Overview of the International Working Group for Alternatives to HIST (Phase I)

Workshop on Animal free Detection of Pertussis Toxin in Vaccines: Alternatives to the Histamine Sensitisation Test

Paul Ehrlich Institute, Langen, Germany
June, 2011

Organized by PEI, NVI, EDQM

Bache, C et al. (2012) Biologicals 40:309-311

Questions and issues raised:

1. Use of different PTx preparations between labs
    - Differing units of measure and activity
    - Not possible to compare/contrast in vitro results

2. Are the in vitro assays as sensitive as HIST?

3. Would in vitro assays detect a vaccine that failed a HIST?
    - Do “failed” vaccines exist?
    - How do we mimic a “failed” vaccine?

Working Group for Alternatives to HIST

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Goals of the Alt. to HIST Working Group:

- Identify a common pertussis toxin preparation for all labs to use
- Collect a common set of vaccines for distribution to interested labs
- Establish a method and concentrations for spiking vaccines with PTx
- Identify labs interested in participating in this project
- Distribute vaccines, PTx, and methods to all labs on time for ICCVAM workshop

BSP114 Collaborative Project

BSP 114 Collaborative Project

- > 40 labs/individuals contacted to determine their interest
- EDQM:
  - supplied PTx reference standard (Ph. Eur. BRP, Batch 1)
  - collected vaccines
  - distributed to all participating labs
- Participants asked to spike supplied vaccines at:

  2 IU/ml ≈ HSD5
  10 IU/ml ≈ HSD50
  20 IU/ml

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Donated Vaccines

Manufacturer	Vaccine	Adjuvant
GlaxoSmithKline	Vaccine A	$Al(OH)_3$
GlaxoSmithKline	Vaccine B	$Al(OH)_3 + AlPO_4$
GlaxoSmithKline	Vaccine C	$Al(OH)_3$
Sanofi Pasteur Canada	Pediacel	$AlPO_4$
Sanofi Pasteur France	Tetraxim	$Al(OH)_3$
Statens Serum Institute	DTaP-IPV	$Al(OH)_3$
Statens Serum Institute	aP	$Al(OH)_3$

BSP 114 Collaborative Project

- Instructions provided on reconstitution and storage of PTx
- PTx should be allowed to adsorb for 1 hour
- Suggested methods for desorption of vaccines also provided
    - EDTA buffer
    - Citrate buffer
- Samples sent in June, 2012
- Labs could use which ever in vitro assay they prefer
- All participants requested to present and/or submit their data

Participating labs:

National Institutes for Food and Drug Control (NIFDC) – China

National Institute of Infectious Diseases (NIID) – Japan

Korea Food and Drug Administration (KFDA) – Korea

Korea Vaccine Co., Ltd – Korea

Boryung Pharmaceutical Co – Korea

Green Cross Corp. – Korea

National Institute for Biological Standards and Control (NIBSC) – U.K.

Paul Ehrlich Institut (PEI) – Germany

Netherlands Vaccine Institute (NVI) – The Netherlands

University of Applied Sciences Utrecht – The Netherlands

Norwegian Medicines Agency (NoMA) – Norway

GlaxoSmithKline (GSK) – Belgium

Sanofi Pasteur – Canada

Health Canada

Assays under evaluation:

1. Biochemical
    - Fetuin binding assay (ELISA)
    - Enzyme-based HPLC (eHPLC)

2. Cellular
    - Production of cAMP
    - Decrease in ATP

3. Genomic

Where does the WG go from here?

Phase II: dependent on outcome of this workshop.