Technology Transfer from the Perspective of IFPMA vaccine members

WHO – Workshop on Technology Transfer for Local Manufacturing Capacity of Vaccines
Michael Watson (Sanofi Pasteur)
Chair of IFPMA Biologicals and Vaccines Committee
What is Technology Transfer?¹

What?
Transfer of skills, knowledge, technologies, methods of manufacturing, samples of manufacturing and facilities

To whom?
Within or outside an organisation, a geography or an industry/discipline

Why?
1. To increase access to scientific and technological developments
2. To allow further development of the technology into new products, processes, applications, materials or services
3. Increase manufacturing capacity and access to products
4. Share Know-How & Intellectual Property
5. Lower Cost of Goods?
6. Because it is mandated?

¹ Adapted from http://en.wikipedia.org/wiki/Technology_transfer
Many Types of Technology Transfer

- R&D capacity
- Clinical trials
- Laboratory testing
- Quality assessment
- Supply chain management and logistical issues
- Training of personnel
- Information technology
- Project / human resource management
- Local production

Health-related technology transfer is not solely the remit of industry
The Principle of Technology Transfer

Give a man a fish, he'll eat for a day

Teach a man to fish, he'll eat for a lifetime
Technology Transfer in the context of barriers to access:

- **Political versus Cultural situation**
  - Political priorities – Fish are OK to eat
  - Politico-economic stability – The next government will not be vegetarian
  - Budgetary priorities – Spend on nets rather than shotguns or scythes
  - Sustainable ability to pay – Will be able to repair broken nets
  - Cultural and social barriers and modifiers – The French eat pike but the Brits do not

- **Programmatic factors:**
  - Policy making capacity and capability – Able to plan the fishing trip
  - Sustainable health care system and logistics – Fuel for boats, able to get fish to market
  - Epidemiological, disease and safety surveillance capability and capacity – Know which fish are where and when and how to manage stocks
  - Regulatory capacity and capability (requirements, review timelines) – Develop and enforce rules on fishing methods and quotas
  - Adapted healthcare solution – the product – Equipment adapted to local species and conditions
Today’s vaccine technology balance is a result of 200 years of evolution in vaccines and vaccination
Prior to 1930s, low-tech, low reg, low quality made for easier transfer and equity

Balmis Expedition
• 22 orphan boys (8 to 10 years old) as successive carriers of the vaccine.

Making yellow fever vaccine ……..probably

Smallpox (Vaccinia) vaccine

WHO Vac TT mtg, Nov. 30-Dec.1, 2010, Geneva
1930s to 1990s: National Public Health institutes, not industry, drove technology transfer
1950s to 1980s: new vaccines, technology and regulations

Developed world commercial producers able to meet costs & standards > global disparity

- **New vaccines**
  - Polio (Salk & Sabin)
  - Measles
  - Mumps
  - Hepatitis B
  - Meningococcus
  - Haemophilus influenza
  - Combinations

- **New technologies**
  - Culture on chick embryos (Goodpasture, Walter Reed, 1931)
  - Tissue culture (Enders, 1949)
  - Recombinant vaccines (1980s)
  - Conjugate vaccines (1980s)
  - Plus improved production and assay techniques

- **New regulations**
  - “Jim” and Biologicals Act: 1902
  - Cutter incident: 1955, led to creation of Division of Biologics Standards in NIH, now FDA
  - GMP and management of input materials 1963 and 1976
  - Management of air pressure – 1978/87
  - WHO developed a prequalification system – 1987
  - Documentation and Team Biologics -1990s
  - Many more regulatory and quality standards
Fewer producers + pressure of global eradication programs

**Demand**
- Increased supply at minimum cost/profit
- Increasing costs of R&D, quality and production

**Supply**
- 10 of 14 developed-world manufacturers partially or totally stopped production of traditional vaccines during 1998-2001 (UNICEF)
- EPI/UNICEF faced severe shortages and high prices as suppliers merged and reached capacity limits during 1990s
Today: new technologies, new possibilities

- Genomics, proteomics & Genetic engineering
- Cell culture, expression & production
- Immunology & adjuvants

+- Funding, Financing & partnerships

- Cost & time of R&D & Production

- Growing Global Market
- Increasing low cost competition
- Increased technological solutions
- Improving epidemiology & surveillance
- Global focus on Public health

- Risks of litigation
- Quality and Regulatory Requirements, Costs & Risks
- Oligopsonistic purchasers
- Uncertain return on investment (Risk of investment in other sectors)
- Increasing low cost competition
## Vaccine Technology Transfer: Summary

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Technology</th>
<th>Economics</th>
<th>Politics</th>
<th>Regulation</th>
<th>Legal &amp; IP</th>
<th>Technology Transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre 1930s</td>
<td>Low</td>
<td>Low cost</td>
<td>Colonial policy plus altruism</td>
<td>Nearly absent</td>
<td>Absent</td>
<td>Word of Mouth</td>
</tr>
<tr>
<td>1930s – 1980s</td>
<td>Moving</td>
<td>Increasing cost</td>
<td>National health programs</td>
<td>Strengthening from a low base</td>
<td>Absent</td>
<td>WHO, national institutes, meetings, education?</td>
</tr>
<tr>
<td>Eradication Programs</td>
<td>Increasing complexity, sophistication, cost</td>
<td>Pressure from buyers</td>
<td>Altruism, global budget issues</td>
<td>Increasing Regs. Increasing qual. standards WHO PQ</td>
<td>Starting to appear</td>
<td>WHO, expert groups, donor funding</td>
</tr>
<tr>
<td>1990s to 2010</td>
<td>High</td>
<td>High cost/low margin, economies of scale</td>
<td>Self-sufficiency, biotechnology, donor politics, privatization</td>
<td>Very high domestic and parallel WHO prequalification</td>
<td>Strengthening but mainly on intermediates and processes</td>
<td>WHO DCVMN, biotechnology programs, corporate strategic alliances, donors &amp; Education</td>
</tr>
<tr>
<td>2011+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
However vaccines are not cars, or even like small molecules
Vaccines are more like Michelin 3-star food

➢ The place

➢ The product

➢ The people

WHO Vac TT mtg, Nov. 30-Dec.1, 2010, Geneva
Understand the Technology before transferring it

Nature of Vaccine R&D & Production in 2010

| High and rising Regulatory and Quality Hurdles |
| High and rising capital investment for production |
| More know-how than IP barriers |
| High and rising R&D costs |
| Some Gov & NGO funding of R&D and Production |
| High investor expectation of return on investment |
| High and rising technical complexity |

Implications for Vaccines

| Technology transfer |
| High and sustainable skills, competence & quality |
| Significant Capital cost + Know-how transfer |
| Hardware without know-how will not work |
| Sig, supporting Clinical & pharmaceutical data |
| Look for local or NGO partnerships |
| Innovative financing support e.g. AMC |
| Confident of respect for IP and Know-how |

Not a quick fix: Long, expensive & risky

- At least two committed partners
- Sustained and sustainable commitment
- 5-10 yrs for the transfer!
- Sustainable funding: $50-100+ Million required
- Will it really improve access and/or decrease cost/price?
- The Local know-how & trainable people?
- Independent competent National Control Authority
- A mature production process
- 10-30 year pay-back time:
  - Political stability
  - Sustainable demand

WHO Vac TT mtg, Nov. 30-Dec.1, 2010, Geneva
A stepwise approach securing downstream processes prior to developing bulk production capacity

Phase 1
Packaging and Distribution of Finished Product
Implementation of:
- Basic Quality Control
- Labeling
- Cold chain
- Distribution network
- Adverse event reporting
- etc.

Phase 2
Phase 1 + Filling of Bulk
Implementation of:
- Sterile filling unit
- Sterility assurance
- QC expertise
- Validated suppliers
- Quality Assurance
- etc.

Phase 3
Phase 2 + Production of Active Principle
Implementation of:
- Engineering
- Bulk production expertise
- Sustainability
- Economic viability
- etc.

Key choice is what stage to transfer first
## Examples of Vaccine Tech Transfer and Joint Venture Programs

<table>
<thead>
<tr>
<th>Partners</th>
<th>Types of vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bharat Biotech (India) – Wyeth (Pfizer)</td>
<td>Hib</td>
</tr>
<tr>
<td>Bio Farma (India) – Biken</td>
<td>polio, measles</td>
</tr>
<tr>
<td>Bio Kangtai (China) – sanofi pateur</td>
<td>JE, influenza</td>
</tr>
<tr>
<td>Bio Manguinhos (Brazil) – Biken</td>
<td>Measles, polio, rubella</td>
</tr>
<tr>
<td>Bio Manguinhos (Brazil) – GSK Bio</td>
<td>Hib, MMR, OPV, pneumococcal conjugate, Rotavirus</td>
</tr>
<tr>
<td>Biological E (India) – Intercell</td>
<td>JE</td>
</tr>
<tr>
<td>Birmex (Mexico) – sanofi pasteur</td>
<td>influenza</td>
</tr>
<tr>
<td>Butantan (Brazil) – sanofi pasteur</td>
<td>influenza</td>
</tr>
<tr>
<td>China – GSK</td>
<td>Various vaccines, including influenza</td>
</tr>
<tr>
<td>China – Merck</td>
<td>HepB</td>
</tr>
<tr>
<td>Egypt - GSK</td>
<td>DTP-HepB, MMR, Meningitis, OPV</td>
</tr>
<tr>
<td>India - GSK</td>
<td>Various vaccines</td>
</tr>
<tr>
<td>India - Novartis</td>
<td>rabies</td>
</tr>
<tr>
<td>Panacea Biotech (India) – Novartis</td>
<td>DTP-Hib</td>
</tr>
<tr>
<td>Russia – GSK</td>
<td>Various vaccines</td>
</tr>
<tr>
<td>Thailand – Merck (Nobilon)</td>
<td>influenza</td>
</tr>
<tr>
<td>Ukraine – GSK</td>
<td>MMR</td>
</tr>
</tbody>
</table>
## Technology Transfer & Local Production is Ongoing for Influenza Vaccines

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PRODUCTION INITIATIVE</th>
<th>COMPANY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil (Sept 2009)</td>
<td>Agreement with Butantan to produce and supply pandemic influenza H1N1 vaccines to Brazilian government; vaccine formulation, filling and packing in Brazil</td>
<td>sanofi pasteur</td>
</tr>
<tr>
<td>Mexico (Mar 2009)</td>
<td>Agreement to build a facility to manufacture seasonal and pandemic influenza vaccines in collaboration with Birmex, a Mexican federal vaccine manufacturer</td>
<td>sanofi pasteur</td>
</tr>
<tr>
<td>WHO / Thailand (Feb 2009)</td>
<td>License granted to WHO for egg-based seasonal and pandemic live-attenuated influenza vaccine technology; WHO to sub-license to developing country public sector vaccine manufacturers; Thailand is the 1st country to request sub-license</td>
<td>Merck &amp; Co. (Nobilon)</td>
</tr>
<tr>
<td>China, Hong Kong &amp; Macau (Nov 2008 / June 09)</td>
<td>Joint venture agreement with Shenzhen Neptunus Interlong Bio-Technique Co Ltd to develop &amp; manufacture seasonal influenza vaccines and pre-pandemic / pandemic influenza vaccines</td>
<td>GSKBio</td>
</tr>
<tr>
<td>China (Nov 2007)</td>
<td>Agreement with the Chinese authorities to build a facility to manufacture seasonal and pandemic influenza vaccines</td>
<td>sanofi pasteur</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Agreement with Bio Farma to build a facility to manufacture seasonal influenza vaccines</td>
<td>Biken</td>
</tr>
<tr>
<td>Brazil (1999)</td>
<td>Agreement with Butantan to build a facility to manufacture seasonal influenza vaccines</td>
<td>sanofi pasteur</td>
</tr>
</tbody>
</table>
Conclusions: Sustainable Vaccine Technology Transfer

- Tech Transfer is one of many factors that influence access to vaccines

- Tech Transfer should be a realistic pragmatic collaboration not a political quick fix

- It requires careful consideration of:
  - Cost
  - Feasibility
  - Time
  - Resources
  - True impact/benefit
  - Sustainability
  - Long term commitment by all partners

- In many circumstances, for very good reasons, tech transfer is not possible,
  - in this case the R&D-based industry ensures access to vaccines through other mechanisms

- Maintaining a free and healthy market is key to ensure the sustainability of innovation and affordability of vaccines