Vaccine Development & Deployment in Thailand

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Outline

✓ Vaccine introduction & immunization program
✓ Vaccine development & production
✓ TB problem & vaccine development plan
Thailand Selected Demographics

Population: 67 millions (est)*
Live Birth (2009): 733,014 /year
Total fertility rate: 1.66* (est)
Infant Mortality: 15.0/1,000 live births (2006 estimate)
GNI per capita: 2,698 USD* (PPP 8,703 USD)**

2011, http://www.indexmundi.com/thailand/demographics_profile.html,
http://www.tradingeconomics.com/thailand/gdp-per-capita

Thailand’s Perspective on Vaccines

✓ Modern & cost-effective public health tool for primary disease prevention & control, mostly having externality benefit

✓ Relatively not difficult to implement & access

✓ Having high risk for shortage of procurement
Vaccine Introduction & Immunization Program
Basic Immunization - EPI

Target populations:
- New born babies & children
  - Pregnant women
  - High-risk groups

EPI established since 1977 under technical & strategic advisory of NAICP

Nationwide coverage >90%, except in border areas & high terrains

Vaccine procurement, technical support, evaluation are organized at national level

All hospitals & HC provide immunization service, free of charge

National Advisory Committee on Immunization Practice (NACIP) established since 1970
# EPI Immunization Schedule of Thailand

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccines (11 immunogens)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td></td>
</tr>
<tr>
<td>At birth</td>
<td>BCG, HB₁</td>
</tr>
<tr>
<td>2 months</td>
<td>OPV₁, DTP₁, HB₂</td>
</tr>
<tr>
<td>4 months</td>
<td>OPV₂, DTP₂</td>
</tr>
<tr>
<td>6 months</td>
<td>OPV₃, DTP₃, HB₃</td>
</tr>
<tr>
<td>9 - 12 months</td>
<td>MMR₁</td>
</tr>
<tr>
<td>Older children</td>
<td></td>
</tr>
<tr>
<td>1 ½ - 2 yrs</td>
<td>OPV₄, DTP₄, JE₁, JE₂</td>
</tr>
<tr>
<td>2 ½ - 3 yrs</td>
<td>JE₃</td>
</tr>
<tr>
<td>4 yrs</td>
<td>OPV₅, DTP₅</td>
</tr>
<tr>
<td>Students</td>
<td></td>
</tr>
<tr>
<td>4 - 7 yrs</td>
<td>MMR₂</td>
</tr>
<tr>
<td>12-16 yrs</td>
<td>dT</td>
</tr>
<tr>
<td>Adults</td>
<td>Seasonal Flu in HCWs &amp; High risk group</td>
</tr>
</tbody>
</table>
Timeline of vaccine introduction in Thai EPI since 1977

<table>
<thead>
<tr>
<th>Year Interval</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977-1981</td>
<td>BCG x 1</td>
</tr>
<tr>
<td>1982-1996</td>
<td>DTP x 2</td>
</tr>
<tr>
<td>1987-1991</td>
<td>DTP x 3</td>
</tr>
<tr>
<td>1992-1996</td>
<td>DTP x 4</td>
</tr>
<tr>
<td>1997-2001</td>
<td>DTP x 5</td>
</tr>
<tr>
<td>2002-2006</td>
<td>DTP-HB x 3</td>
</tr>
<tr>
<td>2007-2011</td>
<td></td>
</tr>
<tr>
<td>2012-2016</td>
<td></td>
</tr>
</tbody>
</table>

- **BCG**: Bacille Calmette-Guérin
- **DTP**: Diphtheria, Tetanus, Pertussis
- **OPV**: Oral Poliovirus
- **M**: Measles
- **R**: Rubella
- **HB**: Hepatitis B
- **JE**: Japanese Encephalitis
- **TT**: Tetanus
- **Typhoid**: Typhoid
- **Influenza**: Influenza
- **Flu in HCW**: Flu in Healthcare Workers
- **Flu in HR**: Flu in High Risk Groups

Source: EPI / DDC / MOPH, 14 July 2011

HR* – High risk groups
Decision making process for introduction of new vaccines in Thai EPI

1. The disease is a major burden.
   - Cases/ deaths/ disability
   - Social & economic impacts

2. Vaccination is a priority intervention.
   - Safe & efficacious vaccine
   - Vaccine effectiveness
   - Other interventions less promising

3. Vaccination is a good investment.
   - Cost benefit /cost-effectiveness/cost saving
   - Financing feasibility

4. Vaccination is programmatically feasible.
   - Operation and logistic feasibility under existing health infrastructure
   - Public acceptance & political will

5. Programmatic feasibility is proven in a pilot.
   - Pilot program conducted with the feasibility for sustenance if pilot outcome is promising.
Licensed or registered
Decision to introduce in EPI

Promote / monitor vaccine use in private sector

Policy process, Pilot project, Expansion, Nationwide

Private sector
Public sector

- Verify disease burden
- Establish CB / CE
- Ensure programmatic feasibility
- Ensure affordability & sustainability
- Obtain policymaker advocacy

Based on experience with introduction of HB (1985-1992), JE (1990’s), DTP-HB (since late 1990’s)
Practical steps in vaccine introduction

- Licensed or registered
- Decision to introduce in EPI
- Promote / monitor vaccine use in private sector
- Policy process
- Pilot project
- Expansion
- Nationwide
- Public sector
- Private sector

Hib, Pneumo, HPV, Rota

- Verify disease burden
- Establish CB / CE
- Ensure programmatic feasibility
- Ensure affordability & sustainability
- Obtain policymaker advocacy

Based on experience with introduction of HB (1985-1992), JE (1990’s), DTP-HB (since late 1990’s)
Planning and budgeting for national immunization program

- **Budget Bureau**
  - Prepare plans & budget proposal with justification
  - Review, prioritize & further put forward

- **MOPH & NHSO**

- **EPI & DDC**

- **NACIP**
  - Advice

- **Cabinet**
  - Propose & defend

- **Parliament**
  - Approval

- **Budget approved**
EPI under UC

• NHSO takes care of financing for vaccines and vaccine delivery, including procurement and supply of vaccines to all health care providers.

• MOPH is responsible for:
  – Policy / strategy development and guidance, as well as technical support to health care providers
  – Vaccination service
Vaccine Development
Challenges on Vaccine Development in Thailand

✓ Vaccine researches
  - Depend on individual interest
  - Domestic vaccine candidate: in pre-clinic
  - Clinical testing—phase I-III & bridging studies
    - Imported vaccine candidates
## Current Vaccine R&D (Pre-clinical phase) in Thailand

<table>
<thead>
<tr>
<th>Disease</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue</td>
<td>- Live attenuated tetravalent; Chimeric Den-YF, tetravalent; DNA</td>
</tr>
<tr>
<td>JE</td>
<td>- Inactivated cell culture; Live attenuated; Chimeric JE-YF, Dengue 2 PDK53</td>
</tr>
<tr>
<td>HIV</td>
<td>- Candidate vaccines under development and clinical studies - phases I, II, III</td>
</tr>
<tr>
<td></td>
<td>- Phase III (prime-boost, MOPH/ RTA/ Mahidol/ US)</td>
</tr>
<tr>
<td>Influenza</td>
<td>- R&amp;D on seed virus (H5) initiated (Biotec &amp; Mahidol)</td>
</tr>
<tr>
<td></td>
<td>- Clinical trial on candidate H5 vaccines under preparation (DMS); Live-attenuated-product</td>
</tr>
<tr>
<td></td>
<td>- Registered (GPO); Siriraj Hospital (Universal flu vac)</td>
</tr>
<tr>
<td>Chikungunya</td>
<td>Inactivated cell-based GPO</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Pre-clinical (DMS)</td>
</tr>
</tbody>
</table>

*Incomplete list*
## Current Vaccine Production in Thailand

<table>
<thead>
<tr>
<th>Producers</th>
<th>Vaccines</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. GPO</td>
<td>1. JE Vaccine (inactivated, MB derived)</td>
<td>Upstream to downstream</td>
</tr>
<tr>
<td>2. Thai Red Cross</td>
<td>2. BCG</td>
<td>Upstream to downstream</td>
</tr>
<tr>
<td></td>
<td>3. ERIG</td>
<td>Upstream to downstream</td>
</tr>
<tr>
<td></td>
<td>4. Anti-venom</td>
<td>Upstream to downstream</td>
</tr>
<tr>
<td>3. GPO-MBP</td>
<td>5. Measles</td>
<td>Formulation &amp; filling</td>
</tr>
<tr>
<td></td>
<td>6. OPV</td>
<td>Filling</td>
</tr>
<tr>
<td></td>
<td>7. MMR</td>
<td>Formulation &amp; filling</td>
</tr>
<tr>
<td></td>
<td>8. Hepatitis B</td>
<td>Filling</td>
</tr>
<tr>
<td></td>
<td>9. Vero cell rabies</td>
<td>Formulation &amp; filling</td>
</tr>
<tr>
<td></td>
<td>10. Influenza</td>
<td>Filling</td>
</tr>
<tr>
<td>4. Livestock department</td>
<td>13 animal vaccines</td>
<td>Upstream to downstream</td>
</tr>
</tbody>
</table>

Source: NVI, DDC, 2008
Challenges on Vaccine Development in Thailand

✓ Vaccine researches
  ➢ Depend on individual interest
  ➢ Domestic vaccine candidate: in pre-clinic
  ➢ Clinical testing—phase I-III & bridging studies
    ▪ Imported vaccine candidates

✓ Vaccine production
  ➢ Number of human vaccines domestically produced has been decreased over time
National Vaccine Committee (NVC) 2001

Cabinet

- NVC
- Subcommittees
  - R&D
  - Production
  - QA/QC
  - ACIP

National Vaccine Policy & Plan

Governmental Organizations

- NGOs

Private Sector

R&D / Production / QA&QC / EPI
National Vaccine Policy & Strategies 2005
National Vaccine Policy & Strategies 2005

Aim: To promote development on specific vaccines for vaccine self-reliance, vaccine security, and capacity building on vaccine development

- Promote development on vaccine science and technology: from research to production, QA/QC & immunization
- Promote the investment in domestic upstream vaccine production industry
- Encourage collaboration between governmental and private sector
- Establish the National Vaccine Institute (Public Organization)
National Vaccine Agenda 2011

10 projects in 10 years

- Dengue vaccine development
- BCG production & New TB vaccine development
- DTP-HB production
- Japanese encephalitis vaccine (JEV), cell-based, production
- Acellular pertussis vaccine development & production
- GMP pilot plant establishment
- Bio-medical & vaccine resource center establishment
- Human resource development
- NVI Establishment as a center for policy driver on vaccine development and immunization of the country
Tuberculosis
BCG Production

Mahidolvongsanusorn Building
**Current BCG Manufacturing Process**

1. **BCG culture (S₂ culture)**
   - Harvesting
   - Wash

2. **Semi-dry mass**
   - Grinding
   - Add solution

3. **Conc. BCG Suspension**
   - Add solution

4. **Final Bulk**
   - Filling

5. **0.5 ml of vials (half-closed stopper)**
   - Freeze-drying
   - Capping
   - Inspection

6. **Freeze-dried BCG Vaccine**
   - Labelling / Packaging

7. **Final Product**
EPI Vaccine Coverage in Thai Children 1-year Old

Source: National vaccine coverage survey
Selected Thai EPI Vaccine Coverage and Disease Incidences

- **Diptheria**
- **Polio**
- **Pertussis**
- **Tetanus neo.**
- **Measles**
- **HB**
TB Case notification from 2001-2012

Source: Bureau of TB, Dept. of Diseases Control, MOPH (updated 31 July 2013)
Trends in notified new smear-positive TB cases by age group among males, 2001-2012

Source: Bureau of TB, Dept. of Diseases Control, MOPH (updated 31 July 2013)

<table>
<thead>
<tr>
<th>ITEMS</th>
<th>Newly Treated Cases</th>
<th>Previously Treated Cases</th>
<th>Combined Drug resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Pct</td>
<td>N</td>
</tr>
<tr>
<td>Total tested</td>
<td>1456</td>
<td>100.00%</td>
<td>175</td>
</tr>
<tr>
<td>Fully sensitive</td>
<td>1216</td>
<td>83.52%</td>
<td>110</td>
</tr>
<tr>
<td>Any resistance</td>
<td>240</td>
<td>16.48%</td>
<td>65</td>
</tr>
<tr>
<td>H+R resistance (MDR-TB)</td>
<td>27</td>
<td>1.85%</td>
<td>29</td>
</tr>
<tr>
<td>Mono-resistance</td>
<td>164</td>
<td>11.26%</td>
<td>32</td>
</tr>
<tr>
<td>Two drugs resistance</td>
<td>47</td>
<td>3.23%</td>
<td>3</td>
</tr>
<tr>
<td>Three drugs resistance</td>
<td>2</td>
<td>0.14%</td>
<td>1</td>
</tr>
<tr>
<td>Four drugs resistance</td>
<td>3</td>
<td>0.21%</td>
<td>4</td>
</tr>
<tr>
<td>Any H-resistance</td>
<td>174</td>
<td>11.95%</td>
<td>46</td>
</tr>
<tr>
<td>Any R-resistance</td>
<td>30</td>
<td>2.06%</td>
<td>39</td>
</tr>
<tr>
<td>Mono H-resistance</td>
<td>99</td>
<td>6.80%</td>
<td>16</td>
</tr>
<tr>
<td>Mono R-resistance</td>
<td>2</td>
<td>0.14%</td>
<td>7</td>
</tr>
</tbody>
</table>

Note: Total = 1747 cases, 116 cases are waiting for analysis, NTRL NTP-May2013
TB Burden

Number of TB cases of 22 countries

- Thailand: 2,553
- France: 1,100
- Italy: 94,000
- Ethiopia: 86,000

Map showing the number of TB cases in 22 countries, with Thailand having 2,553 cases, followed by France with 1,100 cases, and Ethiopia with 94,000 cases. The map also highlights other countries with notable numbers of cases.
National Vaccine Agenda 2011

10 projects in 10 years

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New BCG & new TB vaccine plant
Conclusion

- Thailand has a strong policy on immunization and vaccine development for vaccine security and self- & regional-reliance
- New TB vaccine has been emphasized & included in the national vaccine development agenda
- Field trial & domestic production could be possible ways of collaboration
Thank you