieved pain and distress
 - Are there ways to further reduce pain and distress?
- Share experiences
 - What has worked, what has not
 - New research findings, research needs
- Identify opportunities for further progress



Acknowledgements:

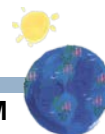
Workshop Organizers and Co-Sponsors

■ Organizers:

- National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)
- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)
- European Centre for the Validation of Alternative Methods (ECVAM)
- Japanese Center for the Validation of Alternative Methods (JaCVAM)
- Health Canada

■ Co-Sponsors

- Center for Veterinary Biologics, USDA
- International Alliance for Biological Standardization (IABS)



ICCVAM Interagency Biologics Working Group

U.S. Food and Drug Administration

Richard McFarland, PhD, MD (CBER) (Co-Chair)

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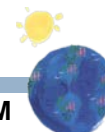
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EURL ECVAM Liaison

Marlies Halder, DVM

JaCVAM Liaison

Hajime Kojima, PhD



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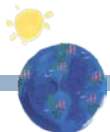
Organizing Committee

BWG Members

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NIEHS
USA
- Jodie Kulpa-Eddy, DVM (Co-Chair)
USDA
USA
- Richard McFarland, PhD, MD (Co-Chair)
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- Karen Brown, PhD,
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- Randy Sebring, PhD
Animal Health Institute
USA
- Hans Draayer, MSc
GV Biological Consulting
USA



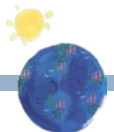
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National Institute of Environmental Health Sciences

William S. Stokes, D.V.M., DACLAM	<i>Director</i>
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Debbie McCarley	<i>Special Assistant</i>

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Steven Morefield, M.D., *Project Manager*
Vivian Doelling, Ph.D.
Brett Jones, Ph.D.
Nelson Johnson, B.S.
Linda Litchfield
Anna Lee Mosley
Catherine Sprankle





International Workshop on Alternative Methods for Leptospira Vaccine Potency Testing: State of the Science and the Way Forward

Workshop Introduction and Objectives

Jodie Kulpa-Eddy, DVM, USDA

Richard McFarland, MD, PhD, FDA

Co-Chairs, ICCVAM Biologics Working Group

September 19, 2012

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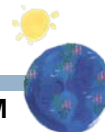


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Leptospira Workshop Objectives

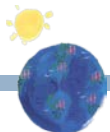
- Animal and Public Health Perspectives
 - Identify and review public health needs
 - Regulatory requirements for potency testing of *Leptospira* vaccines
- State of the Science
 - Review the state of the science of currently available alternative methods for *Leptospira* vaccine potency testing
- Implementation
 - Identify any unresolved data gaps and develop an implementation strategy to achieve global regulatory acceptance of alternative methods
- Future considerations
 - Identify best practices for current and future integrated approaches to *Leptospira* vaccine potency testing



Workshop Program – Day 1

Session 1: Overview of Public Health Needs, Regulatory Requirements, and Research Initiatives for *Leptospira* Vaccine Potency Testing State of the Science

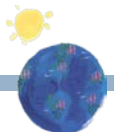
- Leptospirosis: Public Health Perspectives
- Leptospirosis: Animal Health Perspectives
- USDA Regulatory Guidelines and Practices for Veterinary *Leptospira* Vaccine Potency Testing
- European Regulatory Framework and Practices for Veterinary *Leptospira* Vaccine Potency Testing
- International Regulatory Requirements for *Leptospira* Vaccine Potency Testing Roundtable: Current Requirements and Opportunity for Harmonization
- Next-Generation Human *Leptospira* Vaccines
- Current NIH Research In Human *Leptospira* Vaccines



Workshop Program – Day 2 (1)

Session 2: *In Vitro* Replacement Alternatives for Potency Testing of *Leptospira* Vaccines: Development, Validation, and Implementation Leptospirosis: Public Health Perspectives

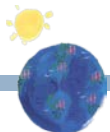
- Successful Development of an *In Vitro* Replacement Assay for *Leptospira* Vaccine Potency Testing
- Successful Validation of an *In Vitro* Replacement Assay for *Leptospira* Vaccine Potency Testing
- Product Specific Validation of an *In Vitro* Assay for *Leptospira* Potency Testing: An Industry Perspective (1)
- Product-Specific Validation of an *In Vitro* Assay for *Leptospira* Potency Testing: An Industry Perspective (2)
- Development of *Leptospira In Vitro* Potency Assays: EU/Industry Experience and Perspectives
- Expansion of the *In Vitro* Assay for *Leptospira* Potency Testing to Other Serovars: Case Study with *Leptospira hardjo*
- **Breakout Session #1:**
***In Vitro* Replacements Methods for Potency Testing of *Leptospira* Vaccines: Validation Status, Data Gaps, Implementation Strategies, and Expanding the Serovars**



Workshop Program – Day 2 (2)

Session 3: Reduction and Refinement Alternatives for Potency Testing of *Leptospira* Vaccines: Development, Validation, and Implementation

- Development and Validation of a Serological Potency Test for the Release of *Leptospira* Vaccines in the European Union
- Product-Specific Validation of a Serological Potency Test for Release of *Leptospira* Vaccines in the European Union
- **Report from Breakout Session #1: *In Vitro* Replacement Methods for Potency Testing of *Leptospira* Vaccines: Validation Status, Data Gaps, Implementation Strategies, and Expanding the Serovars**



Workshop Program – Day 3

Session 3: Reduction and Refinement Alternatives for Potency Testing of *Leptospira* Vaccines: Development, Validation, and Implementation

- Opportunities and Strategies to Further Reduce Animal Use for *Leptospira* Vaccine Potency Testing
- Opportunities and Strategies to Further Refine Animal Use for *Leptospira* Vaccine Potency Testing
- **Breakout Session #2:**
Reduction and Refinement Alternatives for Potency Testing of *Leptospira* Vaccines: Validation Status, Data Gaps, Implementation Strategies, and Expanding the Serovars
- **Report from Breakout Session #2: Reduction and Refinement Alternatives for Potency Testing of *Leptospira* Vaccines: Validation Status, Data Gaps, Implementation Strategies, and Expanding the Serovars**
- Summary of Workshop Recommendations and Next Steps
- Adjournment

