International Workshop on Alternatives to the Murine Histamine Sensitization Test (HIST): State of the Science and the Path Forward

Workshop Introduction and Objectives

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William H. Natcher Conference Center
Bethesda, MD
Workshop on Alternatives to the Murine Histamine Sensitization Test (HIST) for Acellular Pertussis Vaccines

- November 28-29, 2012
- William H. Natcher Conference Center
  National Institutes of Health, Bethesda, MD
- Experts from government, academia and industry expected to attend
- Plenary and Breakout Group Sessions
- NICEATM coordinating with the International working group on alternatives to HIST
- Review of in vitro safety data on spiked Pertussis toxin vaccine preparations
- Workshop report to be published
- 47 registrants to date from 11 countries

Further information, including registration, is available at:
http://iccvam.niehs.nih.gov/meetings/HISTWksp-2012/HISTWksp.htm
Alternatives to HIST Workshop Objectives (1)

- Review the usefulness and limitations for alternative *in vitro* test methods proposed to replace the current *in vivo* HIST
- Review *in vitro* protocols and data generated by participants of the International Working Group on Alternatives to HIST
  - Use of common set of vaccines, pertussis toxin (reference standard), and protocol for spiking
  - *In vitro* assays tested
    - Biochemical assays
      - Binding assay: used to assess the amount of pertussis toxin/toxoid binding activity to the glycoprotein fetuin.
      - Enzymatic assay: monitors the residual ADP-ribosylation of the pertussis toxin
    - Cell-based assays
      - Human cells measuring ATP reduction
      - Rat cells measuring cAMP increase
      - CHO cell (morphological, cytopathic)
Alternatives to HIST Workshop Objectives (2)

- Discuss application of *in vitro* assays for monitoring consistency of vaccine manufacture as alternatives to the HIST
- Establish framework for international collaboration to validate *in vitro* assay(s) for acellular pertussis vaccine testing
- Identify regulatory acceptance requirements for *in vitro* assays as alternatives to the HIST
Opening Session

- Plenary Presentation: The Many Faces of Pertussis Toxin
- Current Regulatory Requirements for Residual Pertussis Toxin Testing of Acellular Vaccines
- 2010 International Collaborative Study on Validation of an \textit{In Vitro} Assay System as an Alternative to the Current Histamine Sensitization Test for Acellular Pertussis Vaccines
- Overview of the International Working Group for Alternatives to HIST (Phase 1)
Session 1: Alternatives to HIST: Methods and Evaluations

- Analyses of Pertussis Toxin ADP-ribosyltransferase and Carbohydrate-Binding Activities as an *In Vitro* Alternative to the *In Vivo* HIST
- *In Vitro* Assays for the Detection of Pertussis Toxin: BSP114 Collaborative Study Results
- Alternative *In Vitro* Methods for Detection of Pertussis Toxin in Component Pertussis Vaccines: Results of a BSP114 Phase 1 International Collaborative Study
- Characteristics of Enzymatic and Binding Activities of Pertussis Toxin According to Chemical Detoxifying Agents
- Detection of PTx in Acellular Pertussis Vaccines Using a CHO Cell Clustering Assay, a Carbohydrate-Binding Assay, and an Enzymatic/HPLC Assay
Session 1: Alternatives to HIST: Methods and Evaluations cont.

- Cell-Based Assays for Detection of Pertussis Toxin in Acellular Vaccines: The Pertussis ATP Test (PAT) and the cAMP-PTx Assay
- Using Pertussis Toxin-Sensitive Genes in Dendritic Cells to Evaluate the Safety of Acellular Pertussis Vaccines
- Summary Analysis of Reported Data Sets

- Session 1B: Alternative *In Vitro* Methods to the Murine Histamine Sensitization Test
- Roundtable Discussion
Session 2: The Path Forward: Gaps to Cross and Bridges to Build in the Road Toward the Adoption of Alternatives to HIST

- Plenary Presentation: Pertussis Toxin and the CHO Cell Response

- Session 2A: CHO Cell Assay: Potential Use for Standardization and as an Alternative to HIST
- Roundtable Discussion

- Session 2B: Issues with Pertussis Toxin Adsorption/Desorption
- Roundtable Discussion
Session 2C: The Path Forward: Harmonizing the Adoption of Alternative Assays

- Roundtable Discussion

- Session 3: Next International Collaborative Validation Study on Alternative Assay(s) with Spiked Vaccines
  - Roundtable Discussion

- Closing Remarks and Adjournment
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