NVI Experience and Concept of Central Technology Hub

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Netherlands Vaccine Institute (NVI)

MSF/Oxfam Consultation improving access and stimulating vaccine development for use in resource pour settings

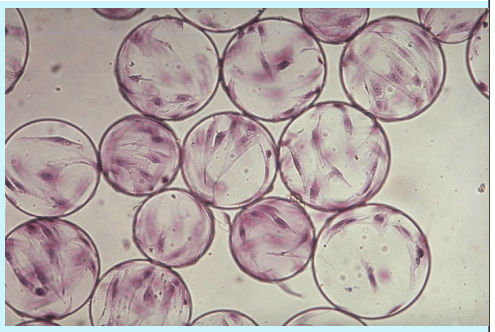
25 January 2010

Geneva, Switserland

The Netherlands Vaccine Institute

- **Unique Values:**
  - Over 100 years vaccinology know-how
  - Independent
  - Production infrastructure covering entire value chain
- **Transition-Change:**
  - Privatise production (2009 -2012)
- **Challenges:**
  - Maintain the entire value chain
  - Access to production infrastructure
  - R&D capable to transform research into practice

Technology Transfer from Bilthoven



- EPI vaccines (DTP and others)
- Hib-conjugate vaccines
  - barriers and enabling factors
- Recently initiated projects with WHO
  - inactivated polio vaccines
  - influenza vaccines (“hub”)

Developing Countries Vaccine Manufacturers Network (DCVMN)

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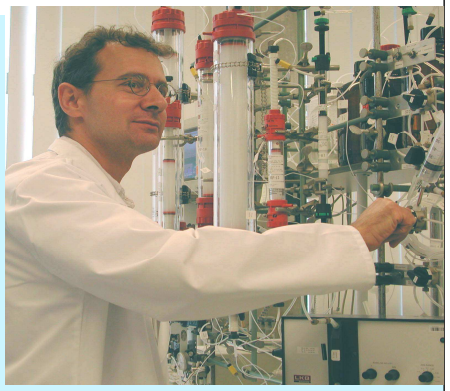
Objectives
Hib-conjugate vaccine project
1999 - now



-Develop an **up-scalable and patent free production process** for the large-scale production of Hib conjugate vaccine

-**Transfer the technology to developing countries** to ensure a sustainable supply of affordable and quality vaccine

-

Hib-conjugate vaccine development and tech transfer

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theHibinitiative
TAKING ACTION TO PREVENT CHILDHOOD PNEUMONIA & MENINGITIS

NEWS

Serum Institute of India obtains first ever Indian license for its Hib vaccine developed through technology transfer from the Netherlands Vaccine Institute

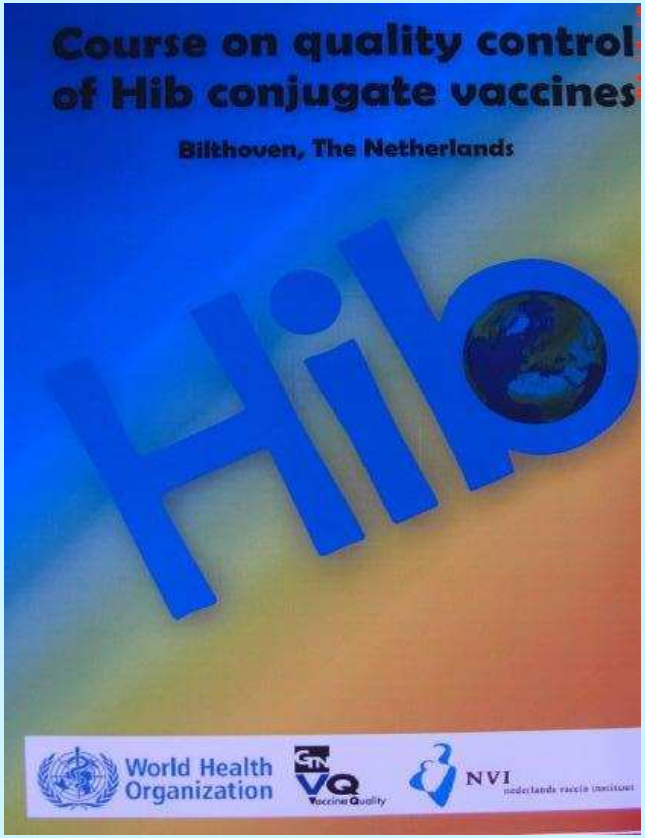
May 3, 2007

Serum Institute of India Ltd (SII Ltd) has developed a vaccine against Hib (Haemophilus influenzae type b) and obtained a license from the Indian Government for its indigenous production. The pilot process technology know-how came from the Netherlands Vaccine Institute (NVI). This is the first time that through intensive joint development and technology transfer a developing country vaccine manufacturer successfully develops a Hib vaccine and obtains a license for it.

Jadhav et al. Vaccine (2008) Mar 20; 26 (13): pg. 1611

Training of National Regulatory Authorities in quality control of Hib vaccines

The NVI experience obtained in the Hib development project was used to develop and run Hib QC training courses under the WHO Global Training Network



Barriers/challenges

- **Patent and proprietary know-how issues complicate the access to Hib technology**
- **Regulatory issues complicate the use of alternative conjugate technology** as lot release criteria are product specific
- **Ethical issues complicate the use of alternative conjugate technology** as it is difficult to justify clinical trials with these conjugates in the presence of licensed Hib vaccines which are highly safe and effective
- Due to the presence of competing vaccines already on the market **donors were not willing to fund the project as this would have been seen as unfair competition**

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Enabling entities & factors

- **GAVI has created a market for Hib conjugate vaccines** and reliable supply- and demand- forecasts
- **WHO has recommended incorporation of Hib vaccine in all infant immunization programs**
- **The NVI Hib technology transfer project has created access to critical Hib technology for local manufacturers and NRA's in developing countries**.
- **Local manufacturers play a critical role to meet the MDG 4 on the reduction of child mortality .**Thanks to their large scale production capabilities and global market experience they are able to produce Hib vaccine for their national immunization programs and ensure sustainable supply of affordable and quality Hib vaccines in the world

Technology transfer hub for pandemic influenza vaccine

- A **technology platform** for transferring a single robust production process at pilot scale with relevant documentation (SOPs, Batch Process Records, validation procedures, analytical methods and release criteria)

- A **technology package** transferable to interested developing country vaccine manufacturers, upon request and without IPR hurdles

- Selected technology: **Inactivated whole virion influenza vaccine produced in embryonated eggs**

Friede et al. Vaccine 27 (2009), 631 - 632

2009 Tech Transfer Activities

1. Website : www.itpiv.nl

2. QA/GMP - Workshop for 13 participant
   - 7 DCVM

3. Generic Training Course for 10 participants
   - 6 DCVM

4. Partner identification for bilateral Tech Transfer agreements

Training Course 2009

- 10 bench places
- Two volume Course Manual
- Hands-on: demonstration dedicated “training” run
- Two groups: Production & Quality Control

Access to:

- ❑ Technical advice
- ❑ Process and production technology
- ❑ Documentation
- ❑ Assays
- ❑ (Pre)clinical support




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Tech Transfer projects since 1990

Project	Vaccine(s)	Recipient	Country	Approach	IP-issues
World Bank Vaccine Project (1990 – 1998)	DTP, MV, OPV	SIBP, LIBP, KIMB, (NCL)	China	turn-key	none
Hib – Project (1999 – now)	Hib conjugate	Bio Farma SIIL, BE Ltd Glovax/SIBP	Indonesia India Korea/China	development and transfer of pilot process	non-exclusive license; fees and/or royalties
WHO ITPIV (2007 – now)	**egg-based inactivated influenza**	**VACSERA IVAC Others?**	**Egypt Vietnam**	**1-generic, hub based 2- bilateral TT agreements**	**non-exclusive license; modest fees; no royalties**
WHO Sabin-IPV (2008 – now)	new safer polio	t.b.d.; potentially several	*Brazil?* *China?*	1-generic, hub based 2- bilateral TT agreements	non-exclusive license; modest fees; royalties

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Concluding Remarks

- Not IP but transfer of know-how is the main impediment.
- Tech Transfer to local manufacturers from EU-based Vaccinology Institutions like NVI works through different models.
- Hub-concept with WHO on flu and polio bears promise.
  - For other products as well?

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BACK UP SLIDES

Access to vaccine technology is determined by three factors

- Intellectual Property

- ***Technical know-how***

- A viable market

Batson and Milstien. Health Affairs (Millwood) (2008), 27(1), pg 140

What is next: a new generic conjugate course?

- Strategic Collaboration IVI - NVI
- Need for generic course for new conjugate vaccines:
  - Pneumo, Meningo, Vi-typhi, Shigella,….
- Aim: achieve earlier introduction of new conjugate vaccines developed by DCVM to the global market
- Target audience:
  - NRA/NCL-staff
    - **QC tests in addition to batch review**
  - DCVMN Members
  - Biotech and Industry?
- 5 year program; 2 courses annually / different locations
- Funding (around €2 million) not yet in place

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World Health Organization

ITPIV

INTERNATIONAL TECHNOLOGY PLATFORM FOR INFLUENZA VACCINES

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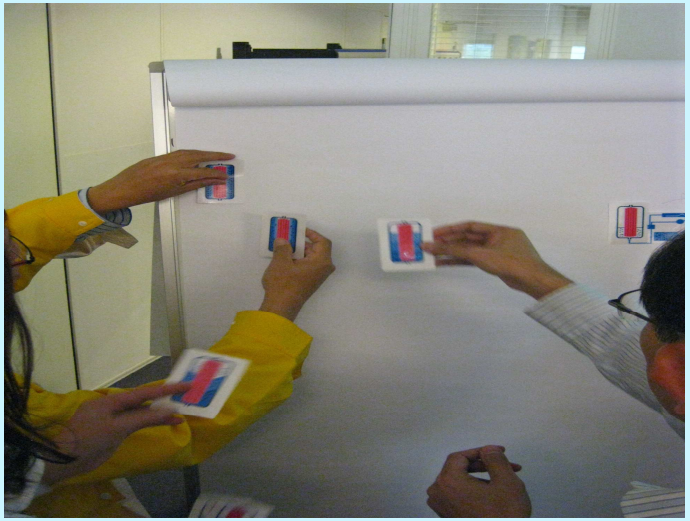
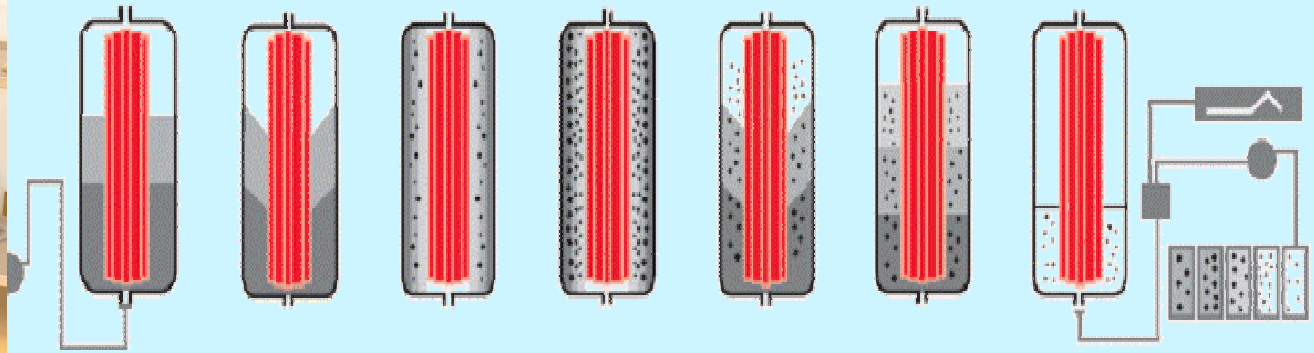
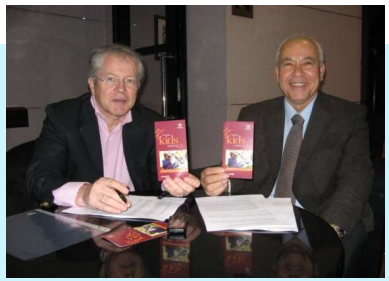
Process development & characterization

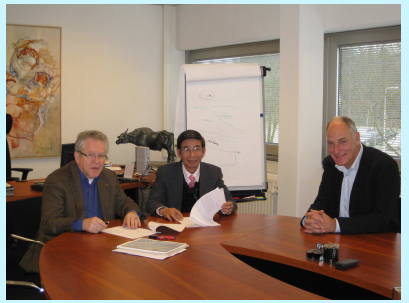
World Health Organization





Status on potential bilateral partners





- Vacsera – Egypt
  - First agreement signed Sept'09
- IVAC – Viet Nam
  - First agreement signed Dec'09
- RAZI – Iran
  - Fact finding NVI visit to Iran pending

- Other interested parties from China, Kazachstan, Argentina, India, and South Korea

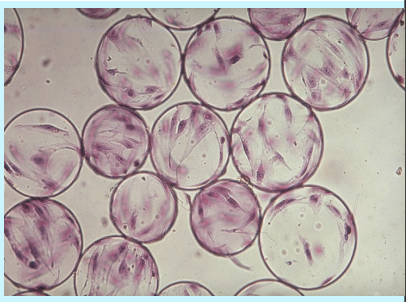
Planning for 2010

- Confirm process for pandemic strain (WIV)
- Process development for sub-unit vaccine
- At least two training courses (March – April)

- Carry out agreements with Egypt and Vietnam

A safer polio vaccine

Sabin-IPV
based on NVI Salk-IPV
Vero/microcarrier process



Planned activities (2008 – 2011):

I. **Clinical lot preparation & process fine tuning / optimization**

II. Proof of Principle clinical studies and licensing

III. **Training and Tech Transfer :**

- **Generic training courses**
- Bilateral Tech Transfer agreements with DCVM

NB: items in **bold** financed through a BMGF grant to WHO's Polio Eradication Initiative