3rd Regional Pneumococcal Symposium

13-14 February 2008
Istanbul, Turkey

Dr. Akira Homma
Bio-Manguinhos, Fiocruz
DCVMN
Developing Countries Vaccine Manufacturers Network
-DCVMN-

Formed in 2000, Bandung, Indonesia; formally organized July 2005

- To provide quality vaccines at affordable prices to the developing world
  - 19 members (Brazil, Cuba, China, Egypt, India, Indonesia, Iran, South Africa, Senegal, South Korea, Thailand);
  - 7 members WHO pre-qualified;
WHO Pre-qualified vaccines currently available from DCVMN

- BCG, DTwP, OPV, MMR, MR, Hep B, Yellow Fever, Rabies
- Made available through UNICEF, WHO and PAHO – also private export markets

DCVMN provides 2/3 of vaccines used in the world

- Most are expanding capacity and adding new technologies and products
- R&D efforts towards Hib, Rotavirus, Pneumococcal, Meningococcal, JE and others
**DCVMN Pneumococcal Vaccine Development Projects**

- **Biological Evans** - 7-10 valent conjugate - 2012/15;
- **BioMed CPS** - 11 valent conjugate - 2009/12;
- **Shantha Biotech** - conjugate and protein technology
- **BioVac Institute** - Regional approach;
- **Finlay Institute** - 8-13 valent - synthetic vaccine; Conjugation tech 4 years for clinical study;
- **China National Biotechnology Co.** - 23 valent PS
- **Serum Institute of India** - 14 valent conjugate
- **Bio-Manguinhos / Fiocruz** - conjugate & proteins - 2017
- **Butantan** - PS (3-Valent) - PspA (2-3-Valent) conjugate; Whole cell non-encapsulated inactivated/Harvard
Declines in invasive pneumococcal disease following vaccination, USA

Sentinel surveillance

Population-based surveillance

Kaplan, Pediatrics 2004

Whitney, New England J 2003
Vaccine-Type Invasive Disease in Children <5 Years
ABCs 1998-2005

CDC unpublished data and MMWR Sep 16, 2005
Hospitalization for invasive pneumococcal disease, ≥65 yr olds (Medicare data)

PCV7 in children

- 43.0%
- 40.7%
- 38.3%

Baseline

McBean, Vaccine 2005
Cobertura de Vacunas
Conjugadas para Neumococos

Mexico
62%
55%
69%

El Caribe
65%
79%
83%

Venezuela
70%
70%
81%

Colombia
70%
84%
87%

Brasil
63%
80%
82%

Chile
41%
66%
73%

Paraguay
60%
80%
84%

Argentina
53%
76%
81%

Uruguay
51%
76%
86%

América Latina
58,9%
71,0%
77,0%

Fuente:SIREVA-
BRAZIL/SIREVA: Distribution of S. pneumoniae isolates during 30 years in Brazilian states - 1977-2006

Nr of strains:
1977-1992: 1.622 (16 years)
1993-2006: 8.267 (14 years)
Total nr of strains: 9.889

SIREVA 1993
Brazil: S. pneumoniae - 2000-2006 (7 years), 5,842 strains

2000-2006
North: 1.2%
Northeast: 22%
Mid West: 6.2%
Southeast: 58.3%
South: 12.3%

< 5 years: 2,380 strains
Brazil: *Streptococcus pneumoniae* - 2000-2006, 5.842 strains

**Clinical Material**
- L. pleural: 11%
- Blood: 31%
- LCR: 57%
- Others: 1%

**Clinical Diagnostic**
- Meningitis: 62%
- Pneumonia: 28%
- Bacteremia: 2%
- Others: 2%
Vaccination against Pneumococcus

Background

• 1999: introduction of pneumococcal 23-valent vaccine for elderly people (annual campaign) and for special groups (institutionalized elderly and chronic diseases).

• 2002: introduction of conjugated pneumococcal 7-valent vaccine in the Special Reference Center for Immunobiologicals (CRIE).
## Pneumococcal Vaccine – PNI Demand

### 7-Valent, conjugated

<table>
<thead>
<tr>
<th>Year</th>
<th>Laboratory</th>
<th>Quantity</th>
<th>Price/Dose (USD)</th>
<th>Total (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td></td>
<td>20,000</td>
<td>46.68</td>
<td>933,660.00</td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td>3,500</td>
<td>53.30</td>
<td>193,559.61</td>
</tr>
<tr>
<td>2005</td>
<td>Wyeth</td>
<td>26,500</td>
<td>54.84</td>
<td>1,453,135.00</td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td>26,250</td>
<td>53.00</td>
<td>1,391,250.00</td>
</tr>
<tr>
<td>2007</td>
<td></td>
<td>40,000</td>
<td>NA</td>
<td>NA</td>
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</tbody>
</table>

### 23-Valent

<table>
<thead>
<tr>
<th>Year</th>
<th>Laboratory</th>
<th>Quantity</th>
<th>Price/Dose (USD)</th>
<th>Total (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>Sanofi Pasteur</td>
<td>700,000</td>
<td>7.33</td>
<td>5,131,430.00</td>
</tr>
<tr>
<td>2004</td>
<td>Sanofi Pasteur</td>
<td>300,000</td>
<td>8.18</td>
<td>2,455,056.53</td>
</tr>
<tr>
<td>2005</td>
<td>Sanofi Pasteur</td>
<td>170,000</td>
<td>8.67</td>
<td>1,474,574.32</td>
</tr>
<tr>
<td>2006</td>
<td>Merk</td>
<td>370,000</td>
<td>7.98</td>
<td>2,952,600.00</td>
</tr>
<tr>
<td>2007</td>
<td>NA</td>
<td>370,000</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
## Potential Global Vaccine Market

<table>
<thead>
<tr>
<th>Dosing Regimen</th>
<th>High Income Markets</th>
<th>Middle Income Markets</th>
<th>Low Income Markets</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>3 (?)</td>
<td>3 (?)</td>
<td>--</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Market (Mi doses)</th>
<th>High Income Markets</th>
<th>Middle Income Markets</th>
<th>Low Income Markets</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>130 (?)</td>
<td>135 (?)</td>
<td>305 (?)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Price/Dose (average est.)</th>
<th>High Income Markets</th>
<th>Middle Income Markets</th>
<th>Low Income Markets</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>$60</td>
<td>$20 (?)</td>
<td>$2 (?)</td>
<td>--</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Market ($B)</th>
<th>High Income Markets</th>
<th>Middle Income Markets</th>
<th>Low Income Markets</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>$2.4</td>
<td>$2.6 (?)</td>
<td>$0.3 (?)</td>
<td>$5.3 (?)</td>
<td></td>
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</table>

Production capacity: 100 Mi doses - Deficit of 200 Mi doses
DCVMN producers can come into market: 5-10 years

AMC, 2006

(?) questionable
A Role for DCVMN in the production of Pneumococcal conjugated vaccines for middle income countries

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>High Income</th>
<th>Middle Income</th>
<th>Low Income</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price/Dose (average est.)</td>
<td>$60</td>
<td>$20</td>
<td>$2</td>
<td>--</td>
</tr>
<tr>
<td>Vaccine Market (Mi doses)</td>
<td>40</td>
<td>130</td>
<td>135</td>
<td>305</td>
</tr>
<tr>
<td>Population (Mi)</td>
<td>10</td>
<td>43</td>
<td>45</td>
<td>98</td>
</tr>
</tbody>
</table>
CHALLENGE FOR MIDDLE INCOME COUNTRIES:
ACCELERATE THE INCORPORATION OF PNEUMOCOCCAL VACCINE

- Most of governments are convinced of the importance
  - data of impact of disease
  - epidemiological surveillance - serotype prevalence studies
  - cost-benefit studies
  - SAGE/WHO recommended
  - Sabin Institute
  - pneumoADIP

- Push mechanisms - New approach for vaccine development by big pharma; DCVMN laboratories; support from PATH, Bill & Melinda GATES, governments R&D investments - ??? years;

- Today’s situation - High demand and few offer of the conjugated vaccine = high price = big obstacle for introduction in middle income countries
CHALLENGES for new production plant in DCVMN countries

- Requires several serotypes for production;
- Complex PS/protein conjugation technology
  - CRM197; TT; DT; Hib D protein;
- Combination of > 10 different vaccines
- Requires very high investment (AMC)
  - New plant of production - US$ 180 million
  - Start-up - US$ 50 million
  - Period for production - 5 years with Tech Transfer

- More complex Regulatory requirements
- High cost and time consuming clinical studies
- WHO pre-qualification
ACCELERATE THE INCORPORATION OF PNEUMOCOCCAL VACCINE PRODUCTION TECHNOLOGY IN DCVMN COUNTRIES

- More producers must be involved faster in the production - increase availability and make its price affordable for middle income countries
  - Joint development work between/among DCVMN's members - there are members with high technology capabilities - must get together;
  - Strengthen the Public-Private partnership for new technological development;
  - Transfer of Technology - create a win-win situation - requires a deep commitment from parties involved.
Thank you!

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