Examples of Vaccine Know-How Transfer

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Netherlands Vaccine Institute (NVI)

Washington, DC, US

11-13 January 2010

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

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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; <u>no</u> 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

Hib-conjugate vaccine development and tech transfer

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the Hib initiative
TAKING ACTION TO PREVENT CHILDHOOD PNEUMONIA & MENINGITIS

NEWS

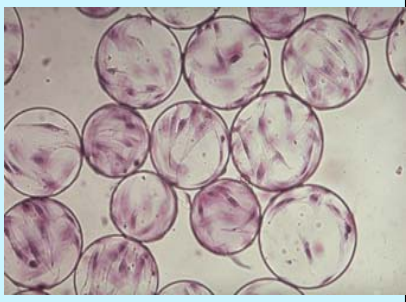
Serum Institute of India obtains first ever Indian license for its Hib vaccine developed through technology transfer from the Netherlands Vaccine Institute

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

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

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World Health Organization

ITPIV

INTERNATIONAL TECHNOLOGY PLATFORM FOR INFLUENZA VACCINES

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)

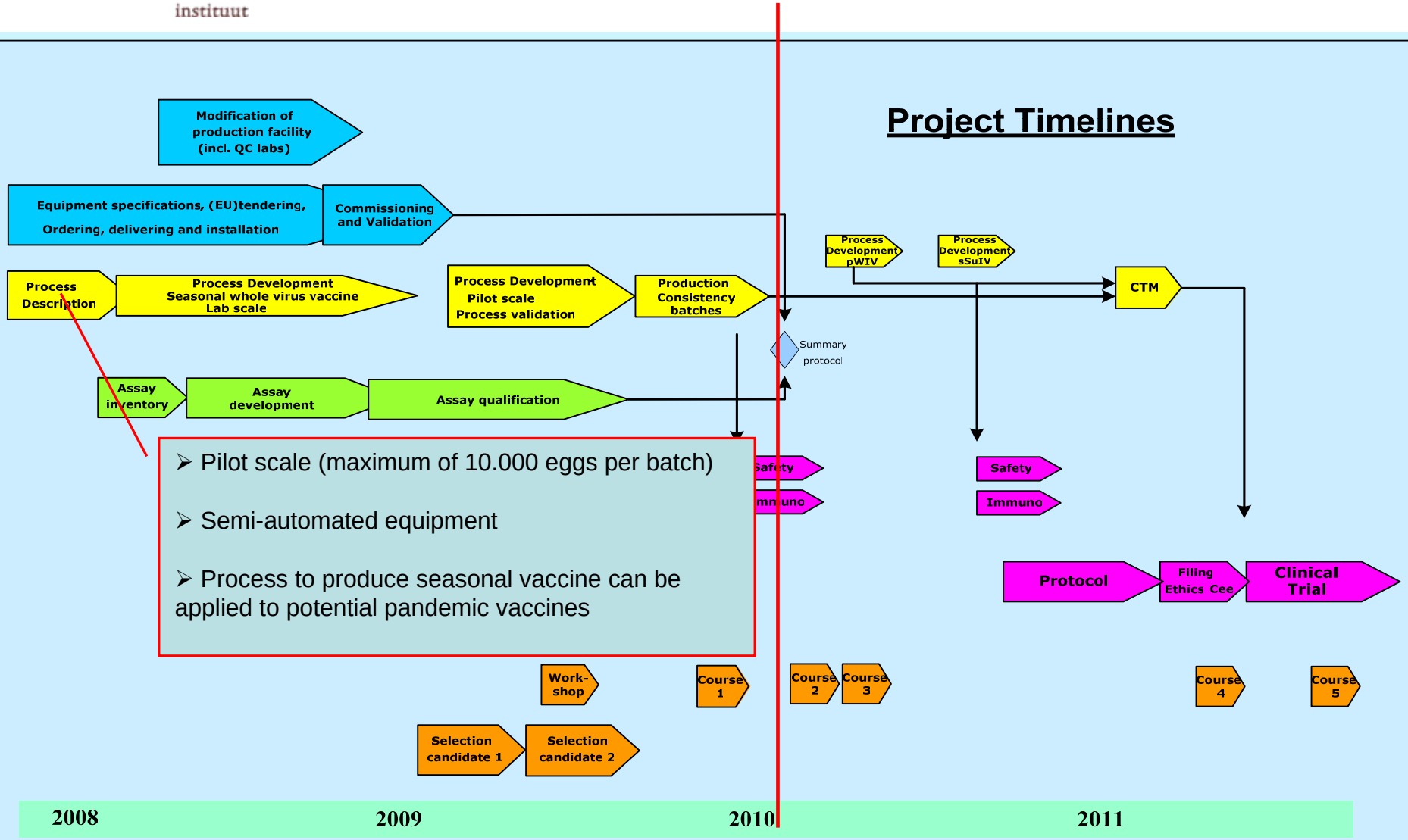
- A **technology package** transferable to interested developing country vaccine manufacturers, upon request and without IPR hurdles

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

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

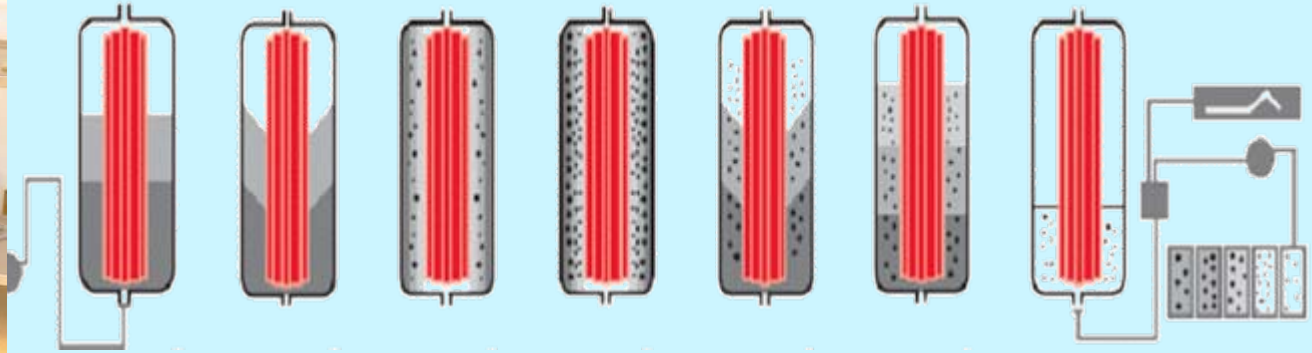
ITPIV

Project Timelines

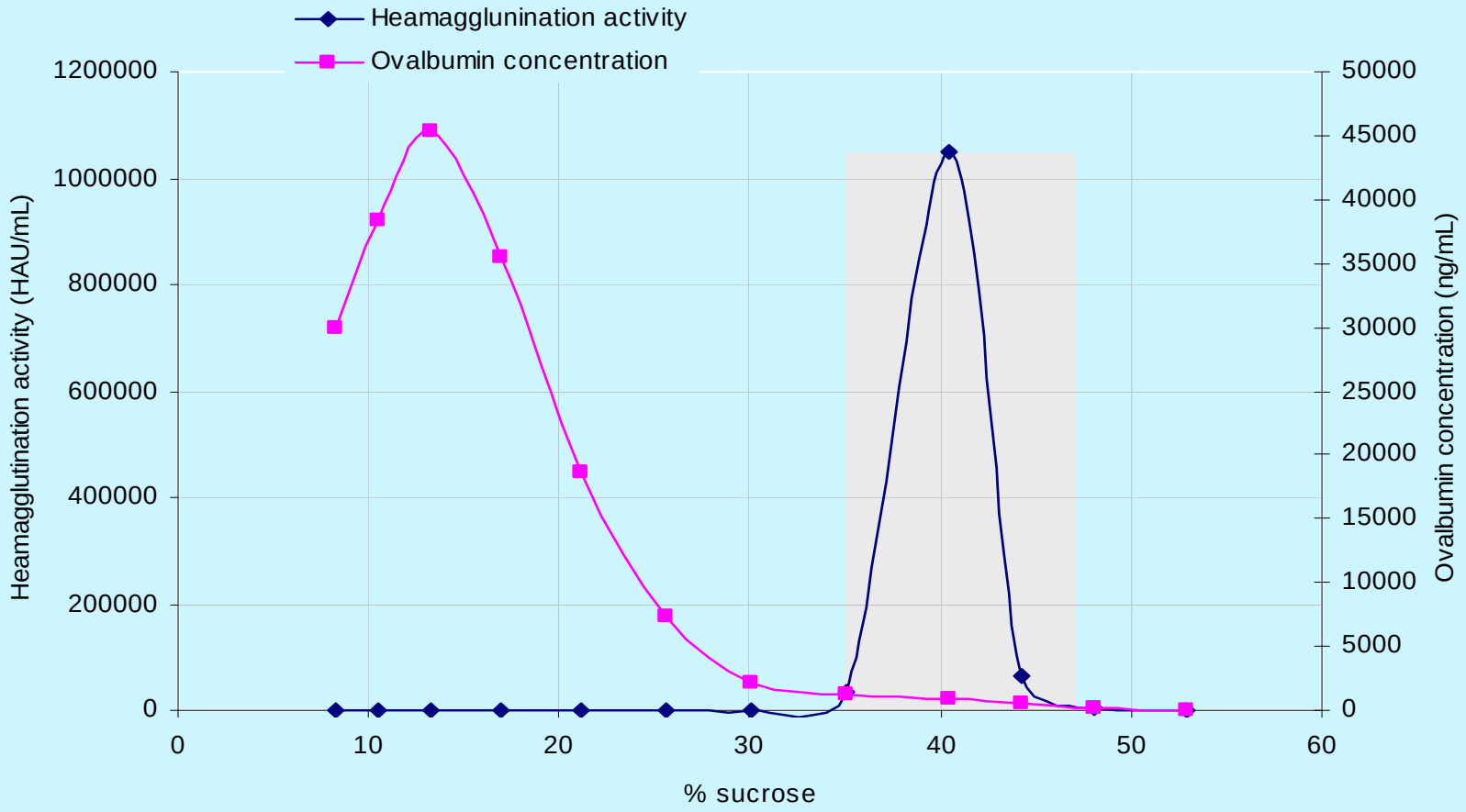


- Pilot scale (maximum of 10.000 eggs per batch)
- Semi-automated equipment
- Process to produce seasonal vaccine can be applied to potential pandemic vaccines

Process development & characterization



Ovalbumin and HA profile in zonal sucrose gradient



Process development

Overall yield of the process (corrected for volume losses due to sampling).											
Batch #	unit	09FLU04	09FLU05	09FLU06	09FLU07	09FLU09	09FLU011	09FLU012	09FLU13	09FLU14	09FLU15
Desired dose potency	ug	45	45	45	45	45	45	45	45	45	45
Overall rec (corrected for sampling)	%	22	20	40	22	35	54	55	35	49	48
HA in bulk (corrected for sampling)	mg	165	103	250	121	388	673	629	388	482	671
Overall yield (corrected for sampling)	dose/egg	0.5	0.3	0.8	0.4	1.2	1.5	1.4	0.9*	1.1	1.5

*The overall performance of batch 09FLU013 has been negatively affected by a zonal power failure.

2009 Tech Transfer Activities

1. Website : www.itpiv.nl

2. QA/GMP - Workshop for 13 participants

3. Generic Training Course for 10 participants

4. Partner identification for bilateral Tech Transfer agreements

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Traini

World Health Organization

- A two volume Course Manual was developed
- Hands-on: demonstration of one dedicated "training" run
- 2 sub groups: production and quality control

Access to:

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

- cleanroom design
- water system
- HVAC
- equipment
- maintenanc
- trouble sho
- etc.

- seedlot preparation
- egg handling systems
- zonal ultra centrifuge
- virus inactivation
- process validation

- specifications
- validation plans and reports
- BPR
- SOP's

- in-process and release tests
- specification
- set-up
- assay
- etc.

- IMPD
- safety and efficacy studies
- clinical plan
- study protocols
- etc.

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
  - *Both include tailor- made group training in Netherlands*

PEAK
PEAK
PEAK

GPO
IVAC
NHA TRANG. VIÊT NAM
- 1978
- NT: 1,5 hec
- SD farm: 125 hec
Production VACCINE for EPI
Products for market
R&D
DTP
TT
BCG
Vi. Typhoid
SAT . ImBCG
SAR . SAD
SAV . INFα.2b
PPD . Td
...
Pentavalent (DPT. Hib. HeB)
Pandemic Flu vaccine
Sera anti Tehodotoxin
Food and Drug
Mump
Employee : 200
Colabrating : UNICEF, WHO, RIVM, CLB, NIH_US
Looking for : - Combo vaccine,
- Influenza (Seasonal vaccine, new technology)
- MMR, Varaccella, Cancer vaccine
- VLP and Specific Adjuvant, Denger
Be

International Faculty