
Welcoming Remarks and Introduction

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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
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 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 Agriculture
- Department of the Interior
- Department of Transportation
- Environmental Protection Agency
- Food and Drug Administration
- 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 1999
- 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
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.
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 diptheria (2013)

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

- 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

- September 19-21, 2012
- USDA Centers for Animal Heath
  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*
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)
- Abigail Jacobs, PhD (CDER)
- Suzanne Fitzpatrick, PhD, DABT (CFSAN)

U.S. Department of Agriculture
- Jodie Kulpa-Eddy, DVM (Co-Chair)
- David Dusek, PhD
- Donna Gatewood, DVM
- Geetha Srinivas, DVM, PhD

Centers for Disease Control and Prevention
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Department of Defense
- Leonard Smith, PhD
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Department of Interior
- Tonie Rocke, PhD

National Institute of Allergy and Infectious Diseases/NIH
- Suman Mukhopadhyay, PhD

National Institute of Environmental Health Sciences/NIH
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- Warren Casey, PhD, DABT

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- Michele Regimbald-Krnel, PhD

EURL ECVAM Liaison
- Marlies Halder, DVM

JaCVAM Liaison
- Hajime Kojima, PhD
Acknowledgements: Organizing Committee

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Workshop Introduction and Objectives

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Co-Chairs, ICCVAM Biologics Working Group

September 19, 2012
National Centers for Animal Health
Ames, Iowa, USA
NICEATM-ICCVAM Workshop on Alternative Methods for Leptospira Vaccine Potency Testing

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Co-organized with ICATM partners

Will address how to further implement replacement methods for potency testing, and 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
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

- Leptospirosis: Public Health Perspectives
- Leptospirosis: Animal Health Perspectives
- 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
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
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
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