Economics of Vaccine Development

A Vaccine Manufacturer’s Perspective

Gerald Voss
The Value of Vaccines
29 diseases are currently preventable by vaccination

‘Vaccines are one of the greatest achievements of biomedical science and public health’

Global public health

Cervical cancer
Diphtheria
*Haemophilus influenzae* type b
Hepatitis A
Hepatitis B
Herpes zoster
Human papillomavirus
Influenza
Measles
Meningococcal
Mumps
H1N1 flu
Pertussis
Poliomyelitis
Pneumococcal
Rotavirus
Rubella
Smallpox and vaccinia
Tetanus
Tuberculosis
Varicella

Regional focus

Anthrax
Cholera
Japanese encephalitis
Monkeypox
Tick-borne encephalitis
Typhoid fever
Rabies
Yellow fever

Making the case for vaccines

• Vaccines are important tools to combat infectious diseases globally and have proved to reduce mortality and morbidity caused by several pathogens
In 1988, polio was endemic in 125 countries.
In 2013, polio remains endemic in 3 countries

WHO. Global Polio eradication initiative. Available at: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek/Poliocasesworldwide.aspx (accessed August 2013);
Making the case for vaccines

• Vaccines are important tools to combat infectious diseases globally and have proved to reduce mortality and morbidity caused by several pathogens

• We manufacture vaccines and provide access for all to existing and new vaccines that are:
  – Immunogenic/efficacious and effective
  – Of high quality with an acceptable safety profile
  – Affordable
Vaccination on a global scale

- Vaccines account for 2-3% of the global pharmaceutical market. Market size has increased from 5 bn in 2000 to 24 bn US $ in 2013

- Every year up to 3 million deaths are prevented and 750,000 children are saved from disabilities through vaccination

- GSK’s contribution
  - For **over 50 years** we have supplied polio vaccines for elimination and eradication efforts worldwide
  - In 2010, we delivered **1.4 billion vaccines doses to 179 countries worldwide**
  - Up to **70% of our volumes are distributed in low and middle income countries**
  - GSK has a **tiered pricing policy** to enable pricing to be aligned to a country’s ability to pay

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4 GSK Corporate Brochure 2011
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• Vaccines are highly cost-effective
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• Important savings are generated with polio and measles vaccination
  – For every dollar spent in those vaccines 6 USD and 13.5 USD of direct and indirect cost are saved\(^1\)
  – Savings from the Global Polio Eradication Initiative is expected to reach 40-50 billion USD over 1988-2035 period\(^2\)

• Average Cost per Death Averted and Cost per DALY for the Traditional Immunization Program by Region\(^3\)

<table>
<thead>
<tr>
<th>In 2001 US$</th>
<th>East Asia and the Pacific</th>
<th>Europe and Central Asia</th>
<th>Latin America and the Caribbean</th>
<th>Middle East and North Africa</th>
<th>South Asia</th>
<th>Sub-Saharan Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated cost/death averted</td>
<td>434</td>
<td>3,540</td>
<td>1,030</td>
<td>993</td>
<td>205</td>
</tr>
<tr>
<td></td>
<td>Estimated cost/DALY</td>
<td>85</td>
<td>395</td>
<td>438</td>
<td>166</td>
<td>16</td>
</tr>
</tbody>
</table>

\(^1\) CDC MMWR 1999/48(12); 243-248
\(^2\) Tebbens, Vaccine, 2011
\(^3\) Jamison, World Bank, 2006
Economic rationale for new vaccine development
Economic rationale for vaccine development

• Development risk (and upfront investment)
  – Scientific concept
  – Technical approach
  – Clinical development
  – Regulatory landscape

• Potential return
  – Medical need
  – Product properties (including cost of goods)
  – Financial return on investment
Overall value proposition

• Individual health
  – Reduction in morbidity and mortality

• Public health improvement
  – Control, elimination and eradication
  – Herd immunity

• Economic benefit
  – Direct (healthcare cost)
  – Indirect (economic development)

• Societal benefit
  – Equity
  – Human capital

• Developer/manufacturer business model
  – Financial return on Investment
Building a target product profile

- Unmet medical need
  - Global or regional
  - Epidemiology

- Target population
  - Age (infants, adults, elderly)
  - Special populations (immuno-compromized, travellers, maternal immunization)

- Administration
  - Route
  - Schedule (and co-administration)
  - Boosters

- Vaccine composition and presentation
  - Live-attenuated, whole-killed, recombinant, vector

- Implementation
  - Anticipated standard of care
  - Future recommendations
Vaccine development challenges
Vaccine development is a complex multistep process requiring significant time and financial investment.

Up to 1 bn $
Scientific challenges and innovation

- Pathogens or diseases: malaria, HIV, TB, CMV etc.
- Populations: infants, elderly, immuno-compromised etc.

- New Antigens
- New antigen presentation (DNA)
- New Delivery strategies (live vectors)
- New Adjuvants

CMV = Cytomegalovirus; HIV = Human Immunodeficiency Virus; TB = Tuberculosis

Vaccine production: bulk manufacturing

Making/releasing a vaccine lot can take up to one year

Cell culture is used to grow viruses and bacterial media to grow bacteria

Pathogens (virus, bacteria)

Whole pathogens, split antigens or recombinant proteins are recovered from culture media or expression systems

• Purification
• Sterile filtration
• Aseptic manufacturing
• Batch release

Whole pathogens (inactivated or live attenuated)

Split antigens

Subunit vaccine

Recombinant proteins

Quality control is key at every step of the vaccine manufacturing process

Challenges in clinical development

- Clinical development is complex and costly

  - Limited utility of preclinical animal models
  - **First-time-in-human trials have unique challenges** – safety first, incremental enrollment, strict holding rules
  - Progression to target population (age de-escalation/escalation), robust dose ranging, adjuvant justification, formulation selection increasingly required by regulators
  - Proof of Principle (POP) or Proof of Concept (POC) may require human challenge studies or involve complex study designs that approximate Phase III settings
  - Phase III programs are often multi-center and multi-country trials and very challenging to execute well
  - **Phase IIIb/IV programs including significant post-licensure commitments add to cost and complexity**
• Regulatory requirements
  – are ever increasing (paediatric legislation, post-approval safety/effectiveness studies, ….), requiring additional investments during vaccine development
  – are not entirely aligned between agencies and may differ by region and country, thereby adding complexity to licensure

• Regulatory approval does not mean a vaccine is recommended and reimbursed, and recommendations vary by region and country
Conclusions and future perspectives

• Development of new vaccines is becoming ever more demanding and faces multiple challenges that impact the balance between risk and return.

There are two levers to meet those challenges:

• Innovation at all levels from Discovery to Implementation
  – New vaccine technologies
  – Improved clinical trial design
  – Adapted regulatory pathways
  – Delivery science

• Partnerships are needed to render future vaccine development sustainable
  – Reward innovation
  – Define future public health needs (elderly populations, ….)
  – Product Development Partnerships for Diseases of the Developing World
  – Create broad alliances for implementation
Thank you