Status of the WHO Influenza Vaccine Technology Transfer Programme

Dr Laszlo Palkonyay

World Health Organization, Initiative for Vaccine Research (IVR)

3rd Meeting with International Partners on Prospects for Influenza Vaccine Technology Transfer to Developing Country Vaccine Manufacturers

Nha Trang, Vietnam, 5-6 May 2010
Framework of the WHO programme

Objective:

In the context of the WHO Global Action Plan to increase supply of pandemic influenza vaccine (GAP), to facilitate acquisition of influenza vaccine production capacity in developing countries by supplying funds & facilitate technology transfer to eligible developing country producers.

Financial support:

- US Department of Health & Human Services
- Government of Japan
- Asian Development Bank
- Government of Canada
- UK Government
Evaluation of Technologies available in the short/medium term: timeline and cost strategies

- **IIV**: Inactivated Influenza Vaccine
- **LAIV**: Live Attenuated Influenza Vaccine

![Graph showing investment required vs time required to establish seasonal vaccine production](image)

- **Investment required (arbitrary scale)**
- **Time required to establish seasonal vaccine production (years)**

- **IIV Egg**
- **IIV Tissue Culture Established cell line**
- **IIV Tissue Culture New cell line**

Legend:
- **Whole virus**
- **Split virus**
- **Subunit (surface antigen)**
- **Live attenuated**
## Two rounds of project initiation since the GAP inception (2006)

<table>
<thead>
<tr>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bio Farma, Indonesia</td>
<td>Cantacuzino Institute, Romania</td>
</tr>
<tr>
<td>Birmex, Mexico</td>
<td>Green Cross Corporation, Korea</td>
</tr>
<tr>
<td>Instituto Butantan, Brazil</td>
<td>Razi Institute, Iran</td>
</tr>
<tr>
<td>IVAC, Viet Nam</td>
<td>Torlak, Serbia</td>
</tr>
<tr>
<td>Governmental Pharmaceutical Organization (GPO), Thailand</td>
<td>Vacsera, Egypt</td>
</tr>
<tr>
<td>Serum Institute of India (SII), India</td>
<td></td>
</tr>
</tbody>
</table>
Technologies developed by the 11 manufacturers

- Time required to establish vaccine production
  - IIV Egg
  - LAIV Egg
  - IVAC
  - Tissue Culture
    - Established cell line
  - BIOFARMA
  - Green Cross
  - Cantacuzino
  - Birmex
  - Razi
  - Butantan
  - Thai GPO
  - Serum Institute of India
  - Vacsera
  - Torlak

Investment required
- BioFarma
- Green Cross
- Cantacuzino
- Birmex
- Razi
- Butantan
- LAIV Egg
- IIV Egg
- IVAC
- Tissue Culture
  - Established cell line
- BIOFARMA
- Green Cross
- Cantacuzino
- Birmex
- Razi
- Butantan
- Thai GPO
- Serum Institute of India
- Vacsera
- Torlak
Map of current and new influenza vaccine manufacturers
The "Technology Hub" Concept

Major challenges encountered during Phase 1 of the programme

- Finding a technology provider proved very difficult
- Limited human resources at new manufacturer site

A possible solution: to create a "technology hub" to serve as technology provider

- A technology platform for transferring a robust production process with relevant documentation (SOPs, Batch Process Records, validation procedures, analytical methods and release criteria) > established at the Netherlands Vaccine Institute
- A technology package transferable to interested developing country vaccine manufacturers, upon request (and possibly against fees), without IPR hurdles
- Selected technology: Inactivated whole virion influenza vaccine produced in embryonated eggs. Inactivated split virion technology under development with the support of a recent WHO grant
Provision of access to technology: the Russian LAIV

Institute of Experimental Medicine (IEM), St Petersburg, Russian Federation:
master donor strains (producing virus strains) and know how for the development and manufacture of live attenuated, seasonal and pandemic influenza vaccines.

BioDiem, Ltd., Australia:
exclusive license in all countries of the world, excluding Russia and the Commonwealth of Independent States.

Nobilon The Netherlands:
exclusive license in certain geographical areas, including all Developing Countries.

WHO
1) non-exclusive license for egg-based vaccines in all Developing Countries, with the right to grant a sublicense to private companies or governmental or non-governmental organizations in developing countries
2) right to use the virus strains supplied by IEM.

Developing country vaccine manufacturer
Achievements of the WHO Influenza Vaccine Programme: 2007-2010 – 1/2

- Financial and technical assistance with intense WHO monitoring was provided to **11 developing country manufacturers:**
  - Brazil - Mexico - Republic of Korea (new 2009)
  - India - Thailand - Iran (new)
  - Indonesia - Vietnam - Egypt (new)
  - Serbia (new) - Romania (new)

- **Six** of the 11 have produced **clinical lots of A(H1N1) vaccine,** four have completed or are conducting clinical trials of pandemic vaccine, two have registered this vaccine for use in humans. Additional three-four registrations are expected to be secured during the upcoming months of 2010.

- A royalty-free license was negotiated by WHO with Nobilon-Schering-Plough-Merck on the **LAIV technology**. A sublicense was provided to 3 developing country vaccine manufacturers (China, India, Thailand).
The Technology transfer & training center established at the NVI campus in Bilthoven, the Netherlands is fully operational.

NVI through contractual agreements is engaged in bi-lateral technology transfer projects with developing country vaccine manufacturers (Vacsera, Egypt and IVAC, Vietnam - other agreements pending).

(More information on the technology "hub" and on LAIV in Jan Hendriks' and Larisa Rudenko 's respective presentations)
Next steps

It will be essential

- to sustain both technical and financial support for the new manufacturers until registration of a product;
- to strengthen capacity of their respective National Regulatory Authorities; and
- to initiate new projects in underserved regions, notably Sub-Saharan Africa and Eastern Europe

Thank you!