Vaccine in new century

**success of leveraging market methods**

- Measles deaths dropped by 60% 1999 – 2005
- 4.3 million measles deaths averted 2000 – 2008

> “This is a historic victory for public health,”
> -- Dr. Margaret Chan

- GAVI: 4.1 billion $ committed 2000 – 2015
- 5 million lives saved by UNICEF vaccine

Challenges

• 2 M/year vaccine preventable childhood deaths
• Sustainable procurement
• Supply security
• Financial risks
• Gap
• Mid-income countries

GAVI helped fund the center that administered this yellow fever vaccination.
www.miller-mccune.com
Challenges

- 2 M/year vaccine preventable childhood deaths
- Sustainable procurement
- Supply security
- Financial risks
- Gap
- Mid-income countries

Can vaccine ToT address these challenges ??
Landscape of technology transfer in vaccines

-- A study conducted for WHO/IVR as part of WHO project on improving access to medicines in developing countries through technology transfer

By Wenfeng Gong
Duke University- Sanford School of Public Policy
Outline

- Rationale: vaccine vs. drugs in ToT
- Objectives and scope
- Results & finding
  - Players
  - Disease target
  - Models of ToT
  - Trends
- Key issues from interviewees
## What’s different for vaccine ToT?

<table>
<thead>
<tr>
<th></th>
<th>Medicines</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tech natures</td>
<td>Various, chemical synthesis may easy to establish</td>
<td>Complicated</td>
</tr>
<tr>
<td>Intellectual property</td>
<td>Significant barrier for newer drugs</td>
<td>Patents not major barrier in past, but know-how critical</td>
</tr>
<tr>
<td>Market force</td>
<td>Private sector dominated</td>
<td>Highly national policy regulated; global procurement;</td>
</tr>
<tr>
<td>Market dynamics</td>
<td>Various, good competition for generics</td>
<td>Limited manufacturers; &gt;90% by 15 companies; IFPMA+DCVMN; fewer ToT</td>
</tr>
<tr>
<td>Public Health Impact</td>
<td>Not all drugs have significant impact</td>
<td>Vaccines generally cost-effective</td>
</tr>
</tbody>
</table>
UNIDO statement in 1975:

“By 2000, 25% of pharmaceutical products would be produced in low- and middle- income countries”.

Currently, only 7% medicines made in LMICs. But, over 80% vaccines made in LMICs.

However, the 80% vaccines only take 20% of the sales.
Landscape analysis: objectives and scope

- Conducted, during June to Aug 2010, for WHO/IVR
- Broad review of existing ToT cases
- Drivers, barriers, & trends
- Provide an evidence-based reference for decision making in future ToT.

Cases included:
- ToT Initiated or completed in the past two decades.
- North-South, South-South
Combination of
1. internet research,
2. manufacturer survey
3. interviews with suppliers, recipients of technologies & others with interest in the process.

3 different questionnaires for tech suppliers, recipients & transfer sponsors.

Questions included:
1. Manufacturer’s information
2. Nature of technology and transfer
3. Intellectual Property (IP) and Licensing
4. Achievements
5. Issues, including external factors
Landscape analysis: results

- 101 identified: completed, abandoned, or ongoing
- **92 valid**, covered nearly all major cases
- Initiated or completed in past two decades
- Drivers and barriers varies among regions/sectors

- Semi-Quantitative studies:
  - Players
  - Models of ToT
  - Trends
Landscape analysis: results

- Recipient Countries:
Landscape analysis: results

- Recipient Countries:
Landscape analysis: results

- Technology Suppliers:
Landscape analysis: results

- Disease Targets:
  - Influenza (20)
  - Polio (4)
  - Hepatitis B (13)
  - Haemophilus influenzae type b (HiB) (6)
  - Measles and Measles Contained (7)
  - Rotavirus (11)
  - Meningococcus (1)
  - Japanese Encephalitis (JE) (4)
## Landscape analysis: results

- **Maturity of technology being transferred:**

<table>
<thead>
<tr>
<th>Step</th>
<th>R &amp;D stage</th>
<th>Pilot stage</th>
<th>Large-scale production</th>
<th>Fill-finish process</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Upstream transfer (Seed w/ know-how)</td>
<td>![transfer_symbol]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Seed w/ tech platform</td>
<td>![transfer_symbol]</td>
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<td></td>
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<tr>
<td>3. Pilot-stage transfer</td>
<td></td>
<td>![transfer_symbol]</td>
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<td></td>
</tr>
<tr>
<td>4. Large-scale production or Turn-Key transfer</td>
<td></td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
</tr>
<tr>
<td>5. Fill-finish transfer</td>
<td></td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
</tr>
<tr>
<td>6. Stepwise transfer</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
</tr>
<tr>
<td>7. R&amp;D Tech support w/o mature concept</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
</tr>
<tr>
<td>8. QC/QA Tech support</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
<td>![transfer_symbol]</td>
</tr>
</tbody>
</table>

- **transfer symbol**: transfer of vaccine-specified tech
- **transfer line**: self-development w/ support
- **dashed line**: self-development
### Landscape analysis: results

- Maturity of technology being transferred:

<table>
<thead>
<tr>
<th>Maturity of Technology</th>
<th>Quantity</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Upstream transfer (Seed w/ know-how)</td>
<td>5</td>
<td>NIH-Bharat, Typhoid Vi-DT</td>
</tr>
<tr>
<td>2. Seed w/ tech platform</td>
<td>11</td>
<td>NIH-Sinopharm, with PATH, Rota</td>
</tr>
<tr>
<td>3. Pilot-stage transfer</td>
<td>25</td>
<td>NVI-SII, Hib</td>
</tr>
<tr>
<td>4. Large-scale production or Turn-Key transfer</td>
<td>17</td>
<td>JPRI-BioFarma, OPV</td>
</tr>
<tr>
<td>5. Fill-finish transfer</td>
<td>6</td>
<td>Sanofi-GPO Merieux, MMR</td>
</tr>
<tr>
<td>6. Stepwise transfer</td>
<td>7</td>
<td>Sanofi-Butantan, seasonal Flu</td>
</tr>
<tr>
<td>7. R&amp;D Tech support or joint development</td>
<td>9</td>
<td>GSK-Fiocruz, dengue</td>
</tr>
<tr>
<td>8. QC/QA Tech support</td>
<td>5</td>
<td>GSK-Vacsera, general tech support</td>
</tr>
</tbody>
</table>
## Landscape analysis: results

- **Approach of transfer:**

<table>
<thead>
<tr>
<th>Approach of transfer</th>
<th>Diagram</th>
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<tbody>
<tr>
<td>1. Bilateral know-how transfer or joint development</td>
<td><img src="image1" alt="Diagram" /></td>
</tr>
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<td>2. Joint venture and acquisition</td>
<td><img src="image2" alt="Diagram" /></td>
</tr>
<tr>
<td>3. <em>de-novo</em> manufacture</td>
<td><img src="image3" alt="Diagram" /></td>
</tr>
<tr>
<td>4. Single recipient joint development w/ active input by facilitation entity</td>
<td><img src="image4" alt="Diagram" /></td>
</tr>
<tr>
<td>5. Shared technology platform</td>
<td><img src="image5" alt="Diagram" /></td>
</tr>
<tr>
<td>6. Technology transfer “hub”</td>
<td><img src="image6" alt="Diagram" /></td>
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## Landscape analysis: results

- **Approach of Transfer:**

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<th>Quantity</th>
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<tr>
<td>1. Bilateral know-how transfer or joint development</td>
<td>41</td>
<td>Biken-GPO, JE</td>
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<tr>
<td>2. Joint venture and acquisition</td>
<td>12</td>
<td>Sanofi-GPO Merieux</td>
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<tr>
<td>3. <em>de-novo</em> manufacture</td>
<td>8</td>
<td>GSK-India, HPV</td>
</tr>
<tr>
<td>4. Single recipient joint development w/ active input by facilitation entity</td>
<td>8</td>
<td>NIH-SII, with MVP, Men A</td>
</tr>
<tr>
<td>5. Shared technology platform</td>
<td>9</td>
<td>NIH-Shantha, with PATH, Rota</td>
</tr>
<tr>
<td>6. Technology transfer “hub”</td>
<td>1</td>
<td>NVI-11 DCVM, with WHO, Flu</td>
</tr>
</tbody>
</table>
Purposed strategic model analysis

- For future work
- Evaluation of Models:
Landscape analysis: more results

- ToT Financing: most recipient self-financed; public companies with support from government; limited cases supported by NGOs
- Budget is usually short, but resource prioritization is more a concern
- Cost of ToT is not a concern, licensing fee and royalty more mentioned
- Local policies have positive effects on ToT
- General production facility is usually good, Clinical trial expertise, QC equipment, satisfaction with NRA vary
# PAST Examples of Public health impact of vaccine ToT

- **vaccine ToT** → **local capacity** → **sufficient and stable supply** → **global procurement** → **price reduce** → **increased access** → **positive PH outcomes**

### Disease target

<table>
<thead>
<tr>
<th>Disease target</th>
<th>Recipient countries</th>
<th>Donor</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HiB</strong></td>
<td>Brazil, India, Indonesia, China</td>
<td>GSK, NVI, ICGB</td>
<td>100% of local needs met, 42% of UNICEF purchases met.</td>
</tr>
<tr>
<td><strong>HepB</strong></td>
<td>Brazil, India, Korea, China</td>
<td>ICGB, Merck, Rhein</td>
<td>100% of local needs met, 42% of UNICEF purchases met.</td>
</tr>
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</table>
Public health impact of vaccine ToT in the PAST

Number of countries having introduced HepB vaccine* and global infant HepB3 coverage, 1989-2009

- Merck to BIBP & Kangtai/China
- Green Cross to BioFarma/Indonesia
- CIGB to Panacea/India
- NVI to BioFarma/Indonesia
- Rhein to SII and Bio E/India

* Year of introduction can be the year of partial introduction
** Includes India and Sudan with partial introduction

Vaccine ToT for public health impact in the FUTURE

- **Why** ToT to LMICs?
  - **Competitive manufacturers**
    - Lower price? Price negotiation; price ≠ cost
    - Global procurement: supply security? sufficiency?
    - Facilitate global access to vaccine
- **Which** disease target? (Public health need)
- **When** should transfer be considered?
- **Who** are the transferors, transferees, and facilitators?
  - Emerging market countries: ability & need
- **How** should the ToT be conducted?
Trends:
Bilateral Transfer vs. Acquisition, Merging, & Establishing:
Major Vaccine ToT Events with For-profit Suppliers

DCVM→IFPMA: research-based pharma

Space for “me-too” manufacturers in the future?
Key issues from interview/survey

Recipients’ side (n=30 in cases):

1. R&D ability for supporting ToT; innovation capacity
   70% of manufacturers rate their capacity ≤3 out of 5
   - Human resource for R&D

2. General production facility, and GMP facility for ToT

3. Prioritization of resources in company level

4. License negotiation skills and training

5. Evaluation/assessment for quality of technologies

6. NRA capacity weakness (reported in some countries)
Key issues from interview/survey

Suppliers/sponsors’ side (n=3 of survey + n=5 of interview):

1. R&D ability for supporting ToT;
   - R&D budget to support ToT
2. Business case/sustainability
3. Clinical trial expertise
4. QC facility and human resource
Limitations

- Some questions in survey not answered
- Relatively low survey response rate
  from suppliers/sponsors comparing to recipients, but interviewed.
- Number of cases ≠ volume of cases
- Only single response for some cases, lack confirmation
- Recipients’ perspective ≠ suppliers’ perspective
- Lack of understanding of attainment of the cases
- Lack of Public Health outcome evidence
- Cannot link the landscape of TT to the outcomes
- Correlation ≠ casual relationship
- Small n, few statistical significant results
Thank you

And thanks to the many participants of survey