Working Paper No. 2011/36

Perspectives on Public Private Partnership: The R&D Based Vaccine Industry

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23 November 2011

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AMC</td>
<td>Advance Market Commitment</td>
</tr>
<tr>
<td>ADIPS</td>
<td>Accelerated Development and Introduction Plans</td>
</tr>
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<td>AVI</td>
<td>Accelerated Vaccine Initiative</td>
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<td>BMGF</td>
<td>Bill &amp; Melinda Gates Foundation</td>
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<td>BVGH</td>
<td>Bio Ventures For Global Health</td>
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<tr>
<td>CBA</td>
<td>Cost Benefit Analysis</td>
</tr>
<tr>
<td>CEA</td>
<td>Cost Effectiveness Analysis</td>
</tr>
<tr>
<td>CSCR</td>
<td>Cross-Sector Collaborative Relationships</td>
</tr>
<tr>
<td>EC</td>
<td>European Commission</td>
</tr>
<tr>
<td>EIB</td>
<td>European Investment Bank</td>
</tr>
<tr>
<td>FDA</td>
<td>U.S. Food and Drug Administration</td>
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<td>GAVI</td>
<td>Global Alliance for Vaccines and Immunization</td>
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<td>GCP</td>
<td>Good Clinical Practices</td>
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<tr>
<td>GDP</td>
<td>Gross Domestic Product</td>
</tr>
<tr>
<td>GNI</td>
<td>Gross National Income</td>
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<tr>
<td>GMP</td>
<td>Good Manufacturing Procedures</td>
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<td>GSK</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
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<td>HDI</td>
<td>Human Development Index</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papilloma Virus</td>
</tr>
<tr>
<td>IFFIm</td>
<td>International Financing Facility for Immunization</td>
</tr>
<tr>
<td>IMF</td>
<td>International Monetary Fund</td>
</tr>
<tr>
<td>ISS</td>
<td>Immunization Support Services</td>
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<tr>
<td>MDG</td>
<td>Millennium Development Goals</td>
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<tr>
<td>MFN</td>
<td>Most Favored Nation</td>
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<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
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<tr>
<td>PPP</td>
<td>Purchasing Power Parity</td>
</tr>
<tr>
<td>R &amp; D</td>
<td>Research and Development</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
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<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
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<td>WHO</td>
<td>World Health Organization</td>
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</table>
Abstract
Public and private stakeholders, including the industrialized countries vaccine industry, have since its launch in 2000 been a member of the Global Alliance for Vaccines and Immunization (The GAVI Alliance), a public private partnership that strives to save children’s lives and protect people’s health by increasing access to immunization in the poorest countries of the world. This paper examines the R&D-based industry’s strategic intent and operational model, and contributions to innovation, supply and delivery of vaccines. Building on the World Health Organization’s (WHO) general concept of global access to medicines, the purpose is to provide insights into the commitments as well as challenges faced by the innovation-driven industry, and this in the following main areas: (i) The Quest for Global Health – Vaccines for the World; (ii) Availability – Innovation, Manufacturing and Supply; (iii) Affordability – Universal Access, Equity and Pricing; (iv) Adoption – Financing and Public Awareness; and (v) Alliances – Building a Strong Public Private Partnership.
1. INTRODUCTION

Preventing disease through vaccination on a global scale significantly contributes to the enhancement of health, security and prosperity. This is a formidable task and collaboration between key stakeholders is needed. The industrialized countries vaccine industry has since its launch in 2000 been a member of the Global Alliance for Vaccines and Immunization (The GAVI Alliance), a public private partnership that strives to save children’s lives and protect people’s health by increasing access to immunization. The aim of the GAVI alliance is to mobilize key forces around the common goal of saving more lives through enhanced collaboration.

This paper argues that through a solution-focused exploration of the link between global health outcomes and sustainable vaccine-related business models, a win-win situation can be created for all stakeholders and their respective constituencies, regardless of whether these members are looking at the challenges through the lens of the public or the private sector. Each partner brings unique skills and resources to the alliance, making the whole stronger than the sum of its parts.

The purpose is to provide insights into the research commitments and contributions of the innovation driven vaccine industry, and to stimulate dialogue between public and private sector members whose interests and viewpoints may differ but who ultimately all subscribe to the GAVI Alliance’s common goal of saving children’s lives. The paper explains industry’s strategic intent and operational model, and the challenges with regard to innovation, supply and procurement. It explores the conditions under which industry can improve its performance as a partner of the alliance in order to continue inventing and supplying new and existing vaccines that benefit developing countries while respecting and operating within established legal and economic trade confines.

Building on the World Health Organization’s (WHO) concept on global access to medicines, the paper includes the following main sections: (i) The Quest for Global Health – Vaccines for the World; (ii) Availability – Innovation, Manufacturing and Supply; (iii) Affordability – Universal Access, Equity and Pricing; (iv) Adoption – Financing Systems and Public Awareness; and (v) Alliances – Building Strong Public Private Partnerships. The final section concludes.
2. THE QUEST FOR GLOBAL HEALTH – VACCINES FOR THE WORLD

During the past decade, health has achieved unprecedented prominence as a key driver of social and economic progress, and more resources than ever before are being invested in the health sector. In particular, immunization is recognized as one of the most efficient, successful and cost-effective health investments in history. Five million lives have been saved through the Global Alliance for Vaccines and Immunization (GAVI) supported immunization programs in the past 10 years alone. But even with this compelling evidence, 23 million children, mainly in the developing world, are still not vaccinated against common but life-threatening diseases. The barriers are multiple, but thanks in part to the support of The GAVI Alliance in introducing innovative solutions, vaccine makers have been able to further increase their commitment to developing and introducing vaccines that developing countries need. Looking forward into the 21st Century, vaccine makers are committed to furthering The GAVI Alliance’s mission and programs both collectively and individually.

2.1 Global Health and the Value of Vaccines

Vaccination has probably saved more lives than any other public health innovation with the possible exception of improvements in sanitation and water safety [1]. It has led to the eradication of smallpox and the elimination of poliomyelitis and measles from large parts of the world, saving millions of lives. However, despite these successes, vaccination has the potential to make an even greater contribution to global health. Three million children still die each year from vaccine preventable diseases [2]. Pneumonia, meningitis and diarrhea account for a quarter of childhood deaths, many of which could be prevented with currently available vaccines. Malaria and improved tuberculosis vaccines are on the horizon and vaccination against human immunodeficiency virus (HIV) may ultimately become possible. The scope of diseases that can be prevented by vaccination is expanding. Hepatitis B virus (HBV) and human papilloma virus (HPV) vaccines are already being used successfully to prevent liver and cervical cancers, and progress is being made on the therapeutic use of vaccines in the treatment of cancer and in the management of non-communicable diseases such as hypertension, diabetes and drug and alcohol addiction.
Given the social and economic importance of health and the unique role that vaccines play in global health, vaccines should be valued both for their ability to prevent disease and to supporting good health worldwide. Unlike traditional pharmaceuticals, vaccines are prophylactic medicines designed to prevent rather than treat disease. Table 1 summarizes their key benefits to individuals and society as a whole.

Table 1: Contributions of Vaccines to Health & Well-being

- **Societies**
  Societies benefit from ‘herd immunity’. When a high percent of vaccination is achieved, communities benefit as the spread of disease declines. One generation benefits subsequent generations when eradication or elimination is achieved.

- **Governments**
  Governments benefit as vaccination compares favorably with other preventive health measures, such as screening, counseling and behavior change interventions (i.e. diet modification for lower risk of heart disease, and screening for breast, cervical and colorectal cancer).

- **Employers**
  Employers benefit from a healthy, more productive workforce.

- **Families**
  Families benefit when the main wage earners stay healthy and family members do not need to make up for lost income, parents do not miss work caring for sick children, and vaccination is a ‘point of contact’ with the health system for the entire family for other interventions, health education and routine childhood examinations.

- **Individuals**
  Individuals benefit because vaccines reduce the pain, suffering, disability and death from disease, thereby lowering individuals’ costs for medical care, minimizing days of work lost due to illness or the need to care for an ill family member. Furthermore, ‘herd immunity’ protects vulnerable individuals, who are not or cannot be vaccinated.

Vaccination is one of the world’s most important and cost-effective public health measures, and has wider socio-economic effects on society. Despite these positive
external effects, cost-effectiveness (CEA) and cost-benefit (CBA) analyses of vaccines often take a narrow view of the benefits of vaccination, and fail to take account of recent academic work on the effects of health on incomes. According to Bloom et al. [3] there are several problems with both types of analysis, as they have been used in the past. First, the experience of development over the past half century shows that good health fuels economic growth, just as bad health strangles it. Second, neither type typically takes account of the cost of averted infections that may occur several years later. Healthy children perform better at school, and healthy adults are both more productive at work and better able to tend to the health and education of their children. Healthy families are also more likely to save for the future; since they tend to have fewer children; resources spent on them go further, thereby improving their life prospects. Third, healthier societies may be a stronger magnet for foreign direct investment and tourism than those where disease poses a constant threat. Neither type of analysis factors in these effects generating additional savings through vaccination.

### Table 2: Summary of Recently Introduced Vaccines

<table>
<thead>
<tr>
<th>VACCINE TARGET</th>
<th>DISEASE IMPACT</th>
<th>VACCINES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cervical cancer caused by human papillomavirus (HPV)</strong></td>
<td>HPV is the major cause of cervical cancer, which is responsible for 240,000 deaths worldwide and affects 500,000 women each year, 80% of whom are in the developing world.</td>
<td>Two vaccines are available that protect against the 16 and 18 subtypes of the virus, which are responsible for 70% of HPV cervical cancers. One of the vaccines also protects against the 6 and 11 subtypes, which are responsible for genital warts.</td>
</tr>
<tr>
<td><strong>Meningococcal disease</strong></td>
<td>Meningococcal infection can lead to meningitis. Several meningococcal sub-types exist, with subtype A prevalent in the African ‘meningitis belt’ causing frequent epidemics. Of those infected, between 10% and 20% die, and of the survivors 20% are likely to suffer permanent</td>
<td>Polysaccharide vaccines are used during outbreaks, but are not highly effective in young children and do not result in long-lasting immunity. A number of conjugate vaccines against type C are now available whereas others targeting different subtypes are in development. A conjugate vaccine covering subtypes</td>
</tr>
<tr>
<td><strong>disability, such as hearing loss, mental retardation or paralysis. Subtype B is prevalent in industrialized countries. Generally, severe cases can also be caused by type C.</strong></td>
<td><strong>A, C, W and Y, which account for many cases of the disease, is also available in a number of countries. Monovalent MenA conjugate vaccine has recently been launched in the countries of the African ‘meningitis belt’.</strong></td>
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</tr>
<tr>
<td><strong>Pandemic and pre-pandemic influenza virus</strong></td>
<td><strong>Previous influenza pandemics have resulted in large numbers of deaths. The largest pandemic of the last century, in 1918-19, caused 40-50 million deaths. Scientists predict that a future pandemic could result in millions of fatalities and cause great disruption to society.</strong></td>
<td><strong>Several vaccines have received preliminary approval for use during a pandemic, once the exact virus strain is available for production. Others based on potential pandemic strains (such as H5N1) have been developed for stockpiling or use prior to the occurrence of a pandemic.</strong></td>
</tr>
<tr>
<td><strong>Pneumococcal diseases</strong></td>
<td><strong>Pneumococcal diseases are responsible for approximately 1.6 million deaths worldwide each year. Many of these deaths occur in young children, particularly in the developing world. WHO recommends routine vaccination, particularly where child mortality is high.</strong></td>
<td><strong>The first pneumococcal vaccines were based on polysaccharides and given to older children and the elderly. They are not as effective in children under 2 years old. However, new conjugate vaccines offer protection to this important at-risk group. There are now two PCVs on the market – a 10-valent and a 13-valent presentation.</strong></td>
</tr>
<tr>
<td><strong>Rotavirus diarrhea</strong></td>
<td><strong>Rotavirus is an important cause of acute diarrhea, and in 2004 was responsible for the deaths of over 500,000 children under the age of five, the majority of whom were in the developing world.</strong></td>
<td><strong>Two vaccines are now available and used in a number of countries. The vaccines have undergone extensive clinical testing to establish their safety, following the occurrence of rare but serious complications called intussusception with an earlier unrelated rotavirus vaccine.</strong></td>
</tr>
<tr>
<td><strong>Chickenpox caused by varicella zoster virus</strong></td>
<td><strong>Varicella zoster virus is responsible for chickenpox, a highly contagious disease prevalent in children. Chickenpox is usually mild, but can be severe in adults and those with compromised immune systems, such as those with HIV.</strong></td>
<td><strong>Vaccines against the disease are available and are used in many industrialized countries.</strong></td>
</tr>
<tr>
<td><strong>Shingles caused by varicella zoster</strong></td>
<td><strong>After recovering from chickenpox, the varicella zoster virus remains in the body and can cause a</strong></td>
<td><strong>A vaccine specifically designed to protect against shingles is available. Testing in thousands of adults</strong></td>
</tr>
<tr>
<td>virus</td>
<td>painful skin rash commonly called shingles years later. The disease is quite prevalent, with an estimated 1 million cases annually in the US alone, most commonly in those over 50 years old.</td>
<td>showed that the vaccine can reduce the incidence of shingles by approximately half, and neuralgia was reduced by two-thirds.</td>
</tr>
</tbody>
</table>

Source: WHO/IFPMA

### 2.2 Investing in New and Improved Vaccines

Investment in research and development, largely by the pharmaceutical and biotechnology industry, has resulted in a broad range of vaccines targeting over 25 infectious diseases.

During the last 30 years, scientists have made further breakthroughs by harnessing the power of biotechnology, genetic decoding and information technology, and the pace of vaccine development has accelerated.

As a consequence, the vaccine industry has recently introduced a number of new vaccines such as those against cervical cancer (human papillomavirus), meningococcal infection, pandemic-potential influenza, pneumococcal diseases, rotavirus, diarrhea, and varicella zoster [4]. Table 2 reviews recently introduced vaccines.

As biological sciences continue to advance rapidly, the pharmaceutical and biotechnology industry is making significant investments to further extend the range of available vaccines. Scientists continue to work on preventing infectious diseases, including those that disproportionately affect the developing world, such as HIV/AIDS, malaria and tuberculosis.

A number of vaccines are now in development designed to treat diseases such as cancer.

Unlike more traditional vaccines, these cutting-edge vaccines aim to focus the immune system on attacking established disease, rather than offering protection against infections. Table 3 provides an overview of vaccines in development by R&D based vaccine companies.
Table 3: Overview of Vaccines in Development

<table>
<thead>
<tr>
<th>Bacterial diseases</th>
<th>Viral diseases</th>
<th>Parasitic diseases</th>
<th>Therapeutic treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clostridium difficile</td>
<td>Cytomegalovirus</td>
<td>Hookworm</td>
<td>Allergic rhinitis (hay fever)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Dengue fever</td>
<td>Leishmaniasis</td>
<td>Alzheimer’s</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Ebola</td>
<td>Malaria</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>Helicobacter pylori</td>
<td>Epstein-Barr</td>
<td>Schistosomiasis</td>
<td>Cervical cancer</td>
</tr>
<tr>
<td>Meningococcus B</td>
<td>Genital herpes</td>
<td></td>
<td>Ebola</td>
</tr>
<tr>
<td>Plague</td>
<td>Hepatitis C</td>
<td></td>
<td>Dengue fever</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>Hepatitis E</td>
<td></td>
<td>SARS</td>
</tr>
<tr>
<td>Aeruginosa</td>
<td>Herpes simplex</td>
<td></td>
<td>West Nile</td>
</tr>
<tr>
<td>Shigella</td>
<td>HIV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>Influenza (universal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococcus group</td>
<td>Parainfluenza</td>
<td></td>
<td></td>
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<tr>
<td>A &amp; B</td>
<td>Respiratory syncytial virus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>SARS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>West Nile</td>
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<td></td>
</tr>
</tbody>
</table>

Source: WHO/IFPMA

2.3 Global Public Private Partnership (GAVI)

The GAVI Alliance has an impressive track record. In the partnership’s first decade, over 5 million child deaths were prevented through increased coverage of existing vaccines and the accelerated introduction of new vaccines in low-income countries. GAVI pioneered the use of innovative financing mechanisms, most notably the International Financing Facility for Immunization (IFFIm), and the Advance Market Commitment (AMC). It was among the first of this past decade’s new international health initiatives to require co-financing from participating countries; a pivotal pre-condition to leveraging partner governments to invest, politically and financially, in vaccines; establishing them as a national priority and sustaining the programs over time. GAVI established an Accelerated Vaccine Initiative (AVI) (former ADIPs - Accelerated Development and Introduction Plans) to support the introduction of new vaccines in developing countries where these vaccines would be appropriate and needed. GAVI
also was an early proponent of results-based aid, conditioning the disbursement of a portion of its Immunization Support Services (ISS) funding to measured progress in vaccination coverage. Its policy and financing instruments have been independently evaluated multiple times and have received high marks.

The many achievements notwithstanding, much work remains to be done. At the World Economic Forum in Davos, Switzerland, in January 2010, the Bill & Melinda Gates Foundation (BMGF) launched the Decade of Vaccines by pledging US$10 billion to support worldwide efforts to develop and deliver vaccines to the world’s poorest children in the next decade. Although this pledge could save the lives of more than 8 million children, this sum still does not enable vaccines to reach their full potential towards contributing to the achievement of Millennium Development Goal (MDG) # 4: to reduce the mortality rate in children under 5 years of age by two-thirds between 1990 and 2015. Partners in the Decade of Vaccines know that there are crucial gaps in policy, resources, advocacy, and funding that need to be addressed. Table 4 explains why this is the right time for partners to start planning for the next decade.

The vaccine industry is a key partner in global health and is committed to increasing global access, availability and affordability of vaccines, including those that are underused or newly introduced. For many years, industry has supplied vaccines for use in the developing world at preferential prices through international agencies such as UNICEF, and this commitment continues. Industry also makes donations of vaccines to improve public health in the poorest countries. Although newer vaccines, which are based on complex new technologies, are inevitably more expensive due to their significant development costs, a strong and enduring partnership between industry, governments, public health authorities, international organizations and special purpose alliances, such as the GAVI Alliance, can help ensure that vaccination remains one of the world’s most important and cost-effective public health measures.
Table 4: Past Achievements and Future Opportunities for Vaccines

✓ Great progress made over the last 10 years
  – An estimated 3M deaths per year are averted by current immunizations
  – 8 new vaccines introduced; coverage of existing vaccines significantly expanded
  – Gap between high and low income countries significantly reduced

✓ Continued unmet need
  – Vaccine preventable diseases still account for significant mortality and morbidity
  – Coverage deficits and delivery challenges, especially in rural and poorer areas

✓ Present is promising and opportune
  – Increased country ownership (and therefore greater likelihood of long-term commitment and sustainability, especially in less developed countries)—More diseases are becoming vaccine preventable
  – Unprecedented middle-income country growth and therefore, for leveraging and co-financing vaccine programs
  – Information technologies combined with higher levels of education, especially among women and poor, leading to better information dissemination about vaccine benefits and more informed patient population, leading to higher rates of adoption.

✓ ...But also challenges
  – Challenging macro-environment
  – Shifting geopolitical forces
  – Turbulent economic environment

Source: BMGF

3. ‘AVAILABILITY’ – INNOVATION, MANUFACTURING AND SUPPLY

Vaccine makers have a proven track record for inventing, producing and supplying high quality products. Nevertheless, vaccine research and development (R&D) is time consuming, risky and expensive. While pharmaceutical development takes many years and involves major investment and risk, vaccine R&D can take even longer and involve even higher costs. There are many reasons for this, the main one being that vaccines are used in very large quantities and on healthy populations. Clinical testing of vaccines
can involve tens of thousands of subjects over long periods of time, and may involve extensive monitoring even after a vaccine receives regulatory approval in a country. While often claimed to be a panacea, technology transfer from highly industrialized nations to developing countries may lower costs but because of the high degree of advanced technology involved, this should happen under specific conditions and in collaboration with the original manufacturer. Vaccine manufacturing is both a science and an art and requires the right combination of skills.

3.1 Value Chain of Vaccine Development & Delivery
The value chain of vaccine development and delivery is complex and requires significant resources. Multi-stakeholder support and expertise is needed to advance innovative products through five stages as illustrated in Figure 1: (1) discovery and research; (2) development of discoveries into usable products; (3) regulatory processes to ensure product safety and licensure; (4) introduction of new vaccines into health systems; and (5) scale-up and effective use of products by populations. Achieving public health impact requires successful and timely progression through this value chain [5].

**Figure 1: Value Chain of New Vaccine Development**

Vaccines are highly regulated not only because of their social importance but also for the fact that they are biological products by nature. Governments are concerned about regulating all aspects of this field, including product safety, clinical testing, pricing and reimbursement, coverage under national and international health care plans and systems, patent protection, and R&D incentives. In light of the fact that societies are becoming increasingly risk averse, the regulation with the greatest impact on both pharmaceutical and biological product development, including vaccines, is that of extensive pre-clinical and clinical testing. This, combined with the associated soaring research and development (R&D) costs and the downward pressure on market prices,
make it increasingly difficult for many pharmaceutical and vaccine companies to recoup their R&D expenditures before the patent expires. The investment risks become even greater when companies develop vaccines or drugs for diseases mainly prevalent in the developing world.

3.2 Vaccine Research, Development & Manufacture

Development of the earliest generation of vaccines was to some extent empirical and involved the use of completely killed organisms, attenuated organisms or inactivated toxins. Development often took place in the absence of the specific molecular understanding of how vaccines work. Development of new vaccines can now take advantage of a much greater knowledge of the complexities of the immune system and of the development of powerful molecular techniques that allow targeted changes to be made in pathogenic organisms and in experimental hosts. Vaccine development has become much more sophisticated, with immunologists working closely with molecular biologists and chemical engineers to design and produce highly purified vaccines that are safe, consistently manufactured and effective.

Vaccine makers must show to the satisfaction of regulatory authorities that the vaccine to be introduced is safe, efficacious and can be produced with consistent quality [6]. This involves extensive characterization of the product to be tested, provision of a suitable antigen dose and administration schedule, and the application of good manufacturing practices to show it can be manufactured in a reproducible way. Antigen dose is based on relevant immune responses in preliminary (Phases I and II) clinical studies, which also monitor the reactogenicity and safety of the candidate vaccine. This stage of development may require the use of the vaccine in hundreds of volunteers of various ages (starting with healthy young volunteers) to determine an acceptable dose and administration schedule for the chosen vaccine formulation. In order to establish the safety, efficacy and consistency of the ‘final’ product studies in greater numbers of subjects using at least three vaccine lots are carried out in Phase III. Up to 100 000 study participants may be needed to demonstrate that the vaccine is safe and efficacious. Finally, the vaccine developer and manufacturer will have to collate a voluminous dossier to submit to competent national and/or supranational regulatory authorities, which will describe, in great detail, the work that has been done
to substantiate the claim that the candidate vaccine is safe and efficacious for the vaccination of humans.

The vaccine manufacturing process is equally complicated and capital intensive. A significant proportion is spent on quality testing and manufacturing controls to make sure the vaccines are of the highest standard. Vaccines are often based on living organisms with inherent variability. The exact molecular elements that provide protection are not always wholly understood so there are significant challenges in completely characterizing the final product. Even tiny variations in the production process may result in products with significantly different biological properties. The result is that vaccine manufacturing must follow highly defined and validated processes and quality control steps to ensure consistent production. Regulatory authorities require strict adherence to these processes, and as a result of this regime, the manufacturer’s product license is intrinsically linked to the manufacturing process and its precise location. Even transferring part of the process within the same production facility requires significant testing, validation and regulatory approval.

The process of researching, testing, gaining regulatory approval and manufacturing vaccines is not only complex but also costly and lengthy. For health-related products in general, but especially for vaccines, the costs and risks have increased over the past few decades because vaccines are unlike traditional drugs in that they are administered to healthy people to prevent infection and disease either immediately or at some future date. The U.S. Food and Drug Administration (FDA) estimates that it takes on average between eight and nine years to study and test a new drug before its approval for use by the public [7]. The development of new vaccines is often more complex and takes even longer. The Biomedical Industry Advisory Group estimated in 2006 that developing a new vaccine takes on average 18.5 years and costs over $500 million [8].
Reasons for rising costs of vaccines:

- R&D costs have risen significantly and tens of thousands of persons must now be tested in clinical studies in order to obtain regulatory approval instead of hundreds or thousands in the past. Authorities have become extremely prudent in granting approval because of liability issues and public pressure (see section 4.3).

- The overall time for inventing and developing innovative medical products has increased despite all modern scientific tools and equipment being mobilized by highly-educated experts; the ‘easy’ diseases have been tackled but huge challenges remain for more ‘difficult’ diseases like TB, malaria, dengue, and HIV, which are of particular interest to developing countries.

- Because of the long lead times, the cost-of-capital must be factored in from an investment and capital-budgeting viewpoint. It should be noted that stricto sensu the ‘opportunity cost’ should also be incorporated (i.e. the opportunity foregone by not developing more profitable products targeted at the more affluent markets in the world).

- Commercial returns on successful medicines have diminished (although this is more the case for drugs than vaccines). Nonetheless, the majority of products on the market fail to cover their R&D cost, leaving research-based companies dependent on the emergence and subsequent marketing of a small number of blockbuster drugs to fund future R&D.

- From the company and investor’s perspective, and in order to generate the necessary (minimum) return-on-investment, the cost of developing and testing vaccines that never reach the market for a variety of reasons must be factored into the price of all products that do.

3.3 Managing Risk: Demand Analysis & Forecasting

Given the unique complexities of vaccine development, manufacturing, and regulatory oversight, supplying current and future products takes significant time and investment to come on stream. Consequently, meeting future demand requires a long-term
commitment to vaccination, combined with careful planning and detailed forecasting from governments and supranational agencies.

Vaccine makers benefit hugely from predictable demand scenarios and mitigating demand risk through adequate forecasting. Stability of forecasting has been referred to by all industry leaders as an important task to focus on for the GAVI Secretariat and related working groups. Not surprisingly, fluctuations in demand are linked to long-term stability in vaccination program management and funding. As one industry leader pointed out during an interview, “we need stable, long-term commitments so we can do our own production forecasting, and achieve those cost savings that will allow us to be able to offer vaccines at the access price. That seems like an easy thing to do. GAVI is talking about five years of funding, but one of the things people don’t understand about vaccine manufacturing is that they have a much longer runway than pills. Our planning horizon is 10 years, not five years. We’ve got to know what we are doing 10 years from now, because if we have to scale up our production capability or change something, it takes that long to commission a vaccine production facility, or de-commission one and change it to do something else” [9].

GAVI’s marshaling of significant and long-term financing for vaccines for low-income countries coupled with improved demand forecasting has provided an important signal to vaccine manufacturers that there is a substantial and viable market for vaccines in low-income countries. These producers have made significant investments and strengthened their industrial capability to become credible players in the global vaccine market [10]. Since production units carry a high fixed cost, and cannot be switched on and off easily long-term planning and forecasting are essential to getting vaccines on the market. However, long term commitments and obligations for the industry, whether on price, supply, etc. need to be both reasonable in their scope and reciprocated by those procuring the vaccines. Currently, GAVI or PAHO nor the novel AMC financing system in support of vaccine procurement have any obligation to purchase the quantities they award although these same quantities are binding obligations on the manufacturers at prices laid down in the contract.
3.4 Technology Transfer - A Collaborative Approach

Technology transfer to developing and emerging economies and local production must take into account issues relating to quality control that inevitably will occur. The original vaccine manufacturers will carefully monitor the quality control and ensure that good governance, manufacturing procedures, and delivery and storage practices are in place. Given the complexity of the process especially in the case of vaccines, it is preferably done in collaboration with the original manufacturer. By the same token, while it is globally recognized that emerging market manufacturers have an important role to play, and several of these companies are now significant suppliers of vaccines to GAVI, it is essential that these companies are required to meet the same high standards for manufactured product quality, clinical development and general regulatory compliance that the research based companies are held to.

Producing safe, high quality vaccines requires many stages of processing and purifying. The manufacturing process takes many months, and sometimes more than a year. A significant proportion of this time is spent on quality testing and manufacturing controls to make sure the vaccines are of the highest standard. Quality testing against strict pharmacopeia standards and biological product regulations is undertaken on every batch produced, at various points in the manufacturing process, to avoid contamination or even minimal alterations in the product. Production under these stringent processes and strict regulatory oversight requires expensive manufacturing facilities, highly skilled and trained employees, and time.

The quality control and testing process for a vaccine can be further complicated if different regulatory agencies use different release criteria and require different testing methods for release in their specific jurisdictions. Therefore, the quality control test profile is specific to each vaccine and to each country of release. The administrative burden is enormous and harmonization of requirements is overdue [11]. While WHO’s pre-qualification process generally assumes this responsibility for GAVI-eligible countries, simplifying these procedures through mutual recognition of regulatory requirements will certainly need to be done over time. Under no circumstances can quality be compromised. Each manufacturer must present extensive information on the product submitted to allow qualified assessment teams to evaluate its quality,
safety and efficacy. Any doubt about standards of product quality, safety and efficacy would rightfully create suspicion and massive problems with patient groups, governments and anti-vaccination lobbies.

Finally, despite local industrial policy aspirations -- in addition to public health motives -- investment in local production must fundamentally make economic sense. The decision to make or buy a vaccine is never easy. However, both options may serve nations well in an era of global trade. Just as it would not make sense to build car factories in every country of the world, the world would not be served by going back to the times when every industrialized country had its own vaccine supplier. The result would be an inability to achieve economies of scale, and an overcapacity of production. The latter may initially be beneficial to patients but ultimately pushes many firms out of business; a situation that jeopardizes supply security. Finally, given the complexity of the manufacturing process and the considerable amount of education and training needed, the advice of experts is to use a stepwise process securing downstream manufacturing processes prior to developing vaccine bulk production capacity. This is illustrated in Figure 2.

**Figure 2: Technology Transfer for Local Manufacturing**

Source: WHO/IFPMA
4. ‘AFFORDABILITY’ – UNIVERSAL ACCESS, EQUITY AND PRICING

Vaccines are recognized as one of the best investments in global health. However, vaccination is a public health tool which should theoretically be funded through national public health budgets, but these are generally limited in low and lower-income countries. This health budgeting ‘silo’ approach could eventually be overcome by a wider recognition of the positive spillover effects on the socio-economic development of a country. Vaccine makers have pledged to continue making efforts to lower the affordability barrier by applying differential pricing or making concessionary price offers to the poorest countries. Differential pricing could go a long way towards making vaccines affordable on a large scale in developing countries, while preserving incentives for R&D. Establishing separate markets and eliminating negative price spillovers across countries is key to achieving differential pricing in practice. Governments and legislators must create an enabling environment for such a policy.

4.1 Reconciling Access and Innovation

In order for the general population in developing nations to have appropriate access to vaccines, existing vaccines must be affordable, and funding for innovation is needed to develop new vaccines. This presents a potential dilemma: prices that are high enough to pay for research and development (R&D) may make vaccines unaffordable in developing markets. Differential pricing (also called tiered pricing or economic price discrimination) can offer a solution, at least for vaccines supplied to both the developing and developed world. Prices in affluent countries – and to a lesser extent in middle-income countries – could generate sufficient revenue to pay for R&D, whereas prices in developing countries need only cover their marginal costs. Differential pricing does not stand in the way of intellectual property rights and vice versa. As will be explained in the following sections, preserving intellectual property rights is the linchpin of achieving not only short term (static) efficiency but also long term (dynamic) efficiency, structurally paving the way for sustainable access to vaccines. Patents on vaccines are not the factor limiting access to vaccines in poor countries, and thus absence of any IP right will not improve access. Nonetheless, differential pricing is not a panacea on its own and has limitations. There are not sufficient revenues from vaccines that prevent diseases that are only endemic in the developing world. Hence,
additional subsidies are indispensable to attract R&D for these diseases. Economic push and pull mechanisms, as discussed at the end of section 3, are needed to create incentives to conduct R&D on vaccines for developing country diseases.

4.2 The Power of Differential Pricing

Charging different prices to different consumers has many benefits and is a common business practice in many industries, including airlines, retail, electric utilities and pharmaceuticals. For medicines (i.e. drugs, vaccines and diagnostics) the ability to apply differentiated pricing strategies depends on the global distribution of a given disease. If a disease is widespread, a large proportion of the fixed R&D costs can be shared with affluent countries, provided rich countries are afflicted by the disease as well. This is fortunately the case (from an economic standpoint) for many of the existing and newer vaccines (that are more expensive); including those currently on the market (hepatitis A and hepatitis B, streptococcus pneumonia, rotavirus, HPV, pandemic influenza, etc.). Furthermore, price differentiation creates economies of scale in the supply processes by offering lower prices to customers who purchase a higher volume and are able to guarantee payment.

Differential pricing leads to a ‘win-win’ situation for both public and private sector stakeholders (government, business, and society). It implies that users with a higher ability-to-pay will be charged higher prices relative to users with a lower ability and willingness-to-pay. If differences in ability-to-pay or willingness-to-pay are primarily determined by differences in income level, differential pricing would be expected to charge users with higher incomes more than those with lower incomes. It has been proven that this not only optimizes social welfare but total business revenue as well (see section 3.3). The concept turns out to be very powerful in the health sector. Here, differential pricing aims to reduce the potential financial barriers to access of drugs or vaccines in low-income countries while simultaneously providing manufacturers with a profitable market in affluent countries. This gives companies an incentive to invest in building sufficient production capacity as well as in new product research and development. The WHO’s Director General has publicly called for such ‘equity pricing’ to be widely used.
4.3 Is Differential Pricing Equitable?

It is generally acknowledged that R&D of vaccines benefits individuals globally, which raises the question of how to best allocate the ‘joint costs of R&D’ to ‘consumers’ – individual taxpayers and nations at the aggregate level in order to generate the greatest benefit. Considering all consumers in the world as equal based on their needs rather than their ability to pay, leads to prices varying inversely with the consumers’ price sensitivity – a theory of optimal differential pricing known as Ramsey pricing [12]. However, prices must still exceed the marginal cost of production for a significant number of consumers in order for investments in R&D to be recouped. If all consumers were to be charged the same price, then the most price-sensitive consumers would proportionately reduce demand and consequently generate less benefit than the less price-sensitive consumers. In practice, sensitivity to vaccine prices is hard to measure, but a reasonable assumption is that it varies inversely with income. Following this logic, countries with a lower per-capita income would be charged lower prices than countries with a higher per-capita income.

Economic theory asserts that differential pricing promotes greater social welfare than uniform pricing if consumers in aggregate buy more under differential pricing [13], which seems plausible for vaccines. Differential pricing can thus be considered a prime example of equitable pricing. Whereas the term differential pricing stems from business economics, the term equitable pricing is derived from social welfare concepts. These two schools of thought go hand-in-hand and could be considered mirror images of each other, as illustrated in Figure 3. The similarity between the pricing structures that maximize welfare (Ramsey optimal pricing) and those that maximize profits is not surprising. It means that firms, in the pursuit of their own self-interest, will attempt to set price differentials that are both efficient and equitable across markets. In general, differential pricing not only increases the use of existing vaccines (static efficiency) but also results in increased sales revenue (dynamic efficiency) which in turn spurs R&D and increases the output of new vaccines (Figure 4).
In conclusion, to improve access to vaccines worldwide, it is critical for manufacturers to offer vaccines at lower prices to less affluent countries. At the same time, vaccine manufacturers must be able to recover their costs whilst earning a fair return on their investment so as to support continued investment in R&D and scale up of production capacity. This delicate balance can be attained by amortizing expenses *unequally* across countries in such a way that poorer countries pay a relatively lower price, but nonetheless *equitable* share for their products compared to the more affluent...
countries. Consequently, differential pricing can result in significant progress in access to vaccines in both affluent and less economically developed countries. In addition, the principle of differential pricing is applicable to vaccines for the prevention of a range of diseases, not only those confined to poor countries. Section 3.11 describes the supplementary incentives that must be created to promote R&D of vaccines against poverty-related diseases of interest to developing countries (and for which differential pricing is impossible or insufficient).

4.4 Implementing Differential Pricing

As described above, differential pricing inherently includes the notion of equity and has a redistributive effect. The pertinent remaining question is who should pay what share of the R&D costs that are incurred? Because the ‘global joint cost’ of inventing and manufacturing vaccines cannot be attributed to a particular group of vaccinees or country, the cost structure by itself cannot determine the proportion each country or beneficiary should contribute. A country’s gross domestic product, or its ranking in the Human Development Index (HDI), may provide an adequate proxy for its consumers’ ability-to-pay. However, the purchasing power parity (PPP) adjusted Gross National Income (GNI) per capita provides a more refined measure of a nation’s true wealth. This is illustrated by the non-linear function in Figure 5 [14].

As the graph suggests, the ratio of wealth inversely reflects the theoretical discount rate that can be applied to each country compared to a high income reference country. In other words, the steepest discounts are reserved for the poorest countries, while for middle and high-income countries discounts are expected to gradually decrease as the country’s wealth increases, eventually leading to standard prices (without further ‘equity’ discounting). This makes sense from a fairness point of view. If today’s highly developed economies, such as the US, Europe and Japan, find the cost of a vaccine to be a financial burden, low-income countries will certainly experience a relatively greater and heavier financial burden due to the preponderance of poverty among their populations. The curve implicitly shows how the ‘global joint costs’ of research and development, including clinical trials, and those associated with the construction of large-scale manufacturing plants, obtaining regulatory approval, and paying liability insurance fees, among other costs, can be distributed
proportionally across different patient/consumer groups, and in accordance with their respective financial means.

Application of this rationale at the aggregate country level permits a higher-than-marginal-cost price for well-off consumers, who thus absorb a substantial proportion of the fixed costs. For the less affluent consumers, the price gradually declines, so that on average, less fortunate consumers face a cost closer to the marginal costs of production, marketing and distribution. For the poorest countries, a special effort must be made as they may not be able to afford any price, no matter how low the marginal production cost may fall (through economies of scale, licensing third parties, or outsourcing to low-income countries). Here external funding as well as managerial and logistical support is needed, and has been provided by public private partnerships such as GAVI.

The model described above generates a theoretical price index, not the actual market price for drugs and vaccines. The outcome varies by vaccine class since the original benchmark is value-based and usually determined by cost-effectiveness analysis.
Secondly, as part of this process, it is important to consider pricing in the context of volume and long-term supply contracting. Thirdly, depending on the incidence and burden of the disease, additional concessionary prices, which are usually considered on a case by case basis, may be granted. Finally, regardless of their geographic operations, companies can only control *ex-factory* price-setting for their own products and issue guidelines within their own business and trade jurisdiction. Thus, it is only within their own jurisdiction that companies can implement equitable pricing policy. They are not responsible for distribution channel mark ups.

4.5 Barriers to Market Segmentation

Differential pricing is possible only if market separation can be sustained. This means that the low prices that are charged in developing countries cannot be demanded by higher-income nations. In practice, the looming threat of a breakdown of any market separation, and hence of a manufacturer’s ability to maintain appropriate price differentials, is probably the single most important obstacle to implementing lower prices in low-income countries. The primary factors that may lead to this breakdown are two trade-related policies: parallel trade and price referencing between market segments and different countries.

Parallel trade occurs when an intermediary agent exports an originator product from one country or market segment to another to profit from the price differentials set by the original manufacturer. Although proponents argue that parallel trade is a form of free trade, in fact, parallel trade in pharmaceuticals usually results from differences in price regulation, and not from lower, real resource costs. Parallel trade, therefore, offers none of the usual efficiency gains of trade. Fortunately, the case of vaccines is quite different, as the cold-chain distribution requirement complicates matters and acts as a deterrent to parallel trade outside of the regular channels.

The second policy that erodes market separation and promotes price spillovers is external price referencing, which occurs when governments or procurement agencies use low foreign vaccine prices as benchmarks for regulating their domestic prices. In practice, external referencing can be considered the virtual component of parallel trade and consequently equivalent to fully importing a foreign price. The risk that low
prices granted in low-income countries would lead middle and high-income countries to demand similarly low prices is another important obstacle to lower prices in these low-income markets.

Hence, manufacturers adopt differential pricing only if markets remain separate, such that lower prices in one market do not erode potentially higher prices in other markets. Faced with price leakage due to price referencing or parallel trade, a firm’s rational response is to attempt to set a single price or narrow price band of prices instead of practicing differential pricing. If market separation could be guaranteed so that originator firms can sustain differential pricing, then they could charge prices comparable with those of local generic firms in low-income countries. Policymakers, governments and multilateral agencies like The GAVI Alliance must create an enabling environment so that innovation-driven companies can make their commitments sustainable by having a model in place that enables them to deliver results in the short as well as the long term and do what is right from a public health perspective.

4.6 Price Regulation or Competition?
It could be argued that, as an alternative to pricing vaccines according to ability to pay as practiced in differential pricing (see section 3.4), procurement agencies regulate prices by employing a mark-up over audited costs. This approach however faces problems common to all cost-based price setting. Generally, cost-based pricing raises major economic, accounting and political issues. Defining prices based on costs is widely recognized as an inefficient form of regulation in any industry, because cost plus pricing rules reduce incentives to keep costs down [15]. Alternatively, negotiated, confidential price discounts are likely to provide the most efficient approach to achieving appropriate price differences.

Experts agree that regulating price setting of health products based on costs is likely to lead to imprecise and probably downward biased prices because all costs are not fully observable and optimal allocation rules may be unknown or politically unacceptable [16]. First of all, in the case of vaccines, full costs relate to essentially complex, risky and lengthy projects including investments made over 10-15 years, the total cost of which is hard to track. The factor of time cost of investments should be considered, but
is not reflected in accounting statements. Secondly, the full cost of developing new products includes the cost of failures during the research and development process [17]. Third, the degree of shared R&D and production costs is hard to measure. Even if known, the appropriate sharing rule for joint costs between affluent and poorer countries depends on demand conditions in their respective geographies. Fourth, cost-plus pricing proposals leave unspecified whether the marginal cost should include contributions towards building capacity where the supply of developing countries will require construction of additional, costly production capacity.

In conclusion, in the case of vaccines, accounting of costs does not provide an accurate measure of the full economic costs or an appropriate benchmark for price setting. If policymakers or procurement agencies regulate price setting based on allowable costs defined as costs that are clearly attributable to a specific product in a specific country, prices will not cover the total cost. A system that allows for differential pricing is more equitable.

### 4.7 The Limits of Low Price Policy

It is important for vaccine manufacturers to generate volume because of the associated economies of scale and the benefits that production of large batches has on lowering the marginal production cost. Again, the relationship between price and volume is non-linear when trade-offs have to be made. To illustrate the case, take a firm that in a neutral scenario wants to maintain net margins and not just grow its business through geographic expansion and higher patient coverage; a price reduction of 10% would have to be compensated by a volume increase of 15% (starting from the base scenario in the middle of the curve; see figure 6 [18]). With reference to The GAVI Alliance, vaccine prices already enjoy steep discounts and are therefore positioned at the lower end of the equity price curve (which is non-linear and therefore amplifies any increases or decreases made at the extremes of the spectrum). The result is that reducing prices of current vaccines by another 10% or more as sometimes has been suggested [19] would have to be compensated by substantially higher volumes and uptake in order to avoid unduly eroding supplier margins.
In summary, overly focusing on the lowest price instead of the best price is assumed to lead to unanticipated consequences that may not be readily detectable. Although the effect of such a policy on future innovation is hard to measure, it is likely to be negative. The long time lag between initiating R&D and bringing new products to market means that even if current low prices are a disincentive for future innovation and hence future supply of new vaccines, it will be hard to retrospectively attribute this lack of future innovation to the specific policies of today. Whereas larger corporations may be able to incur budgetary losses or afford smaller margins, small and mid-size companies may not have the support to do so. Despite the fact that many of the small and mid-size companies have been encouraged by NGOs such as Bio Ventures for Global Health (BVGH) to invest in vaccines for the poor, many may no longer be capable of investing in this area.

**Figure 6: Optimizing the ‘Price/Volume’ Relationship**

![Graph showing the relationship between price and volume]

### 4.8 Influencing Vaccine Markets

Since GAVI’s inception in 2000, the results obtained through immunization in low-income countries with a Gross Domestic Product (GDP) of less than $1,500 per capita have been impressive. By raising significant new resources for immunization and
focusing on the world’s poorest countries, GAVI has been able to change the way vaccine makers think about developing world markets. In the past, the market was not transparent and high impact products primarily aimed at developing countries were not always commercially attractive. Manufacturers were often not aware of the specific needs, or considered the risks associated with entering these markets too high. As a result, products that are essential from a public health perspective were not developed or manufactured in sufficiently high quantities or provided in presentations tailored to developing countries’ needs. By pooling approximately 70 developing countries that represent over half of the world’s births annually, and using UNICEF’s procurement system, GAVI has helped change the global market dynamic, making this market potentially attractive to vaccine manufacturers of both the developed and developing world.

While suppliers generally welcome the GAVI Alliance’s initiative to create so-called ‘healthy markets’ by mobilizing public and private sector players, and by raising significant additional new resources to ensure that new and existing vaccines are available in the poorest countries as well, there is concern on how this will be implemented. The GAVI Alliance was specifically created to respond to the above mentioned ‘global market failure’ and to facilitate the creation of a ‘market’ on behalf of the developing world. Once this impediment is resolved, the market system will deliver results as in any other vaccine market and will not be in need of any further ‘management’ or ‘shaping’, as implied in the GAVI supply and procurement strategy.

GAVI’s strategic plan comprises a set of objectives under the umbrella of ‘market shaping’; including uninterrupted vaccine supply security, price decreases, facilitating research and development (R&D) of appropriate vaccines for developing countries, and the rapid introduction and accelerated adoption of new and existing vaccines in GAVI-eligible countries. However, ‘market shaping’ in the context of the GAVI Alliance nowadays has become rather complex to implement because the organization is trying to achieve many objectives simultaneously (some of which are in conflict with each other). For instance, it is hard for existing as well as potentially new suppliers to step up investment in developing country markets if products that are the cornerstone of current immunization programs are simultaneously singled out for extra price
reductions. At first glance, this may seem like a reasonable expectation from a buyer’s perspective. From a seller’s viewpoint, this forces companies to operate without a ‘buffer’ or ‘cushion’, which typically are needed to absorb any unforeseen costs or necessary extra investments (e.g. to maintain or upgrade production units, or respond to sudden requests for large supplies when one of the other suppliers cannot deliver). Without a doubt, the GAVI policy risks forcing manufacturers to unsustainably low prices, and thus unintentionally pushing suppliers out of business (ironically bringing us back full circle to the situation that existed prior to the founding of the GAVI Alliance).

A matter of concern is the assumption that ‘market forces’ no longer are the most efficient driver for achieving the best price or the lowest price possible. The GAVI Alliance’s supply and procurement strategy, as outlined in the updated 2011-2015 plan, states that in the past GAVI primarily relied on market forces to influence price and supply security (assuming that competition over time would lead to price decreases but also attract more manufacturers which enhances supply security). Having multiple suppliers in the market is indeed critical to the principle of vaccine security. In the past, there have been instances where supply contracts were not honored simply because of technical problems with the main supplier (causing interruption of vaccination programs). However, the two objectives – having firms invest in manufacturing facilities including attracting newcomers from emerging markets while at the same time reducing price levels – seems contradictory. This is not due to a lack of market forces, but rather a consequence of insufficient funding to match GAVI’s ambition.

It is evident that there may be situations where competition is not possible, but beyond these specific circumstances, competition should be the default in international trade since it has been the most effective driver of price. The most effective approach to reducing vaccine prices in a sustainable way while preserving supply security remains the creation of an attractive market for a larger number of manufacturers. Furthermore, low prices can be obtained through public tenders, which is already common practice. This practice guarantees the lowest prices because UNICEF’s procurement division holds a single buyer (monopsony) position and manufacturers have sunk costs by the time they submit tenders.
4.9 Role of Emerging Economies

As shown in section 3.4, the global nature of what is called ‘joint costs’ of inventing and developing new vaccines (i.e. the costs related to conducting research and development) creates the opportunity and incentive for policy makers and procurement agencies in each country to free ride, paying only the marginal cost and leaving others to pay the joint costs. A sustainable differential pricing structure will only be possible if higher income countries accept the responsibility to pay relatively higher prices, foregoing the temptation to try to obtain the lower prices granted to low income countries; and middle-income countries recognize that it may be appropriate for them to pay prices that provide a return on R&D for at least part of their populations. This threat of free riding would be reduced by effective pricing that keeps prices low in low-income countries and moderate in middle-income countries.

Emerging economies occupy a special position on the ‘fair pricing’ curve in Figure 6, especially in comparison with the human development index (HDI) curve. If evaluated by their national income and HDI, the emerging markets undeniably have the capacity to absorb a considerable part of product research and development costs even at the present time. It would therefore not be defensible if they were not to share some of that cost. That is, not all of the fixed cost burden should be, or perhaps even could be, shouldered only by the cohort of high-income countries (this is overwhelmingly the case at present). Indeed, the world economy is rapidly changing and a modification in policy and practice is needed. Two opposing future trends are likely [21][22]: (i) The United States and Europe struggle on, suffering the repercussions of their financial excesses and political paralysis. They seem condemned by their heavy debt burdens to years of stagnation or slow growth and widening inequality; (ii) whereas much of the rest of the world is brimming with energy. Policymakers in China, Brazil, India, and Turkey are concerned about too much, rather than too little growth. Perhaps for the first time in history, the future of the global economy lies in the hands of developing countries and emerging markets.

Against this backdrop of economic development, middle-income countries (MIC) are likely to play an increasingly important role in the economy of the coming decade. The trend is to increasingly engage the emerging economies in funding GAVI programs in
poor countries and supplying them with vaccines. So far, the majority of vaccines that support GABI programs are supplied by the industrialized country manufacturers. Among the large multinational pharmaceutical companies, Sanofi Pasteur (part of the Sanofi-Aventis Group) and GlaxoSmithKline (GSK) manufacture a broad range of vaccines generally licensed for worldwide use. Others, such as Merck, Pfizer, Novartis and Crucell (part of Johnson and Johnson), offer a narrower range of products addressing particular disease indications or market niches. The situation regarding manufacture and supply is changing due to the growing number of enterprises with headquarters in developing and emerging economies [23].

While GAVI may see its role being to encourage developing and emerging country manufacturers to become suppliers, it should strictly act as a catalyst, and thus maintain its position of neutral broker. In other words, the organization remains impartial and its procurement partners ensure a level playing field and only use criteria like product quality, supply security, and price. Although preferential treatment would definitely distort competition, it is sometimes argued that this also reduces prices. The necessary condition for this to be the case is that licensees or independent vaccine companies in the emerging economies have lower costs than the innovation-driven originator firms, and that these savings are passed on to customers. But labor cost is only a fraction of production costs, and many multinational R&D-based companies have plants in low-wage countries. If originator firms were to have higher costs, this most likely reflects the cost of compliance with ever more stringent animal testing regulations, and environmental and regulatory requirements to which they are held, including among others Good Manufacturing Procedures (GMP) and Good Clinical Practice (GCP).

4.10 Disclosing Price Information
The negative effects of price referencing can be addressed by vaccine makers and purchasers in low-income countries or certain market segments by using confidential rebates as part of their procurement arrangements, so that low prices granted to one purchaser are unobservable to others and cannot be copied. If discounts to low-income countries or populations in lower-middle income countries equally affected by poverty are given as confidential rebates paid directly to the end-purchaser, this
eliminates the opportunity for other purchasers to demand similar rebates. It also eliminates the opportunity for distributors, or other parallel traders, to purchase the product at the low price intended for low-income countries, and export it to higher-price countries. Furthermore, it prevents product leakage between market segments within countries, confining discounts to the intended beneficiaries.

Vaccine companies must comply with international trade regulations and cannot share price information with each other for anti-trust reasons, as creating the possibility of price fixing may limit open competition and thus lead to higher prices. Moreover, companies may resist regulated, transparent discounts, even though they might be willing to offer similar discounts in confidential negotiations. This is both because of the risk of spillovers of these low prices and, more generally, because they might see scheduled discounts as a first step towards a comprehensive system of compulsory price regulation. Such an approach would be highly inefficient given the competitive nature of the pharmaceutical industry.

There is discussion within GAVI circles to proceed to mandatory and public disclosure of the rebates granted to the United Nations Children’s Fund’s (UNICEF) procurement services so that other purchasers can take this as a benchmark. This ignores the fact that, so far, confidential discounts are the chief means by which GAVI-eligible countries get lower prices. Within the GAVI context, steep discounts are aimed at supporting the poorest countries and are closely linked to the use of larger volumes. Another argument for keeping prices confidential is that confidentiality encourages competition whereas publishing bid prices could promote collusion between suppliers. An argument for price disclosure, however, is that transparency increases public accountability, thus enabling the public to see if buyers are doing a good job and reducing the chance of collusion between procurement bodies and bidding companies. In the case of vaccines that are centrally procured and subsequently used in GAVI programs, these disclosure objectives can be achieved by an approved third party audit, without incurring either the adverse spillover effects that result when prices are publicly observable, or the risk of collusion between suppliers.

Yet, it could be argued that if higher-income countries were to accept that taking low-income countries as a benchmark for price referencing is not compatible with poor
countries getting the lowest price in a sustainable manner, price confidentiality is no longer required. Also, the developed country and developing country vaccine manufacturers have, on several occasions, including most recently at the GAVI donor pledging conference in London (June 2011), publicly declared their willingness to widely implement policies that support differential pricing for GAVI-eligible countries and those graduating from the program in the near future. Nonetheless, this issue is complicated by the fact that, in practice, negative spillovers eroding revenues in other markets occur because other countries may request to be treated as preferred nations as well, claiming ‘most favored nation’ (MFN) status (see box). Asking similarly low prices across markets is incompatible with Ramsey’s optimal pricing that is based on sharing the cost burden in an equitable way. As shown, this practice of fair pricing would yield the greatest social welfare for vaccinees.

Blue Box

The controversy over tiered pricing came to a head in 2009, in a dispute with the PAHO Revolving Fund, a pooled procurement mechanism used by most countries of the Latin American region. The Revolving Fund helps member countries to strengthen immunization systems and introduce vaccines, and was able to buy vaccines at prices very similar to those paid by UNICEF on behalf of GAVI. Suppliers insisted that PAHO must pay more than GAVI; PAHO, in turn, insisted on a ‘most favored nation’ (MFN) clause in its contracts that requires that PAHO receive the lowest prices available to any purchaser, including UNICEF [24].

4.11 Stimulating R&D through Subsidies

Clearly, differential pricing in low-income countries can simultaneously reconcile innovation incentives with affordability in low-income countries but it only works in high-income countries for vaccines with significant sales. For diseases that occur predominantly in low-income countries, revenue from vaccine sales elsewhere is not sufficient to stimulate R&D. Industry believes that both ‘push-pull’ subsidies are necessary. While early-stage projects may benefit from ‘push’ incentives, market-based ‘pull’ incentive schemes work better once proof-of-concept has been delivered.
‘Push’ subsidies fund R&D directly, usually through specialized public-private partnerships aiming to develop new vaccines, or antigens, adjuvants, product formulations and presentations adapted to the needs of developing countries (e.g. easy mode of administration, thermo stability, etc.). Whereas push funding aims to support products in the early stages of development (for example, through the innovation fund established by the BMGF), pull mechanisms, in principle, work best when the concept of a new vaccine is ‘proven’ – which means although hard to prove from scientific data alone, the vaccine is somewhere along the transition between research and development. The development stage, which is lengthy and expensive, includes generating empirical evidence through large scale trials in humans, scale-up of production units, quality control and registration. The latter includes obtaining WHO pre-qualification and market authorization to supply developing countries.

An example of a successful ‘pull’ mechanism is The GAVI Alliance itself, which through its long-term purchase commitments, sends a signal to industry that developing countries are a viable and long-term market. However, GAVI’s pull has not been strong enough to stimulate the development of new and sophisticated vaccines [23]. This is largely due to a lack of market or populations with limited buying power. To remedy this failure, supplementary incentive mechanisms need to be mobilized. The Advance Market Commitment (AMC) model is this type of pull mechanism and is designed to stimulate R&D on vaccines that would primarily benefit the developing world.

Under AMC arrangements, donors/governments make a legally binding commitment to pay a specified price for up to a specified number of doses of the vaccine. The vaccine must meet specified criteria, provided that developing countries commit to using the product and paying their share of the price for a number of years. If the disease is predominantly or exclusively prevalent in the developing world, e.g. malaria, TB, dengue and neglected tropical diseases, the subsidy should aim to cover the entire risk-adjusted cost of the project; for illnesses afflicting developing countries as well as affluent countries, these costs can to some extent be recovered by means of differential pricing. The size of the subsidy varies depending on the disease prevalence. The G8 leading industrialized nations expressed their support for AMCs for vaccines at the inaugural conference in Rome in 2005. The appeal of AMCs to donors is that they
pay only if firms successfully develop the appropriate new vaccines, whereas with push subsidies, donors pay in advance and bear the full risk of R&D failure. Industry has expressed its support on various occasions. Meanwhile, the pneumococcal vaccine has been selected by an independent committee of experts to become the pilot project for testing this new incentive mechanism. While well-designed AMCs could play a role in mid-stage development, they are unlikely to be a practical way to drive R&D for challenging early-stage vaccines that face substantial scientific obstacles. In those cases, a combination of ‘push-pull’ will be necessary.

In conclusion, differential pricing alone will not stimulate R&D for vaccines that prevent diseases that occur mainly in developing countries. Supply-side or demand-side public subsidies are necessary for such diseases. The optimal strategy would include the use of both, with AMCs as a demand-side mechanism to stimulate commercialization of promising vaccines that have demonstrated proof of concept. It would be wise for the partners of The GAVI Alliance to prepare now for the next AMC project(s) in spite of the financial and economic turmoil most donor countries are going through at the moment. The opportunity should not be missed in light of other innovative financing facilities currently being discussed at high-level meetings between governments, including, for instance, a tax on international financial transactions (see next section). Lobbying efforts have to start now in order for some of the proceeds to be channeled towards supporting global health initiatives.

5. ‘ADOPTION’ – FINANCING SYSTEMS AND PUBLIC AWARENESS

In many of the poorest countries, health care systems are weak. There is a need for strengthening the infrastructure, and building capacity in management and policy making through training and education. Most importantly, more funds are needed. To bridge the gap in finance, more government resources need to be mobilized, complemented by external funding from donors in industrialized and emerging economies. Vaccination programs are cost-effective and yield a high return in years of life saved, as well as improvement in educational outcomes. But to use their full potential, evidence-based policies need to be systematically developed and the public
at large better educated/informed, which in turn influences the demand for vaccination. Effective communication entails building trust among the public and private sector stakeholders from the start. It also requires reaching out to healthy people – a task that is complicated by the fact that several anti-vaccination lobbies are vocal in dissuading people from becoming vaccinated.

5.1 Innovative Financing and Program Strategy
Over the past 10 years, GAVI has mobilized significant financial support from donors and foundations, including the Bill and Melinda Gates Foundation (BMGF), for immunization. GAVI mobilized this funding not only through traditional means but more importantly, through innovative financing mechanisms, the most notable of which was the innovative International Financing Facility for Immunization (IFFIm), but also through the Advance Market Commitment (AMC). Notwithstanding the important contributions made by these two novel financing mechanisms, and the successful international donor pledging round held in June 2011, more resources will be needed.

Against this backdrop, funds will have to be efficiently managed and it may not be easy to set priorities. There has been heated debate in the past over whether GAVI’s focus on new and underused vaccines detracts from the critical need to maintain, and in some cases, expand access to basic childhood immunizations. Clearly, immunization programs should be sustained, once introduced. Otherwise, health gains are impacted irreversibly and it will not be possible to appreciate GAVI-led program outcomes. While both objectives are important, this type of trade-off will always be difficult to make if financial resources are limited. Without sufficient resources, children, adolescents and adults (in the case of cervical cancer and hepatitis) will continue to die in large numbers from entirely preventable causes. Despite its limited resources though, GAVI has entered into the complex area of health systems strengthening, often without clear policy parameters and at the expense of its core mission [25]. It also struggled to ensure that 1) countries receive the necessary technical expertise to plan for new vaccine introduction and 2) plans are in place for longer-term financial stability as GAVI’s support is phased out.
Funding gaps threaten to limit the scope of GAVI’s ambition and activities in the future. GAVI therefore needs to be clear about what it should be doing but even more importantly, about what it should not be doing. GAVI’s foray into health-systems strengthening may be important and valuable. Nevertheless, it has led to anxieties that GAVI was blurring what should be its central concern – vaccines [26]. Similarly, should GAVI’s remit include developing its own research agenda? Some observers believe this would be a mistake because other organizations are better positioned to fund and conduct vaccine-related research [27].

5.2 Financial Sustainability and Political Support
To guarantee continued success in the next decade GAVI needs and deserves substantial and sustained financial support. Resources will need to come from new and existing innovative financing mechanisms, the private sector, but, most importantly, direct funding from bilateral donors including those in emerging economies. The need for long-term financing of new vaccine development and utilization is daunting. It is estimated that by 2030 there may be as many as 20 vaccines in routine use [28] whose application across the world might cost as much as $20 billion a year, a sum far in excess of the $1-2 billion a year currently available to GAVI [29]. It cannot be expected that donors will contribute all the additional funds required; increased contributions from recipient countries will be essential [1].

GAVI remains an important catalyst for the introduction of new and under-utilized vaccines. Failure to fund the organization would leave an enormous gap in the vaccination landscape of developing countries, and would bring us back to the dire situation we were in about ten years ago. Even so, donors have suggested that their contributions will remain flat, if not reduced, in the next few years, making the GAVI funding gap an unwanted but daunting reality. In that case, GAVI will not be able to fund all new vaccines that its Independent Review Committee (IRC) recommends for approval. Accordingly, countries’ confidence and enthusiasm will diminish. To bridge this ever-widening gap between funding that is needed and that which is available, much more must be done to strengthen GAVI’s funding. Both IFFIm and AMC are great examples of financial innovations to support developing country immunization programs. But more external funding will be needed to maintain coverage at current
levels for existing vaccines and at the same time support the accelerated adoption of new vaccines. The G-20 and the European Commission have officially started a process of exploring a number of novel financing mechanisms (via a so-called ‘Tobin tax’ on speculative financial transactions) to help the developing world cope with a number of problems. Yet the task of securing health initiatives has become difficult given the new and pressing competing needs and strategic imperatives in the world, such as disaster relief due to earthquakes, climate change, green energy, clean environment, etc.

Finally, if GAVI-eligible countries and particularly those that are ‘graduating’ from the GAVI funded program are to achieve sustainable immunization programs, they should take measures to progressively (and wherever possible rapidly) become self-supporting. To achieve this goal, rigorous systems of increasing co-payments must be designed to guide countries in raising and allocating budgets for vaccine procurement and delivery. Such a well-managed transition would lead to greater responsibility and accountability at the country-level. For this to happen, authorities in developed and developing countries must be persuaded that vaccinations are justified as they will need the continuous support of the electorate to spend taxpayers’ money on any globally or nationally-financed vaccination program.

In this context, the story of the value of vaccines must be retold. The core message is the importance of health and of sustaining it, notably through prevention. From this vision flows the vaccines’ ability to prevent or eliminate disease, reduce the severity of disease, protect against complications and disabilities, and protect vulnerable people. Vaccines add value to human life both cost-effectively and efficiently, with benefits accruing not only to the individual, but to societies, governments, families, and employers. Some experts have argued that as a preventive tool, vaccines are under-valued and warrant a different approach [30]. Vaccines have features that require special consideration when assessing their cost-effectiveness. Not all aspects of ill health and time preference are captured by recommended techniques for social and economic evaluation. This may disadvantage the cost-effectiveness of interventions against diseases in children relative to interventions against diseases in adults, and prevention relative to cure. Alternative discounting techniques that deal with social time preference over longer time periods should be used.
5.3 Stakeholder Engagement and Advocacy

To get the ‘value of vaccines’ message widely disseminated, active support is needed from vaccine experts, regulatory agencies, politicians, and the public at large. The Royal Society of the United Kingdom convened a meeting to review the ways in which vaccines are developed and deployed, together with an examination of adequate communication strategies [31]. To have an impact, opinions and recommendations need to come from experts who are independent of profit-making interest groups and of government influence. A proposal was put forward to set up independent vaccine information institutes, committed to the improvement of public knowledge about vaccines, as information dissemination centers. No matter how strong the science may be and how uniform the expert consensus, the general public will remain sensitive to alarms raised by anti-vaccination movements, and will be swayed by the opinions of friends, actions of their peers and the media. This needs to be recognized and responded to by pairing up independent and informed advisors with parents’ groups, opinion leaders and media experts. They can, in turn, address any real or unfounded fears and explain the risks of vaccine apathy as well as vaccine use, adopting the spectrum of modern communication channels to which the younger generation (of parents) is most amenable.

The prejudice against vaccines has fostered the perception that vaccines are great but dangerous. People regularly attribute all those diseases of unknown cause to vaccination (particularly those widely used). For instance, in the absence of a known cause of the rise of autism, many people concluded that it had to be caused by vaccination. First, they associated autism with measles, mumps and rubella vaccination; later, when that was disproven scientifically, others associated autism with the use of thimerosal, a mercury compound used until recently to maintain the sterility of vaccines. Now, even after the association between thimerosal and autism has proven to be unfounded, there are still some skeptics who refuse to accept the scientific evidence and insist that autism is caused by vaccination [32]. How does one increase public trust so that vaccines are again perceived as the best insurance across different generations and geographies? Larson, Cooper, Eskola, Katz, Ratzan [33] argue that public questioning of vaccines and decision making related to vaccine acceptance
is not only driven by scientific and economic evidence, but also by a mix of psychological, socio-cultural, and political factors, all of which need to be understood and taken into account by policy and other decision makers.

A growing body of work suggests that ordinary citizens react to scientific evidence on societal risks in much the same way. People endorse whichever position reinforces their connection to others with whom they share important commitments. As a result, public debate about science is strikingly polarized. The same groups who disagree on ‘cultural issues’ - abortion, for instance – also disagree on whether climate change is real and whether underground disposal of nuclear waste is safe. ‘Cultural cognition’ is a theory of risk communication that takes into full account the effects of culture on decision-making [34][35]. Research suggests that this form of ‘protective cognition’ is a major cause of political conflict over the credibility of scientific data on climate change, environmental risk (and vaccine risk, for that matter). People with individualistic values, who prize personal initiatives, and those with hierarchical values, who respect authority, tend to dismiss evidence of environmental risks, because the widespread acceptance of such evidence would lead to restrictions on commerce and industry, activities they admire. By contrast, people who subscribe to more egalitarian and communitarian values are suspicious of commerce and industry, which they see as sources of unjust disparity. They are thus more inclined to believe that such activities pose unacceptable risks and should be restricted.

In conclusion, unless an active effort is made to improve public confidence and trust in vaccination, there is a risk that gains made in combating the morbidity and mortality of infectious diseases will be lost. Improving communication programs means that we need to learn more about how to present information in forms that are acceptable to culturally diverse groups, and how to structure debate so that it avoids cultural polarization. More research is needed to gain better insight into not just the determinants of public trust, but the mix of factors that are most likely to sustain public trust. The vaccine community demands rigorous evidence on vaccine efficacy, safety, technical and operational feasibility when introducing a new vaccine, but has been negligent in demanding equally rigorous research to understand the psychological, social, and political factors that affect public trust in vaccines.
6. ‘ALLIANCES’ – BUILDING STRONG PUBLIC PRIVATE PARTNERSHIPS

The GAVI alliance forms a strategic alliance between diverse stakeholders from the public and private sector. It is essential to understand what constitutes a public private partnership (PPP), and the often ideologically-driven challenges that must be overcome to make such a partnership work. From that perspective, it is useful to begin by looking at the nature and purpose of public private partnerships. The introduction of PPPs raises a series of political, economic and technical issues. Yet from an organizational standpoint, understanding the group dynamics may be the most important factor in building strong partnerships and building trust because these factors are essential pre-requisites of success in highly diverse groups. By definition, multi-stakeholder decision making processes are bound by cultural diversity. When analyzing the potential diversity that emerges from a social psychological perspective in decision-making groups, stereotypes are of particular importance. Once stereotypical beliefs come into play, they affect people’s perceptions, attitudes, and behavior. Overcoming such stereotypes will allow the partnership to reach its full potential.

6.1 Nature and Purpose of PPPs

In a globalized world, goods and services can be delivered in a number of ways that may involve the government(s) and the private sector to varying degrees. A public-private partnership is generally defined as an agreement between government(s) and one or more private partners (which may include the technical operators and the funders), where the private partners deliver the service or good in such a manner that the public service delivery objectives of the governments are aligned with the profit objectives of the private partners. The effectiveness of the alignment depends on a sufficient transfer of what is called ‘risk’ to the private partners [36].

There is currently no single definition of what constitutes a public-private partnership; the literature offers several possibilities (see Table 5). This lack of definitional clarity may result from the fact that PPPs ‘fill a space between traditionally procured government projects and full privatization’. The distinguishing feature is the focus on ‘partnership’. Some critics object to the use of the term ‘partnership’ in ‘public-private
partnerships’. They argue that partners share the same objectives whereas in a PPP, the public and private partners, given their different natures, do not: ‘the objective of the private sector is to make a profit, whereas governments deliver services to their citizens’. Undoubtedly, this is too narrow of an interpretation of partnership. It denies the reality of corporations acting as good corporate citizens [37]. The argument also brushes aside the fact that public sector work comes at the expense of taxpayers’ money. Moreover, while it is relatively easy for governments to measure their input in setting-up and running a variety of social and economic programs, governments often have great difficulty in measuring efficiency output.

Table 5: Definitions of Public Private Partnerships

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<td><strong>The OECD (2008)</strong> defines a public-private partnership (PPP) as an agreement between the government and one or more private partners (which may include the operators and the financiers) according to which the private partners deliver the service in such a manner that the service delivery objectives of the government are aligned with the profit objectives of the private partners. The effectiveness of the alignment depends on a sufficient transfer of risk to the private partners.</td>
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<td><strong>According to the International Monetary Fund (IMF, 2006:1 and 2004:4),</strong> PPPs refer to arrangements where the private sector supplies infrastructure assets and services that traditionally have been provided by the government. In addition to private execution and financing of public investment, PPPs have two other important characteristics: 1) there is an emphasis on service provision, as well as investment, by the private sector; and 2) significant risk is transferred from the government to the private sector. PPPs are involved in a wide range of social and economic infrastructure projects, but they are mainly used to build and operate hospitals, schools, prisons, roads, bridges and tunnels, light rail networks, air traffic control systems, and water and sanitation plants.</td>
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<td><strong>For the European Commission (EC, 2004),</strong> the term ’public-private partnership’ is not defined at the community level. In general, the term refers to forms of co-operation between public authorities and the world of business which aim to ensure the funding, construction, renovation, management and maintenance of an infrastructure of the provision of a service.</td>
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<td><strong>Standard and Poor’s definition of a PPP</strong> is any medium- to long-term relationship between the public and private sectors, involving the sharing of risks and rewards of multi-sector skills, expertise and finance to deliver desired policy outcomes (Standard and Poor’s, 2005).</td>
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<tr>
<td><strong>For the European Investment Bank (EIB, 2004:2),’ public-private partnership’ is a generic term for the relationships formed between the private sector and public bodies often with the aim of introducing private sector resources and/or expertise in order to help provide and deliver public sector assets and services. The term PPP is thus used to describe a wide variety of working arrangements from loose, informal and strategic partnerships, to design-build-finance-and-operate (DBFO) type service contracts and formal joint venture companies.</strong></td>
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The true advantage of PPPs is to be found in their ability to increase efficiency and to manage risk through cooperation between the stakeholders. PPPs can be situated on a spectrum that represents all possible combinations of public and private involvement in the various forms of service or goods delivery, classified according to the risk allocation between these parties (see Figure 7). In the case of products, the government typically sets the quality and quantity required, and allows the private partner to design and manufacture the asset (e.g. R&D facilities and production plants). Leaving the design to the private partner creates room for the public sector to improve the level of efficiency and cost-effectiveness of the ultimate service that must be provided (e.g. immunization). If the government prescribes the design or builds the asset, and assumes the role of innovator, it would have to carry the risk resulting from faulty design. Governments nowadays prefer to leave that risk, as well as the possible efficiency gains or failures, to the private partners. Firms will try to manage risk factors in such a way that actual outcomes diverge from the expected (or most likely) outcome. Managing risks in a competitive environment drives companies to be technically efficient (obtaining maximum outputs with minimum inputs), while at the same time being X-efficient (preventing the wasteful use of inputs).

Figure 7: Spectrum of Public Private Partnerships (PPPs)

Source: Adapted from Public Private Partnerships, OECD, 2008
6.2 Creating Effective Partnerships

*Blue box*

*Business as usual, government as usual; and perhaps even protest as usual are not giving us the progress needed to achieve sustainable development. Let’s see if we can’t work together to find better paths forward*[38].*

To understand important issues regarding the environment, climate change, health and so forth, and specifically the institutions involved in their governance, observers usually divide the associated organizations into three sectors: government, business, and civil society organizations (CSOs). No one sector has the capacity or legitimacy to solely address these challenges and find sustainable solutions because these challenges generally cross sectors. Consequently, the pressure on entrepreneurs and leaders in each sector forces them to work together in multi-sector collaborations; sometimes called cross-sector collaborative partnerships [39][40][41].

Cross-sector collaborative relationships (CSCR) represent a revolution in governance. Part of what is revolutionary is that the governance of CSCR is not ‘housed’ in any one of the collaborating organizations or sectors. The governance occurs ‘above’ the existing organizations and individual sectors. Another revolutionary aspect is that no one sector controls the governance. In different aspects of the project, one sector may provide more capacity or legitimacy than others. Overall no one sector dominates. Each sector needs the other, and each can stop the project by withdrawing. Executive decision-making is customarily done by consensus, rather than casting votes where the majority then wins.

Unsurprisingly, these sectors are defined by conflicting ideologies, different logic, and conceivably distrust of one another [42]. However, there has been much cross-learning over the past decade. Cross-sector communities will work only if organizations of each sector take the others’ values seriously. In that regard, business has come a long way in terms of corporate social responsibility (i.e. ecological standards, environmental protection, health and security, etc.). CSOs have come to understand the importance of value creation, as measured by efficiency and profit, in the business sector. Government sees its role as a convener and enabler of sound principles promoting sustainability as well as profit making.
GAVI was established as an alliance of governments, international organizations, donors, research organizations, firms and civil society working together to increase access to vaccination. The 27-seat board has one seat for the representative of the industrialized country firms, and one seat for the representative of the developing country manufacturers. Despite industry being a minority partner, this skewed distribution has proven to work well in the past. Every member of the board has a profound interest – at times shared with other stakeholders, at times competing - in the decisions of the alliance. In any event, in the end, this diverse group offers great potential for increased quality of group performance and innovative decision-making. Barder [43] claims that the benefits of having pharmaceutical companies engage in the GAVI alliance are obvious: “they understand the economics of their industry better than anyone else. If the partnership wants to figure out what needs to be done to get more vaccines produced for and distributed in developing countries, it has to work closely with the firms who have the funds and the expertise”.

The richness of the GAVI Alliance lies in the active participation of the main stakeholders. Board members engage in its governance through a process of balanced strategic decision-making, innovation and partner collaboration. Given its collaborative structure, however, conflicts of interest are an unavoidable reality in the conduct of GAVI’s operations, both in the Secretariat and Board. A conflict of interest in and of itself is not wrong and may not be unethical, but members of the Secretariat, Board, Advisory Bodies and others involved in decision-making processes on behalf of GAVI must take appropriate action to ensure disclosure of any actual, perceived or potential conflict of interest. The only solution can and must be that (potential) conflicts continue to be managed through GAVI’s conflict of interest policy and related discussion and decision-making procedures, which the Governance Committee viewed as being successful. As a result, GAVI will be able to properly manage any perceived conflict and thus mitigate the operational and reputational risks inherent in such conflicts.

6.3 Multi-Stakeholder Communication

It is important to understand the multi-stakeholder processes that occur within a public private partnership which aim to bring together all major stakeholders in a new
form of communication, consensus-building, and decision-making around a particular issue. The objective is to improve governance and sustainability and move organizations beyond deadlock and conflict. The increasing popularity of group-based decision-making reflects a widely shared belief that group decision-making offers the potential to achieve outcomes that could not be achieved by any of the individuals or organizations in isolation.

These processes inherently recognize the importance of achieving equity and accountability in the relationship between stakeholders by involving equitable representation of a number of stakeholder groups and their views. In theory, they are based on democratic principles of transparency and participation, and aim to develop partnerships and strengthened networks between stakeholders. When analyzing the potential problems that can emerge through diversity in public private partnerships from a social psychological perspective, stereotypes are of particular importance. Once stereotypical beliefs come into play, they affect people’s perception, attitude, and behavior [44]. Overcoming stereotyping and prejudice is therefore an important component of successful processes with highly diverse groups, which is, by definition, the case for a public private partnership. In many instances, the best strategy to overcome prejudice has proven to be getting mixed groups to work together as this can significantly contribute to reducing prejudice and improving relations between diverse groups.

Finally, it is important to note that membership of The GAVI Alliance does not exist in a vacuum, but depends on the cultural context [45]. NGOs, business and government are also cultures which (can) differ in regards to their background, beliefs and experience. The challenge for international strategic alliances such as GAVI is to move beyond traditional stereotypical expectations, enabling individuals and their constituency to become more aware of their own and others’ assumptions, beliefs and expectations. Effective leadership involves enhancing group performance and maintaining cohesion so that the partnership performs optimally.
7. CONCLUSION

There is no doubt that the private sector can play a significant role as a partner in defining global health and development strategies. The industrialized countries vaccine industry has an established track record of being an involved actor in continually providing vaccines with demonstrated safety and efficacy profiles to the populations of developed and developing countries. Being a key partner in The GAVI Alliance, innovation-driven companies collectively and individually are committed to increasing availability and access to vaccines, including those that are underused or newly introduced. For many years industry has supplied vaccines for use in the developing world at preferential prices negotiated through international agencies such as UNICEF, and is committed to further increase access to vaccines through equitable pricing. The GAVI Alliance which builds on a strong and long lasting partnership between industry, governments, public health authorities, and international organizations provides a sustainable pathway for making these ambitions come through.
8. REFERENCES


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