Evolution of Medical Innovation to Improve Access to Vaccines in Developing Countries

Dr. Seth Berkley, CEO GAVI Alliance

WHO-WIPO-WTO Symposium

Geneva, 5 July 2013
PATENT ON AIDS DRUGS

Before Profit

The US Against the Indian Government

order by: DNP

DNP urge Nova to drop the case

against the Indian Government

Reuters
Key differences between vaccines and drugs

Preventive Biologics Biosimilars
- Process patents
- High capital costs
- Long and complex manufacturing
- Very large clinical trials
- Limited secondary market

Therapeutic Small molecules Generics
- Product patents
- Lower capital costs
- Manufacturing relatively simple
- Smaller clinical trials
- Often significant secondary market
Vaccine development timeline: 1798-1910

With Thanks to Stan Plotkin
Vaccine development timeline: 1910-

With Thanks to Stan Plotkin
Closing the gap between countries

First introduction: 12-year delay

Introduction in 50% of countries: 6-year delay

Percentage of countries introducing HepB vaccine (%)

Year

high-income countries

low-income countries

Launch of GAVI
Innovation needed to address challenges across the value chain

R&D
- Basic research
- Translational research
- Clinical development

Supply
- Manufacturing
- Pricing
- Product quality

Delivery
- Supply chain
- Data
- Health systems
IAVI’s Early positioning in AIDS vaccine R&D

A well-established continuum of players moves new drugs to market

- **Basic research**
- **Applied research**
- **Preclinical development**
- **Clinical development**
- **Advanced development**
- **Large-scale Efficacy trials**

Public sector, academia → Biotech companies → Pharmaceutical companies

IAVI initially worked to ensure a vaccine for the developing world by focusing on product development

- **Basic research**
- **Applied research**
- **Preclinical development**
- **Clinical development**
- **Advanced development**
- **Large-scale Efficacy trials**

Public sector, academia → Biotech companies, pharmaceutical companies

Advocacy
Clinical trial network in developing world
Gap-filling science
IAVI created to address gaps in vaccine R&D

As product failures forced big players out or moved them downstream, a development gap grew …

… and IAVI moved to fill the void, creating new programs as needs arose

- Human Immunology Lab (2001)
- Vectors Consortium (2007)
- AIDS Vaccine Design and Development Lab (2008)
- IAVI Neutralizing Antibody Center at The Scripps Research Institute (2009)
Product development partnership (PDP) model critical to fill gaps

IAVI is an integrated organization that links its …

- Industry-style labs and diverse research portfolio
- Academic, government and private-sector partnerships
- Network of clinical trial centers in Africa and India
- Advocacy and outreach from community to international level
## Need cohorts with **sufficient incidence**

<table>
<thead>
<tr>
<th>RESEARCH CENTER</th>
<th>STUDY POPULATION</th>
<th>PERSON YEARS OF OBSERVATION</th>
<th>CASES PER 100 PERSON YEARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lusaka</td>
<td>Discordant couples</td>
<td>3,468</td>
<td>6.3 (5.5, 7.2)</td>
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<tr>
<td>Zambia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copperbelt</td>
<td>Discordant couples</td>
<td>1,448</td>
<td>7.1 (5.7, 8.5)</td>
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<tr>
<td>Zambia</td>
<td></td>
<td></td>
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<tr>
<td>Kigali</td>
<td>Discordant couples</td>
<td>1,682</td>
<td>2.8 (2.3, 3.3)</td>
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<tr>
<td>Rwanda</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entebbe &amp; Masaka</td>
<td>Discordant couples</td>
<td>1,897</td>
<td>3.4 (2.7, 4.4)</td>
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<tr>
<td>Uganda</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entebbe &amp; Masaka</td>
<td>Fishing community</td>
<td>738</td>
<td>5.6 (3.9, 7.3)</td>
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<tr>
<td>Uganda</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kilifi &amp; Mtwapa</td>
<td>Female sex workers</td>
<td>357</td>
<td>2.8 (1.8, 5.3)</td>
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<tr>
<td>Kenya</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kilifi &amp; Mtwapa</td>
<td>Men who have sex with men</td>
<td>573</td>
<td>8.9 (6.8, 11.7)</td>
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<tr>
<td>Kenya</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rustenburg</td>
<td>Other risk</td>
<td>169</td>
<td>5.3 (1.9, 8.8)</td>
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<tr>
<td><strong>South Africa</strong></td>
<td></td>
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</tbody>
</table>

Source: IAVI
With new antibodies, **new targets**

Conserved determinants in the V1/V2 and V3 loops  
*PG9, PG16*

**CD4 binding site**  
*b12, VRC01, VRC03, HJ16, PGV04*

Mabs from new donors 17, 36 & 39

Glycan shield  
*2G12*

MPER  
*2F5, 4E10, Z13e1*

Better tools to meet key challenges

e.g. Neutralizing Antibody Consortium

Accelerating the search ...

Broadly neutralizing antibodies

Determining structure of novel antigens

High-throughput immunogen design

Assays to rapidly screen immunogens

Characterize sera and identify broadly neutralizing monoclonal antibodies

Structural biology

Immunogen design

Immunogen screening

Clinical development

Protocol G

High-throughput robot

Indian Medicinal Chemistry Program; Innovation Fund

... with new high-throughput approaches
Acceleration in number of PDPs

Selected other public-private partnerships Working on health issues
Egg-based

Relative Efficiency
Number of doses obtained per liter in manufacturing

Relative Cost
Relative manufacturing costs, not including facility

Speed
Time needed to manufacture 300 million doses in existing facilities

One year

Cell culture

Two years

Baculovirus

One year

E. coli

One month
Evolution of number of annual patent filings for human vaccines against influenza virus, 1941-2011

Patents – barriers to access?

In some cases...

- First to identify Hepatitis C (HCV)
- Over 100 patents in more than 20 countries
- High upfront royalty fees impeded R&D

...but not always

- Gardasil (first HPV vaccine) based on research at University of Queensland (UQ)
- CSL and UQ waived royalty fees for sales in GAVI countries
Patents thickets a growing challenge for many new vaccines

Originators
- GlaxoSmithKline
- MERCK
- Pfizer
- sanofi pasteur

Developing country manufacturers
- Serum Institute of India Ltd.
- Panacea Biotec
- Bharat Biotech
- biofarma
- Biological E. Limited

Vaccines:
- Pneumococcal
- Rotavirus
- HPV
Different R&D models – “Push”

103 million people immunised

**Impact:**

*Number of men A cases:*

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2012</th>
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<tbody>
<tr>
<td>Niger</td>
<td>842</td>
<td>0</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>156</td>
<td>0</td>
</tr>
<tr>
<td>Mali</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>
AMC funding sources

AMC Price per dose (US$)

- AMC funds
- GAVI
- Country Co-pay (from US$ 0.20 per dose, initially)*

First eligible vaccine available

Supplier’s share of AMC funds depleted

Supply commitment fulfilled

Year 0 Year 2 Year 4 Year 6 Year 8 Year 10

* Co-financing levels will be in line with the applicable GAVI co-financing policy
Factors Affecting Vaccine Availability
How the co-financing policy works

Source: GAVI Alliance 2012
Ramsey pricing

Source: GAVI Alliance, 2012
Source: GAVI Alliance, 2012

2012 global birth cohort:
135 million

GAVI countries birth cohort:
80 million

GAVI countries birth cohort
Non-GAVI countries birth cohort
Changing the mindset of the vaccine manufacturing industry
Changing the mindset of the vaccine manufacturing industry
Achievements: Encouraging tiered pricing

![Graph showing vaccine price per dose (US$) for various vaccines.]

- **UNICEF/GAVI market (weighted average)**: 2.17, 3.50, 1.88, 4.55
- **US public market**: 34.93, 102.03, 61.11, 97.34

**Vaccine Types**:
- (DTP-hepB-Hib)
- Pneumococcal conjugate
- Rotavirus
- HPV

**Notes**:
1. The UNICEF/GAVI price is the 2012 weighted average across multiple suppliers and presentations of pentavalent vaccine; the US public market price is lowest total 2012 price per dose for DTP, hep B and Hib vaccinations (via separate DTP, hep B and Hib vaccines). The UNICEF/GAVI pentavalent vaccine includes whole-cell pertussis vaccine, while the US public market DTP includes acellular pertussis vaccine.

2. The US public market price is the 2012 price for 13-valent vaccine; the UNICEF/GAVI price is the tail price under the AMC.

3. The UNICEF/GAVI price is 2012 weighted average assuming 3-dose equivalence; the US public market price is the average 2012 price assuming 3-dose equivalence.

4. The UNICEF/GAVI price is the average price of bivalent and quadrivalent vaccines negotiated in 2013; the US public market price is the 2012 average.

Source: UNICEF Supply Division; CDC
Evolving the manufacturing base

2001 – Vaccine supply:
5 suppliers from 5 countries

Source: UNICEF Supply Division, 2013
Evolving the manufacturing base

2012 – Vaccine supply: 10 suppliers from 8 countries

Source: UNICEF Supply Division, 2013

- Russian Federation: 1
- Belgium: 1
- France: 1
- United States: 2
- Brazil: 1
- India: 2
- Republic of Korea: 1
- Indonesia: 1

2012
# GAVI’s vaccine portfolio

## Manufacturers with pre-qualified vaccines in 2013

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Pentavalent (DTP-HepB-Hib)</td>
<td>5</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>2</td>
</tr>
<tr>
<td>Pneumococcal conjugate</td>
<td>2</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>4</td>
</tr>
<tr>
<td>Meningococcal A</td>
<td>1</td>
</tr>
<tr>
<td>Measles-Rubella</td>
<td>1</td>
</tr>
<tr>
<td>HPV</td>
<td></td>
</tr>
</tbody>
</table>
Achievements: Optimizing products

**Penta**: 10 dose vial
Cold Chain volume per dose (cm³): 2.6
Vaccine Vial Monitor: Type 14

**Rota**: 1 dose tube
Cold Chain volume per dose (cm³): 46
Vaccine Vial Monitor: NONE
Packaging Reductions for GAVI Countries

Rotarix 1 dose plastic tube: 85% reduction in packaging size

Rotateq 1 dose plastic tube: proposed 29% reduction in primary container
370 additional million children immunised since 2000
More than 5.5 million future deaths averted since 2000
2013 Measles rubella
2013 HPV
2011 Meningitis A
2009 Pneumococcal
2008 Rotavirus
2007 Measles
2006 Pentavalent
2002 Hib
2001 Yellow fever
2001 Hepatitis B
Accelerating vaccine programmes

- HPV
- measles-rubella
- measles SIAs
- pentavalent
- yellow fever
- pneumococcal
- rotavirus
- men A
- measles 2nd dose

- 33 routine
- 14 campaigns
- 7 demonstration
- 131 routine
- 21 campaigns

- ~600 m
- ~1 bn

In 2000-2012:
- 3 programmes
- 6 introductions
- doses distributed

In 2013:
- 54 introductions

Source: GAVI Alliance
Pentavalent vaccine introduced in every GAVI country by 2014

Source: GAVI Alliance, 2013
Impact of pentavalent vaccine on the ground

Eliminating Hib meningitis in Kenya (Kilifi district)

Source: Anthony Scott, Wellcome Trust Senior Research Fellow in Clinical Science
KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya
The GAVI Alliance: 21st century model of development
Over 22 million children not fully immunised despite progress on supply and pricing

GAVI-eligible: 17.5 million

India: 7.2 million
Nigeria: 3.1 million
Ethiopia: 1.2 million
Pakistan: 0.9 million
DR Congo: 0.8 million
Afghanistan: 0.4 million
Chad: 0.3 million
Uganda: 0.3 million
Côte d’Ivoire: 0.2 million
Cameroon: 0.2 million
Rest of GAVI-eligible: 2.9 million

Non GAVI-eligible: 5 million

Indicator: DTP3 2011
WHO/UNICEF estimates
Children from poor families less likely to be fully immunised

Patterns of DTP 3 vaccination coverage across wealth quintiles since 2005

Source: DHS and MICS data (since 2005)
Courtesy: Save the Children UK, 2012
Improving data

![Graph showing DTP3 coverage from 1999 to 2012 with data points at 37%, 51%, 66%, and 87% and corresponding years and sources.]
Alliance supply chain strategy: initial examples

- Tracking and tracing vaccines through bar codes
- Streamline and improve transparency of short-term forecasting
- New cold chain technology to market
- Private sector expertise
Rapid ramp-up in number of fully immunised children from low base

GAVI 73 countries

Vaccine coverage percentage (%) vs Year

- BCG
- Polio
- Pentavalent
- Rubella
- MCV
- Rotavirus
- Pneumococcal

Fully immunised child (GAVI 73) 47%
Rapid ramp-up in number of fully immunised children from low base
Thank you