Abstract

Objective: Develop a list of knowledge and data gaps that must be addressed to develop alternative methods that can reduce, refine, and replace the use of animals in vaccine potency and safety testing. The workshop was held September 14-16, 2010.

Methods: The childhood vaccine series including the National Institute for Environmental Health Sciences (NIEHS), NICEATM and ICCVAM organized an international workshop held on September 14–16, 2010, to discuss ways to promote international harmonization and/or acceptance of vaccine potency and safety testing. They agreed to develop a list of knowledge and data gaps, as well as a list of criteria for prioritization, to be addressed through international working groups and/or working teams. The workshop was organized by NICEATM, ICCVAM, ECVAM, JaCVAM, and Health Canada. Nearly 200 scientists from 30 countries attended the workshop.

Results: The workshop identified knowledge and data gaps, as well as research, development, and validation needs to address these gaps.

Conclusions: Priority needs and research recommendations were developed by the workshop members, and their implementation is expected to accelerate development and validation initiatives to address these gaps.

Introduction

Vaccines are an extraordinary health intervention that have been shown to be safe, effective, and cost-effective. They are an essential part of controlling infectious diseases, which account for the majority of the global burden of disease. Vaccines are widely accepted as an essential health care intervention, and they are highly cost-effective. By 2020, these interventions are expected to prevent 12 million deaths and 1 million cases of disability worldwide.

In the U.S., the total cost of preventable vaccine-preventable diseases is projected to increase by 2020 to $50 billion, including $33 billion in direct medical costs as well as $17 billion in indirect costs for each U.S. birth cohort. The savings from the use of currently available and/or accepted alternative methods that reduce, refine, and replace the use of animals in vaccine potency and safety testing is estimated to prevent 12 million deaths and 1 million cases of disability worldwide. Vaccines also prevent and control disease by preventing and controlling disease transmission.

Priority needs and research recommendations were developed by the workshop members, and their implementation is expected to accelerate development and validation initiatives to address these gaps.

Workshop Sessions

Session 1: Vaccine Safety Testing: Post-Licensing Reduction, Refinement, and Replacement Methodologies

- Overview of regulatory requirements, including the acceptance of alternative methods that reduce, refine, and replace the use of animals in vaccine potency and safety testing
- Review of the traditional lethal challenge assays and their replacement by serological assays
- Investigation of ways to reduce or eliminate the sources of variation and causes of inconclusive test results
- Examples of veterinary vaccine potency assays for which serological methods have been implemented
- Criteria for prioritization of vaccine safety testing

Session 2: Animal Use for Vaccine Potency Testing: Refinement and Reduction Alternatives

- State of the science of alternative methods that are currently available and/or accepted for vaccine potency testing
- Review of the state of the science of alternative methods for vaccine potency testing
- Examples of human vaccine safety tests that incorporate the 3Rs
- Investigation of ways to reduce or eliminate the sources of variation and causes of inconclusive test results
- Examples of veterinary vaccine potency assays for which serological methods have been implemented
- Criteria for prioritization of animal use in vaccine potency testing

Session 3: Animal Use for Vaccine Potency Testing: Refinement and Reduction Alternatives

- State of the science of alternative methods that are currently available and/or accepted for vaccine potency testing
- Review of the state of the science of alternative methods for vaccine potency testing
- Examples of human vaccine safety tests that incorporate the 3Rs
- Investigation of ways to reduce or eliminate the sources of variation and causes of inconclusive test results
- Examples of veterinary vaccine potency assays for which serological methods have been implemented
- Criteria for prioritization of animal use in vaccine potency testing

Session 4: Vaccine Safety Testing: Post-Licensing Reduction, Refinement, and Replacement Methodologies

- Overview of regulatory requirements, including the acceptance of alternative methods that reduce, refine, and replace the use of animals in vaccine potency and safety testing
- Review of the traditional lethal challenge assays and their replacement by serological assays
- Investigation of ways to reduce or eliminate the sources of variation and causes of inconclusive test results
- Examples of veterinary vaccine potency assays for which serological methods have been implemented
- Criteria for prioritization of vaccine safety testing

Figure 1

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

- Prioritize research needs and recommendations for vaccine safety testing
- Identify earlier humane endpoints for vaccines requiring challenge testing
- Identify earlier humane endpoints for vaccines requiring challenge testing
- Investigation of ways to reduce or eliminate the sources of variation and causes of inconclusive test results
- Examples of veterinary vaccine potency assays for which serological methods have been implemented
- Criteria for prioritization of animal use in vaccine potency testing

Figure 2

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

- Prioritize research needs and recommendations for veterinary vaccine safety testing
- Identify earlier humane endpoints for vaccines requiring challenge testing
- Investigation of ways to reduce or eliminate the sources of variation and causes of inconclusive test results
- Examples of veterinary vaccine potency assays for which serological methods have been implemented
- Criteria for prioritization of animal use in vaccine potency testing

Acknowledgements

This report is the product of the planning workshop on alternative methods to reduce, refine, and replace the use of animals in vaccine potency and safety testing. The workshop was organized by NICEATM, ICCVAM, ECVAM, JaCVAM, and Health Canada. Nearly 200 scientists from 30 countries attended the workshop.

References

For further information, please refer to the ICCVAM website at: http://www.iccvam.org

NICEATM: The National Toxicology Program (NTP) from the U.S. National Institutes of Health (NIH), National Institute of Environmental Health Sciences (NIEHS), National Toxicology Program (NTP), and Food and Drug Administration (FDA).

ICCVAM: The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) is a voluntary, multi-disciplinary, multi-agency initiative that develops, evaluates, and promotes the acceptance of alternative methods to reduce, refine, and replace the use of animals in toxicology testing, as mandated by the Omnibus Budget Reconciliation Act (OBRA-98) and by the NIH. The National Toxicology Program (NTP) was designated as the lead agency by the Congress of the United States to organize ICCVAM. ICCVAM is organized to (a) enhance the development, evaluation, and promotion of alternative methods; (b) facilitate the exchange of information among funding agencies, proposals, and alternative method developers; (c) promote the development of a research and regulatory agenda for alternative methods; (d) support the development of a strategic plan for alternative methods; (e) promote and facilitate the implementation of alternative methods; (f) enhance the implementation of alternative methods in regulatory and research settings; and (g) provide the interagency structure for the coordination of activities to advance the development, evaluation, and promotion of alternative methods. ICCVAM is a voluntary, multi-disciplinary, multi-agency initiative that develops, evaluates, and promotes the acceptance of alternative methods to reduce, refine, and replace the use of animals in toxicology testing, as mandated by the Omnibus Budget Reconciliation Act (OBRA-98) and by the NIH. The National Toxicology Program (NTP) was designated as the lead agency by the Congress of the United States to organize ICCVAM. ICCVAM is organized to (a) enhance the development, evaluation, and promotion of alternative methods; (b) facilitate the exchange of information among funding agencies, proposals, and alternative method developers; (c) promote the development of a research and regulatory agenda for alternative methods; (d) support the development of a strategic plan for alternative methods; (e) promote and facilitate the implementation of alternative methods; (f) enhance the implementation of alternative methods in regulatory and research settings; and (g) provide the interagency structure for the coordination of activities to advance the development, evaluation, and promotion of alternative methods.