Introduction

- Vaccines improve animal and human health and welfare by preventing or controlling infectious diseases
- Vaccines play a major role in (Figure 1)
  - Protecting animal health and public health
  - Reducing animal suffering
  - Enhancing efficient production of food animals to feed the burgeoning human population
  - Reducing the need for antibiotics to treat food and companion animal infections

- NICEATM, ICCVAM, and their ICATM partners organized an International Workshop on Alternative Methods to Reduce, Refine, and Replace animal use for potency and safety testing

Figure 1. Emerging Diseases Affecting Veterinary Medicine

Workshop Goals

- Identify the state of the science of alternative methods that reduce, refine, and replace the use of animals in vaccine potency and safety testing, and discuss ways to promote their implementation
- Identify knowledge and data gaps that must be addressed through research, development, and validation efforts
- Identify and prioritize efforts needed to address these knowledge and data gaps

Workshop Organizing Committee: ICCVAM Interagency Biologies Working Group

- National Institute of Environmental Health Sciences
  - Warren Casey, PhD, DABCP, DACLAM (Director, NICEATM)
  - William Stokes, PhD, DVM, DACLAM
- National Institute of Allergy and Infectious Diseases
  - Richard Isbrucker, PhD
- National Heart, Lung, and Blood Institute
  - Robin Levis, PhD, DABCP
- Health Canada
  - Karen Brown, MSc
- Environmental Health Sciences Network
  - William Stokes, DVM, DACLAM

Workshop Breakout Groups: Vaccines

Objective

- Review the state of the science, knowledge gaps, and priority areas for future research, development, and validation to advance alternative methods for veterinary vaccine potency and safety testing

General Recommendations

- Prioritize Vaccines
- Rabies
- Leptospirosis
- Clostridial
- Encephalitis
- Foreign animal disease vaccines
- Poultry vaccines
- Fish vaccines

Criteiria for Prioritization

- Use of large numbers of animals per test
- Proportion of total numbers of animals annually
- Possibility of animal pain or distress during the challenge testing procedure
- Vaccines for which the functional protective antigen has been identified and characterized
- Vaccines for foreign animal diseases
- Zoonotic organisms that are also dangerous to humans

Achieving Broader Acceptance and Use of Alternative Methods Through:

- Broader access to information
- Harmonization and development of the testing requirements for individual protective antigens and their development
- Increased interaction/communication between regulatory agencies, research institutions, and vaccine manufacturers worldwide through workshops, scientific meetings, and conferences
- Harmonization of requirements, methods, and specifications
- Investigations into the impact of additives on alternative in vitro assays
- Quality assurance and availability of necessary reagents

Vaccine Potency Testing: Replacement, Refinement, and Reduction Methods

Replacement Methods for Veterinary Vaccine Potency Testing

- Allotopic challenge tests
- Intracellular, extracellular, and whole-body challenge tests
- In vitro challenge tests

Refinement Methods for Veterinary Vaccine Potency Testing

- Use of smaller numbers of animals
- Use of non-animal challenge models
- Use of in vitro challenge models

Reduction Methods for Veterinary Vaccine Potency Testing

- Use of fewer animals
- Removal of unnecessary steps in the challenge testing procedure
- Use of alternative challenge models

References


Post-Licensing Veterinary Vaccine Safety Testing: Replacement, Refinement, and Reduction Methods

State of the Science

- Alternative methods are currently available for vaccine safety testing of avian live virus vaccines
- In other cases safety assessment has been incorporated into the vaccine challenge test
- Those are: canine distemper, respiratory syncytial virus, and bovine virus

Priority Research Needs and Recommendations

- Assess the need for the general safety test and determine if this test could be implemented globally
- Continue investigating cell culture and PCR techniques as promising approaches to replace in vivo tests for enteric agents in poultry vaccines
- Determine if an in vivo virus neutralization test could be replaced with cell culture techniques already in use in the European Union for the testing of virus inactivation for human rabies vaccines
- Evaluate, develop, validate, and implement safety testing using various tests in a consistency approach

Conclusions

- This was the first international workshop in the U.S. to bring together stakeholders from both the human and veterinary vaccine communities to discuss opportunities to reduce, refine, and replace animal use for potency and safety testing
- The workshop reviewed the state of the science for existing alternative methods and approaches that could be used to identify, purify, and characterize vaccine protective antigens
- Identified earlier humane endpoints for vaccines requiring challenge testing
- Systematically collect and evaluate all clinical and other objective parameters
- Identify innovative quantitative endpoints, e.g., body temperature changes, body weight
- Collected data and identified clinical endpoints for control groups
- Identified a threshold for the number of controls that would be sufficient to address these gaps and to advance alternative methods for vaccine potency and safety testing
- Advances in science and technology that can and should be applied to these methods were highlighted and identified as priorities for future initiatives
- The workshop emphasized the value and role of international collaboration, coordination, and harmonization in advancing alternative methods for vaccine potency and safety testing
- Increased international cooperation is essential to maximize the impact of new methods and to accelerate their development and implementation
- Implementation of the workshop recommendations is expected to advance new methods for vaccine testing that will benefit animal welfare, enhance control of human and animal disease

Acknowledgements

The Intramural Research Program of the National Institute of Environmental Health Sciences (NIEHS) supported this poster. Technical support was provided by ILS, Inc., under NIEHS contract 1F481-2007.

This poster reflects the views of the authors. The views expressed above have not been reviewed or approved by any U.S. Federal agency and views expressed above do not necessarily represent the official positions of any U.S. Federal agency, other regulatory agencies, or the European Commission.

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