Pertussis, also known as whooping cough, is a highly contagious disease caused by the bacterium Bordetella pertussis. Pertussis was one of the most common childhood diseases of the early 20th century and was once a major cause of childhood mortality in the United States. A whole-cell vaccine introduced in the 1940s reduced the incidence of pertussis by more than 80%. Acellular pertussis (aP) vaccines, which became available in the 1980s, were developed to further reduce, refine (enhance animal well-being and lessen or avoid pain and distress), or replace animal use for aP vaccine safety testing (Stokes et al., 2011).

Two international workshops reviewed currently available alternative in vitro assays to the HIST and discussed a path forward to achieve their validation and adoption (see Table 2). The Workshop on Animal-Free Detection of Pertussis Toxin (PTx) in Vaccines—Alternatives to HIST was held on June 9 and 10, 2011, at the Paul Ehrlich Institute, Germany. An International Working Group for Alternatives to HIST (previously designated as the “Spiked-vaccine Working Group”) was organized to coordinate future studies on relevant alternative methods (Bache et al., 2012; Isbrucker, 2011).

The Alternative Safety Testing Strategies for Acellular Pertussis Vaccines Workshop was held on August 21, 2011, as a satellite meeting to the 8th World Congress on Alternatives and Animal Use in the Life Sciences in Montreal, Canada (Isbrucker, 2011). Participants at this workshop further discussed and clarified regulatory agency requirements to achieve the acceptance of alternative methods to the HIST and agreed that conducting a study using spiked vaccines to compare the sensitivities of the HIST and in vitro assays would be important.

2 Workshop on Animal-Free Detection of PTx in Vaccines—Alternatives to HIST, Langen, Germany, June 9–10, 2011.
3 Alternative Safety Testing Strategies for Acellular Pertussis Vaccines (8th World Congress Satellite meeting), Montreal, Canada, August 21, 2011.
Several in vitro assays have been developed, or are currently under development, with the aim of finding an alternative method to the HIST for monitoring residual PTx activity in aP vaccines. The International Working Group for Alternatives to HIST is coordinating the acquisition and distribution of aP vaccine samples from manufacturers to research laboratories for generation of data using in vitro methods to evaluate vaccines spiked with a known amount of PTx. Data from the various alternative assays will be presented at the upcoming workshop and will form the basis for identifying in vitro methods for future assessment in the next international collaborative study.

The following methods will be evaluated and may be used to generate data to be presented at the upcoming workshop:

1. Binding assay: used to assess the amount of PTx/toxoid binding activity to the glycoprotein fetuin
2. Enzymatic assay: monitors the residual ADP-ribosylation of the PTx/toxoid
3. Cell-based assays: monitor the generation of cAMP or decrease in cellular ATP following exposure to PTx
4. Genetic assays: determine potential genomic markers of PTx activity

This workshop will provide a forum to discuss and review the in vitro protocols and available data from the International Working Group for Alternatives to HIST study and will suggest future collaborative projects using prepared materials. The workshop will also review additional new methods and approaches for aP vaccine safety testing that should improve test accuracy, precision, and efficiency while also reducing or replacing the use of animals in vaccine safety testing. Finally, the workshop will address the path toward global validation, acceptance, and implementation of scientifically valid alternative methods for aP vaccines.

**Preliminary Workshop Agenda and Registration**

Registration information, draft agenda, and additional meeting information are available on the NICEATM–ICCVAM Web site (http://iccvam.niehs.nih.gov/meetings/HISTWksp-2012/HISTWksp_AbstractSubmit-508.pdf) and upon request from NICEATM (see FOR FURTHER INFORMATION CONTACT).

**Call for Abstract Submissions**

NICEATM and ICCVAM invite the submission of abstracts for scientific posters to be displayed during this workshop. Guidelines for the submission of abstracts are available at http://iccvam.niehs.nih.gov/meetings/HISTWksp-2012/HISTWksp_AbstractSubmit-508.pdf. Abstracts must be submitted by email to niceatm@niehs.nih.gov. The deadline for abstract submission is October 12, 2012. The corresponding author will be notified regarding the abstract’s acceptance within 21 working days of the submission deadline. Guidelines for poster presentations will be sent to the corresponding author with notification of acceptance.

**Background Information on NICEATM and ICCVAM**

ICCVAM is an interagency committee composed of representatives from 15 Federal regulatory and research agencies that require, use, generate, or disseminate toxicological and safety testing information. ICCVAM conducts technical evaluations of new, revised, and alternative safety testing methods and integrated testing strategies with regulatory applicability and promotes the scientific validation and regulatory acceptance of testing methods that more accurately assess the safety and hazards of chemicals and products and that reduce, refine, or replace animal use. The ICCVAM Authorization Act of 2000 (42 U.S.C. 285j–3) established ICCVAM as a permanent interagency committee of the NIEHS under NICEATM. NICEATM administers ICCVAM, provides scientific and operational support for ICCVAM-related activities, and conducts independent validation studies to assess the usefulness and limitations of new, revised, and alternative test methods and strategies. NICEATM and ICCVAM welcome the public nomination of new, revised, and alternative test methods and strategies applicable to the needs of U.S. Federal agencies. Additional information about ICCVAM and NICEATM can be found on the NICEATM–ICCVAM Web site (http://iccvam.niehs.nih.gov).

**References**


Stokes WS, Kulpa-Eddy J, McFarland RM.


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