Malaysian Vaccine Program:
Pathway for Malaysia’s Nascent Vaccine Industry

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Agenda

Introduction

GAP: The Case for Influenza Vaccines

The Global Vaccine Scenario

The Malaysian Vaccine Scenario

Vaccine Manufacturing

The Malaysian Vaccine Programme

Conclusion
Introduction
Progression of Outbreaks

- **Outbreak**: Disease occurs in greater numbers than expected.
- **Epidemic**: A localized, rapid spread of an infectious disease to many.
- **Pandemic**: A global disease outbreak.
- **Isolated Cases**

**Epidemics**:
- Dengue
- Cholera
- Meningitis
- Hepatitis

**Pandemics**:
- HIV/AIDS
- Smallpox
- The Plague

**Influenza**
United Nations (UN) Initiatives to Combat Outbreaks

- **UNICEF**: MDG* 4 aims to reduce child mortality by increasing paediatric vaccine coverage
- **WHO**: Global Action Plan (GAP) for Influenza Vaccines
- **WHO**: MDG* 6 aims to combat HIV/AIDS, Malaria, NTDs
- **WHO**: Global strategy for dengue prevention and control, 2012–2020

*MDG – Millennium Development Goal*
MDG 4: Routine Immunization

Increased coverage of paediatric vaccines through inclusion of:

1) Pneumococcal conjugate vaccine (PCV)
2) Haemophilus influenzae type b (Hib) vaccine
3) Rotavirus vaccine

<table>
<thead>
<tr>
<th>Goals</th>
<th>Gains</th>
<th>Pending Work</th>
</tr>
</thead>
<tbody>
<tr>
<td>WFFC* – Fully immunize 90% of children by 2010</td>
<td>Both DPT3 and measles immunization coverage reached 78% in developing countries. In 115 countries, DPT3 coverage reached 95%.</td>
<td>26 million children are still not immunized, 1.4 million children still die from vaccine-preventable diseases.</td>
</tr>
</tbody>
</table>

*WFFC – World Fit for Children (UNICEF)

Source: United Nation’s Children Fund, UNICEF
Key Takeaway: In Oct 2012, WHO included **pneumococcal** vaccinations in their Recommendations for Routine Immunization for all countries.
Meningococcal vaccination is compulsory for those going for Hajj.
Vaccination is pivotal against pandemic and seasonal Influenza.
**Key Takeaway:** MOH Immunization Schedule is currently not updated to WHO’s MDG. Last update was in 2004.

### Table 2: New Immunisation Schedule

<table>
<thead>
<tr>
<th>Immunisation</th>
<th>Age (months)</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>BCG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hep B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*for Sabah only

For immunodeficient children, the recommended schedule is shown below:

### Table 3: Recommended Immunisation Schedule for Immunodeficient Children

<table>
<thead>
<tr>
<th>Immunisation</th>
<th>Immunosuppressive Therapy</th>
<th>HIV</th>
<th>Sibling/Close Contacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hep B</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>DPT</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>OPV</td>
<td>No</td>
<td>Yes (IPV (killed))</td>
<td>Yes (IPV)</td>
</tr>
<tr>
<td>Hib</td>
<td>Yes (3 + Booster dose)</td>
<td>Yes</td>
<td>Yes (IPV)</td>
</tr>
<tr>
<td>Measles</td>
<td>No</td>
<td>Yes</td>
<td>Yes (Asymptomatic)</td>
</tr>
<tr>
<td>MMR</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Key Takeaway: Opportunity for vaccine self sufficiency in Malaysia due to the high penetration. Potential for building vaccine capacity in Malaysia versus foreign importation

Source: Ministry of Health
United Nations (UN) Initiatives to Combat Outbreaks

UNICEF: MDG* 4 aims to reduce child mortality by increasing paediatric vaccine coverage

WHO: Global Action Plan (GAP) for Influenza Vaccines

WHO: MDG* 6 aims to combat HIV/AIDS, Malaria, NTDs

WHO: Global strategy for dengue prevention and control, 2012–2020

*MDG – Millennium Development Goal
GAP*: The Case for Influenza Vaccines

*GAP – Global Action Plan
Deadliest Pandemics in History

**MEASLES**
7th Century BC - 1653
200 million

**HIV / AIDS**
1981 - TODAY
25+ million

**PLAGUE of JUSTINIAN**
541 - 750
25 million

**SMALLPOX**
300+ million
10,000 BC - 1979

**BLACK DEATH**
1340 - 1771
75 million

**SPANISH FLU**
50-100 million
1918 - 1919

**TYPHUS**
4 million
430 BC - TODAY

**CHOLERA**
3 million
1817 - TODAY

**THIRD PANDEMIC**
12 million
1855

**HONG KONG FLU**
1 million
1968 - 1969

*Source: Centres for Disease Control and Prevention, WHO*
Focus on Influenza Outbreaks

**Key Takeaway:** Compared to other pandemics such as the Plague, Influenza still threatens the world.

Sources: “H5N1 Avian Influenza: Timeline of Major Events”, WHO, December 13, 2011
Nature Publishing Group
Global Alert and Response, WHO, April 17, 2013
Influenza Facts

- Avian Flu which resurfaced in China, April ‘13
- Most common Bird Flu
- Mortality rate of 60%
- No human-to-human transmission
- Swine Flu
- Similar strain as Spanish Influenza.
- Resurfaced in ‘09-’10
- “Common Flu” virus
- Caused Asian Flu Pandemic in 1957
- Still Circulates in birds

Sources: CDC, WHO
The H1N1 Pandemic: Race between the Virus and Vaccine

**Key Takeaway:** During the H1N1 pandemic, the vaccine was administered in week 40 after the outbreak occurred. Mortality approx. 18,500

Source: Excerpts from WHO Workshop on Influenza Business Sustainability
The Global Vaccine Scenario
There is a need...

Only 3.6% or 250 million of the global population would receive a full pandemic influenza vaccination.

WHO is actively seeking solutions to address the global shortage of vaccines.

Vaccine Security

Current procurement of influenza vaccines in most South East Asian countries does not meet the needs of the region’s population.

### Influenza Vaccine Sales per 100,000 population

<table>
<thead>
<tr>
<th></th>
<th>2008 trivalent seasonal vaccine</th>
<th>2009 trivalent seasonal vaccine</th>
<th>2010 trivalent seasonal vaccine</th>
<th>2009-2010 monovalent A (H1N1) pdm09 vaccine</th>
<th>2011 trivalent seasonal vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Public</td>
<td>Private</td>
<td>Public</td>
<td>Private</td>
<td>Public</td>
</tr>
<tr>
<td>Brunei</td>
<td>-</td>
<td>480</td>
<td>-</td>
<td>1465</td>
<td>-</td>
</tr>
<tr>
<td>Malaysia</td>
<td>-</td>
<td>367</td>
<td>-</td>
<td>832</td>
<td>-</td>
</tr>
<tr>
<td>Cambodia</td>
<td>0</td>
<td>318</td>
<td>0</td>
<td>832</td>
<td>0</td>
</tr>
<tr>
<td>Lao PDR</td>
<td>0</td>
<td>318</td>
<td>0</td>
<td>832</td>
<td>0</td>
</tr>
<tr>
<td>Myanmar</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Thailand</td>
<td>752</td>
<td>3183</td>
<td>3183</td>
<td>1869</td>
<td>3439</td>
</tr>
<tr>
<td>Vietnam</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thailand†</td>
<td>752</td>
<td>856</td>
<td>3183</td>
<td>1869</td>
<td>3439</td>
</tr>
<tr>
<td>Indonesia</td>
<td>-</td>
<td>128</td>
<td>-</td>
<td>149</td>
<td>-</td>
</tr>
<tr>
<td>Philippines</td>
<td>0</td>
<td>1115</td>
<td>0</td>
<td>2551</td>
<td>0</td>
</tr>
<tr>
<td>Singapore</td>
<td>0</td>
<td>7034</td>
<td>0</td>
<td>12078</td>
<td>0</td>
</tr>
</tbody>
</table>

†Private sales data in this row are from Thailand Food and Drug Administration.
*Excludes Brunei.
Dashed line (-) indicates data were not available.

Global Vaccine Manufacturing

Malaysia is being LEFT BEHIND.

ASEAN (DCVMN*)
• Indonesia
• Thailand
• Vietnam

GLOBAL (DCVMN)
• India
• China
• South Africa
• Brazil
• South Korea

MNC’s
• Global manufacturing facilities
• Manufacturing via collaborations

*DCVMN - Developing Countries Vaccine Manufacturers’ Network
The Malaysian Vaccine Scenario
Gaps

Vaccine Security
- Reliance on external sources, mainly MNC’s
- Shortage of vaccine supply during emergencies (epidemic/pandemic)

Vaccine Capacity
- Lack of self sufficiency for adult and pediatric immunizations
- Lack of regional cooperation to utilize capacity
Impact of Vaccine Security & Vaccine Capacity Issues

Limited Global Capacity for Influenza Vaccines + Unpredictable Influenza Pandemics = TROUBLE.
Vaccine Manufacturing

Comparisons and analysis
## Current & Potential Influenza Vaccine Technologies

<table>
<thead>
<tr>
<th>Old Technologies</th>
<th>Inactivated or Live Attenuated (LAIV)</th>
<th>Recombinant Protein/Peptide</th>
<th>Non-Replicating (ANS1) Influenza Virus</th>
<th>Virus-like Particle (VLP)</th>
<th>Viral Vector</th>
<th>DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Inactivated influenza virus that has been enriched for HA (split) or an influenza virus that has been attenuated so that it can replicate only in specific areas of the human body (LAIV).</td>
<td>Exogenously produced immunogenic influenza proteins or peptides, expressed and purified from a non-influenza source.</td>
<td>Influenza viruses that have been genetically modified by deletion of the genomic segment that encodes for the NS1 protein. This results in a replication deficiency in humans.</td>
<td>A non-infectious particle of highly similar three-dimensional structure to that of the influenza strain from which the genetic material was removed.</td>
<td>Attenuated non-influenza viruses that can carry and express proteins from influenza can be used to express antigenic influenza proteins.</td>
<td>Plasmid DNA that encodes for a mechanism that allows for the expression of antigenic influenza proteins in human cells.</td>
</tr>
<tr>
<td><strong>Manufacturing Platform</strong></td>
<td>Egg/Mammalian-cell culture</td>
<td>Bacterial-cell culture Yeast-cell culture Plant-cell culture Insect-cell culture</td>
<td>Mammalian-cell culture</td>
<td>Bacterial-cell culture Yeast-cell culture Plant-cell culture Mammalian-cell</td>
<td>Mammalian-cell culture</td>
<td>Bacteria-cell culture</td>
</tr>
</tbody>
</table>

**Key Takeaway:** Various Influenza Vaccine technologies under clinical development, newer tech appearing in the market

Source: Centre for Infectious Disease Research and Policy: Game – changing Influenza Vaccines, 2012
The Influenza Vaccine Technology Pathway

Key Takeaways:
* Significant time and funds required to develop an Influenza vaccine from concept to commercialization

* Potential solutions: In-license and do fill-finish activities. Also tie-ups to lock up vaccine supplies during the interim period

Source: Centre for Infectious Disease Research and Policy: Game – changing Influenza Vaccines, 2012
The Malaysian Vaccine Programme (MVP)
The Malaysian Vaccine Program

Objective

Main Reasons for Implementation

- Self Sufficiency
  - Lessen dependency on external sources
- Vaccine Security
  - Pandemics
  - Assurance of availability

Objective

- Assure of availability
- Lessen dependency on external sources
- Pandemics
The Malaysian Vaccine Program

Modes for PPP*

- **R & D**
  - Support for Developmental Activities

- **Commercial**
  - Off-take for Procurement
  - Support for meeting Regulatory Requirements

*PPP – Public Private Partnership
Potential choice of vaccines

- Existing procurement
  - Pentavalent
  - HPV
- Potential Procurement Policy
  - Pneumococcal
  - Meningococcal
  - Seasonal Influenza
National Stakeholder Mapping

SECRETARIAT

MINISTRY

MINISTRY OF HEALTH MALAYSIA

MOSTI

PENANDUNG

ENGAGEMENT UNITS

NKEA Healthcare Steering Committee

ASEAN Economic Cooperation Division
Regulatory - Facilities

- Certification of facilities
- Monitoring to ensure strict adherence to cGMP

- Certification and Monitoring
- Facilitate upgrades of existing laboratories
Regulatory – WHO Pre-Qualification (PQ) & Batch Testing

WHO PQ
- Required for vaccines to be purchased by UN agencies
- Need to meet PQ status requirements?

Batch Testing
- Set up of Batch Testing facilities
Regulatory – Clinical Trials

New Vaccines
- Long clinical trial process 3 – 6 years
- Facilitation in meeting regulatory requirements

Existing Vaccines
- Abbreviated clinical development for products to be manufactured in Malaysia in line with international standards
Financials

Possible Business Models

PPP

Technology Partners
MALAYSIAN - ASEAN VACCINE INITIATIVE (MAVI)
“POTENTIAL FOR A COLLABORATIVE APPROACH TOWARDS BUILDING VACCINE CAPACITY AND CAPABILITIES TO ADDRESS VACCINE SECURITY IN ASEAN”
CONCLUSION
**Current Status**

- Immunization Schedule not updated.
- Gaps: Regulatory, Manufacturing Capacity, Human Capital, Funding, Market Access

**Objectives**

- Vaccine Security
- Self Sufficiency
- Pandemic Preparedness

**Action Plans**

- New or amended policies to justify new vaccine procurement/production.
- Building of Regulatory Infrastructure for Vaccines
Thank You

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