

# **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

Juan Arciniega (FDA, USA)

Christine Bache (PEI, Germany)

Jean-Michel Chapsal (Sanofi Pasteur, France)

Johan Descamps (GlaxoSmithKline, Belgium)

Angele Costanzo (EDQM, France)

Marieke Hoonakker (NVI, Netherlands)

Richard Isbrucker (Health Canada)

Sue Nelson (Sanofi Pasteur, Canada)

CT Yuen (NIBSC, UK)

# 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 PT<sub>x</sub>
- Identify labs interested in participating in this project
- Distribute vaccines, PT<sub>x</sub>, 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

# BSP 114 Collaborative Project

## Donated Vaccines

Manufacturer	Vaccine	Adjuvant
GlaxoSmithKline	Vaccine A	Al(OH) <sub>3</sub>
GlaxoSmithKline	Vaccine B	Al(OH) <sub>3</sub> + AlPO <sub>4</sub>
GlaxoSmithKline	Vaccine C	Al(OH) <sub>3</sub>
Sanofi Pasteur Canada	Pediacel	AlPO <sub>4</sub>
Sanofi Pasteur France	Tetraxim	Al(OH) <sub>3</sub>
Statens Serum Institute	DTaP-IPV	Al(OH) <sub>3</sub>
Statens Serum Institute	aP	Al(OH) <sub>3</sub>

# 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.