Sustainable Supply of Quality Vaccines by DCVMN-A Public Health Driven Alliance

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Overview of Presentation

- Global Vaccine Markets and Supply
- Vaccine development in 21st Century
  - Major trends
  - Future targets
- Affordability of Vaccines and DCVMN
- DCVMN and Access to Newer Vaccines
- Viewpoints
- Summary
Vaccines: Developed World Markets

- World vaccines market expected to be worth US$40 Billion by 2015. - Pediatric proprietary vaccine market is the biggest vaccine sector with more than US$6 Billion market in 2009

- US is expected to lead the vaccine market till 2015

- Four companies (GSK, Sanofi-Aventis, Wyeth and Merck) together control 71% of the vaccines market worldwide.

- Faster growing vaccines:
  - Malaria vaccine (US$ 400 million by 2025) and Cervical cancer vaccine (US $ 4 billion mark) by 2012.
  - Prevnar a Pfizer a product is expected to become the first vaccine to cross US$5 Billion mark by 2015
  - Influenza vaccine market globally is forecasted at 7 Billion US $ by Year 2015.

www.researchandmarkets.org
Developing Countries Markets

Markets*
- Emerging markets growing at 16-17 %.
- China expected to become # 2 market after North America by 2020.

Growth drivers
- Large population, Unmet vaccination needs and low vaccination rates
- Increasing governments focus on prevention/childhood rates
- Fast growing private markets for vaccines
- Innovative international initiatives to meet demand

Future growth Expectations
- Combination vaccines, -Influenza, -Traveller vaccines, Neglected Tropical diseases.

Global Vaccination: Supply scenario

- India, Brazil, China, Indonesia have production capacities to meet their country demands.
- Big Pharma: Assured Market in developed world at high prices.
- Market in developing world through UN agencies (UNICEF, GAVI, PAHO).
- Countries such as Egypt, Mexico, Turkey, Algeria procure vaccine directly from private markets.
- UN agencies: rest of world supplies which constitutes 40% of volume of global vaccine supplies.

Vaccine requirements: Distribution of 128 million children (WHO estimates)
Vaccine Supply

Vaccine manufacturers are classified into: DCVMN and IFPMA.

IFPMA
- Comprise 25 leading international companies. Majority of revenue stake owned by Big 5 Pharma
- Represents research-based pharmaceutical and biotech companies.
- Ability to develop newer products, technologies and introduce them
- Generates 80-85% of total revenue in global vaccine market.
- Contributes 12-15% in volumes to global vaccine requirement.
- Supplies vaccine to developing world through tiered pricing.

DCVMN
- Formed in Year 2000
- Comprise 34 companies over 14 countries in developing world
- WHO prequalified production facilities. High volume low cost business model
- Caters to 86% of total requirement of UN agencies.
- Every second child born on this globe receive DCVMN vaccine.
- Shares only 10-15% of total revenues globally.
- Largely kept prices of traditional vaccines affordable inspite of declining interest of Big Pharma in EPI vaccines.
- Leading example of access, equity and public responsibility
Vaccine Supplies to UNICEF

UNICEF SD
Emerging vs. Industrialized manufacturers
Emerging Market Country Manufacturers make up approximately 50% of procurement volumes in 2010 and 30% by value, predominantly due to lower but increasing participation in new vaccine markets and differing cost bases.

By Volume

By Value

- Developing Country
- Industrialised Country
Where UNICEF Supplies are used.

<table>
<thead>
<tr>
<th>Region</th>
<th>2002</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub Saharan Africa</td>
<td>42</td>
<td>55</td>
</tr>
<tr>
<td>Asia</td>
<td>39</td>
<td>29</td>
</tr>
<tr>
<td>Middle East &amp; North Africa</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Central &amp; South America and the Caribbean</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Central and Eastern Europe</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

UNICEF Forecasting. Presentation at 2012 AGM of DCVMN.
Major Trends (2000-2012)

Growth of the PAHO Revolving Fund

Top ten suppliers of PAHO RF 2003-2008

In 2008, no one manufacturer accounted for more than 25% of PAHO purchases
Global Concerted Responses in 21st Century

DCVM
- Effective vaccines have been introduced in both industrialized and developing countries against infections caused by the hepatitis B virus and *Haemophilus influenzae* type b.
- Vaccine against *Neisseria meningitides* meningitis for sub-saharan African children at a innovative price of less than 50 cents/dose
- Global response to Pandemic Influenza with developing countries manufacturers showing capacity to ready the vaccine for global use.

Big Pharma
- Pneumococcal Vaccine was introduced in 31 countries by end of 2008, up from 20 countries in Year 2007.
- Rotavirus vaccine was introduced in 19 countries by end of Year 2008.
- HPV vaccine was introduced in 22 countries in 2008, as against 10 countries in Year 2007.

Data as on 1 July 2009, WHO estimates. Percentages reported in 193 member countries of WHO. http://www.who.int/immunization/newsroom/GID_english.pdf
State of the World’s Vaccines and Immunization Achievements in 21st Century

- First decade of the 21st century has been the most productive in the history of vaccine development.
  - New life-saving vaccines have been developed for meningococcal meningitis, rotavirus diarrheal disease, avian influenza caused by the H5N1 virus, pneumococcal disease, and cervical cancer caused by human papillomavirus (HPV).

- Increased immunization coverage along with clean water and better sanitization resulted in number of children dying each year below 10 million.

- Vaccines against tuberculosis, diphtheria, tetanus, pertussis, polio, measles, hepatitis B, and Hib disease are preventing 2.5 million deaths each year.

Fact Sheet, UNICEF, 2011
Efforts of the GAVI dramatically increased the introduction of new and underused vaccines that have reached more than 200 million children in developing countries.

For measles alone, since 2000, expanded use of vaccines prompted measles-related deaths to drop from an estimated 750,000 to 120,000 a year.

Surge in vaccine manufacturing capacity in the developing world.

- 14 percent of the vaccines required to meet global vaccine demand are provided by suppliers in industrialized countries.
- Remaining 86% is met by suppliers based in emerging market economies, which are low-cost vaccines, primarily for use in their own or in other low- and middle-income countries—a market that represents 84 percent of the world's population.

Fact Sheet, UNICEF, 2011
Vaccine development in 21st Century Targets

- By the 2020s, eradication of polio and measles from the globe.
- Increase vaccine coverage to plus 90 percent by 2015 to prevent additional two million deaths among children under five years old.
- Considerable number of candidate vaccines in the late stages of research and development and 40% of these candidates aim to protect against diseases for which no vaccines are currently available.
Examples of Re-Emerging Infectious Diseases

- **Cholera**
  - 100% increase worldwide in 1998 (new strain eltor, 0139)

- **Dengue/ DHF**
  - Over past 40 years, 20-fold increase to nearly 0.5 million (between 1990-98)

- **Pertussis**
  - Outbreaks of pertussis (whooping cough) have been reported in Michigan, Ohio, and California (e.g., 9143 cases and 10 infant deaths during 2010 in California). In the United States there were 16,858 cases and 12 infant deaths in 2009 despite high rates of childhood immunization against pertussis as part of the recommended diphtheria, tetanus, and pertussis vaccination series.
  - Year 2012, pandemic was declared in US wherein more than 3500 cases were observed.

SARS: The First Emerging Infectious Disease Of The 21st Century

Lesson learnt from SARS, H5N1 and H1N1

- An infectious disease in one country is a threat to all.
- Tremendous negative economic impact on trade, travel and tourism.
- High level commitment is crucial for rapid containment
- Global partnerships & rapid sharing of data/information enhances preparedness and response.
Vaccine Pricing and Affordability

- Year 1974: EPI program was launched.
- Year 1999: Total cost of full course of EPI vaccine averaged USD 1.37.
- Year 2000: Adding two priority vaccines—Hepatitis B and Hib to EPI vaccines increased the cost to USD10.
- In Past 5 Years: WHO is recommending high unit cost products such as pneumococcal conjugate vaccine and rotavirus vaccine for global use in infants and HPV vaccines for adolescents.
- Year 2011: The expansion of EPI Program have raised the price of purchasing the full course of vaccine in GAVI country to 38.80 USD. (Price does not include programmatic or cost associated with vaccine wastage).
- Price of vaccine became a significant issue for immunization stakeholders in Year 2011, when GAVI faced a US $ 3.7 billion financial shortfall for its 2011-2015 programme implementation.
Pricing and DCVMN

2011 Price Per dose of DTP-Hep-B-Hib (Pentavalent)

<table>
<thead>
<tr>
<th></th>
<th>Crucell</th>
<th>GSK</th>
<th>Serum Institute of India (DCVMN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>Single dose</td>
<td>Two dose lyophilized</td>
<td>Single dose liquid</td>
</tr>
<tr>
<td>Country of manufacture</td>
<td>Republic of Korea</td>
<td>Belgium</td>
<td>India</td>
</tr>
<tr>
<td>2011 price per dose</td>
<td>$2.80-3.20</td>
<td>$2.95</td>
<td>$2.25-2.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Two dose lyo</td>
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<td></td>
<td></td>
<td></td>
<td>$2.25</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Ten dose liquid</td>
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<td></td>
<td></td>
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<td>$1.75-2.1</td>
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DCVMN supplied Pentavalent vaccines, mainstay of GAVI Purchase at prices almost 40% less than Crucell, a European company.

GAVI’s support for pentavalent vaccine has averted 474,000 future deaths.

source: WHO Department of Immunisation, Vaccines and Biologicals’ estimates and projections, November 2010

The Right Shot: Extending the reach of Affordable and Adaptable Vaccines. www.Msfaccess.org; April 2012
DCVMN and Vaccine Development

- In developing world, vaccine prices are substantially lower. UNICEF data demonstrates that vaccine prices are dependent on where a product is produced.

- Developed Country manufacturers spend USD 200 to 400 million USD per vaccine on production facilities, while emerging company manufacturers such as in India, typically spend less than USD 100 million.

The Right Shot: Extending the reach of Affordable and Adaptable Vaccines. www.Msfaccess.org; April 2012
Increasing Access to Vaccines: 
Role of technology transfers in developing production capacities

- Technology transfer and local production proved to be sustainable strategies to address issues of access.
- Access to newer vaccines, such as Haemophilus influenzae B (Hib), rotavirus, pneumonia and human papilloma virus (HPV), between developed and developing countries improved.
- There is a changing dynamic in vaccine technology transfer, with joint ventures, acquisitions and establishment by multinational manufacturers of subsidiaries in developing countries becoming more frequent.
- In most cases, tech transfers to DCVMN has also resulted in lower prices of vaccines.

Increasing access to vaccines, WHO Report on tech transfers 2011
## DCVMN and Access to New Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Potential manufacturer</th>
<th>Country</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **Pneumococcal Conjugate**      | BioManguinhos/GSK, Chengdu Institute/PATr, SII, India/PATr | Brazil, China, India | 10 valent  
Three year project initated in 09 |
| **Rotavirus**                   | Bharat Biotech, Biological E, Serum Institute of India, Instituto Butantan, Chengdu and Wuhan Institutes | India, India, Brazil, China | Phase-3 clinical trials |
| **Meningococcal A Conjugate**   | Serum Institute of India /MVP Project                      | India     | WHO prequalified in 2010.                     |
| **Rabies**                      | Zydus cadilla, Serum Institute, Vabiotech                  | India, India, Vietnam | Prequalified  
Licensed, Not prequalified  
Licensed, not prequalified |
| **JE**                          | Chengdu Institute/PATr, Biological Evans/Intercell, Vabiotech | China, India, Vietnam | -LAIV, licensed in 7 countries (Not prequalified)  
-IC-51, Inactivated vaccine  
-Japanese technology, 3Md/year |
| **Seasonal and Pandemic Influenza** | Vabiotech, GPO, Institute Butantan, Serum Institute of India/Panacea, Bharat Biotech/Zydus cadilla, Biofarma | Vietnam, Thailand, Brazil, India, Indonesia | -Phase III  
- Vaccine Licensed and in market |

Vaccine 2010, 28, 2115-21.
DCVMN and Newer Vaccines
Affordability

Meningococal Conjugate Vaccines

- Tetravalent (A, C, W-135 and Y) vaccines have been developed in Year 2005 and Year 2010. The US CDC price was $82.12 USD per dose.

- A Meningitis conjugate A product (supplied by DCVMN) was WHO pre-qualified in Year 2010 and was priced at 0.50 USD per dose. This product is rolled out in Meningitis Belt countries.

Pneumococcal Conjugate Vaccines

- Year 2000: PCV 7 - CDC Purchase price was $44.25/dose.
- Year 2009: PCV 13 CDC Purchase price was at $71.04/dose.
- Following deliberation in Year 2007, access to PCV 7 and 13 was supported by AMC with initial target price of $2.00 per dose. Finally the price was locked in with tail price of $3.50 per dose.
- No competition from low cost producers as on date. However, some DCVMN members are expected to enter this segment of vaccines by Year 2016.
DCVMN and Rotavirus Vaccines

- Year 2006: $ 15.00 for full course; PAHO supplies
- Year 2011: Big pharma manufacturers reduced the price in range of 5.00 to 10.00 USD per course following sales of 30 million doses.
- Two DCVMN members are expected to have vaccine by Year 2015. One of the members has announced its plan to launch this vaccine at $ 1.00 per dose.

The Right Shot: Extending the reach of Affordable and Adaptable Vaccines. www.Msfaccess.org; April 2012
How DCVMN look forward to Sustaining Vaccine Supply

- Access and partner in Innovative financing schemes.
- Right balance of low price and reasonable returns.
- Equitable access to newer vaccines
Viewpoints-DC Manufacturers

Take Home message

- Global markets signal good opportunities and growth in future
  - DC Manufacturers have shown potential to develop relatively newer vaccines such as influenza, Meningococal Conjugate vaccines, pneumococcal vaccines.
  - DC Manufacturers will continue to play an important role in keeping such vaccines affordable

- Newer vaccine technologies appears promising. Many promising vaccine candidates in advanced stages of vaccine development.
  - Access and affordability of these vaccines?
  - DC manufacturers can play an important role in increasing access, coverage and affordability.
Viewpoints-DC Manufacturers

Take Home message

- Coverage of relatively newer vaccines remain to be low in developing countries.
  - Production capacities and cost effectiveness will remain unique selling points of DC manufacturers in future.

- Global Health Partnerships models showed success.
  - Challenges still remain to address critical issues of better incentives, opportunities for low cost innovative DC manufacturers.
21\textsuperscript{st} Century first decade observed the launch of vaccines targeting Pneumococcal, influenza, rotavirus, meningococcal and HPV vaccines.

Vaccine development in 21\textsuperscript{st} Century will see the launch of vaccine against HIV, malaria, tuberculosis.

Wide coverage of such vaccines needs global production.

DC manufacturers production capacities and high volume low cost business models will be important for ensuring access at affordable prices.

Support from EU is encouraging in terms of funding and excellent expertise of public and private institutes.

EU institutes such as NIBSC, ECAAC, University of Lausanne will be important in facilitating tech transfers to DC manufacturers.
We have to choose between a global market driven only by calculations of short-term profit, or one which has a human face.
— Kofi Annan

We at DCVMN believe in the second option.