

# **SYNTHESIS REPORT: NEW VACCINE ADOPTION IN LOWER-MIDDLE-INCOME COUNTRIES**

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Results for Development Institute



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# Contents

Executive Summary.....	ii
Abbreviations and key terms .....	viii
1. Purpose.....	1
2. Methods.....	2
2.1. Contributors.....	3
2.2. Focus of the Study .....	4
2.3. Study Components.....	4
3. Decision-Making Processes for New Vaccine Adoption .....	5
4. Factors Affecting Vaccine Adoption.....	11
4.1. Broadly Important Factors .....	14
4.2. Factors Important in Multiple Countries .....	22
4.3. Other Factors.....	29
4.4. Potential Factors of Limited Importance.....	39
5. How These Factors Affect Adoption of Four New and Underused Vaccines .....	40
5.1. Hib Vaccine .....	41
5.2. Pneumococcal Conjugate Vaccine.....	41
5.3. Rotavirus Vaccine.....	42
5.4. Human Papilloma Virus Vaccine.....	42
5.5. Japanese Encephalitis .....	43
5.6. Summary .....	44
6. Manufacturer Interviews .....	44
6.1. Summary of Responses .....	44
6.2. Implications.....	45
7. Recommended Interventions .....	46
7.1. Priority One Recommendations.....	51
7.2. Priority Two Recommendations .....	58
8. Recommended Mechanisms for Interventions .....	68
8.1. Priority One Intervention Mechanisms.....	68
8.2. Institutional Roles in Implementation.....	75
Annex A. Study Protocol .....	78
Annex B. Individuals and Companies Interviewed.....	91
Annex C. Data on Lower-Middle-Income Countries and Selected Upper-Middle-Income Countries.....	105
Annex D. Quantitative Analysis.....	122
Annex E. Manufacturer Interview Questions .....	136
Appendix 1. Types of Economic Evaluation for Vaccine Introduction.....	140

## Executive Summary

Lower-middle-income countries (LMICs) receive little external support for their vaccination programs, despite a birth cohort of nearly 80 million and the burden of disease from vaccine-preventable diseases, such as *Haemophilus influenzae* type B (Hib) of which LMICs have 5.6 million cases out of 8.1 million cases worldwide.<sup>1</sup> The GAVI Alliance (Global Alliance for Vaccines and Immunization) assists 41 low-income countries (LIC), as well as some (31) at the lower-income end of the LMIC category.<sup>2</sup> As of 2010, most (86%) of the GAVI-assisted countries (whether LIC or LMIC) had adopted the Hib vaccine in their national immunization programs, but only 54% of the non-GAVI LMICs had done so. Two factors are set to exacerbate the divide between GAVI-supported countries on the one hand and most LMICs on the other. First, countries will begin to graduate from GAVI support as their gross national incomes (GNIs) per capita exceed the reassessed threshold of US\$1,500. When the new policy took hold on January 1, 2011, 16 countries began the process of graduating from GAVI support. Graduating countries will continue to receive support from GAVI's existing commitments for 5 years, though they will be required to fund all purchases of new vaccines from their national resources. Second, additional new vaccines are now on hand, and the countries that GAVI assists have the necessary help to adopt them; however, no such assistance is available for LMICs. For example, GAVI is offering support for the adoption of pneumococcal conjugate and rotavirus vaccines, and yet very few non-GAVI LMICs have adopted these vaccines. All of these vaccines are widely used by upper-middle-income countries (UMICs) and high-income countries. Thus children in LMICs have already fallen behind the rest of the world in their protection from vaccine-preventable diseases and are at risk of falling further behind.

Nevertheless, national immunization programs (NIPs) in non-GAVI LMICs perform well in delivering basic Expanded Program on Immunization vaccines to their birth cohorts. Coverage rates are high, with half of the 24 countries having coverage rates of greater than 90%. The programs are financially self-sufficient, since all costs are paid from national budgets. Thus there is a strong base to build upon.

In 2008, both the World Health Organization's (WHO) World Health Assembly and the Strategic Advisory Group of Experts on Immunization noted that little had been documented concerning the obstacles faced by LMICs in adopting new vaccines. They also acknowledged the importance of vaccinations in LMICs to reach global health goals and recommended that WHO investigate obstacles and mobilize resources for low- and middle-income country adoption of new vaccines.<sup>3,4</sup>

In response, the Bill and Melinda Gates Foundation funded and cochaired (along with WHO) the Advisory Group for this study in order to address these concerns. The Results for Development Institute implemented the study, which analyzed decision making concerning new vaccines, identified and classified factors that influence the decision-making process, and gathered information from vaccine manufacturers and global experts in immunization programs. The study focused primarily on vaccines

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<sup>1</sup> World Health Organization (WHO). Immunization surveillance, assessment, and monitoring: Under five Hib and pneumococcal deaths and cases by country [year] excel file [xls 265kb]. [http://www.who.int/immunization\\_monitoring/burden/Pneumo\\_hib\\_estimates/en/index1.html](http://www.who.int/immunization_monitoring/burden/Pneumo_hib_estimates/en/index1.html)[http://www.who.int/immunization\\_monitoring/burden/Pneumo\\_hib\\_estimates/en/index1.html](http://www.who.int/immunization_monitoring/burden/Pneumo_hib_estimates/en/index1.html). Accessed August 19, 2010.

<sup>2</sup> GAVI now assists 40 low-income countries (LICs) and 16 lower-middle-income countries (LMICs).

<sup>3</sup> WHO. Sixty-first World Health Assembly: Global Immunization Strategy (May 24, 2008). [http://apps.who.int/gb/ebwha/pdf\\_files/A61/A61\\_R15-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/A61/A61_R15-en.pdf). Accessed January 12, 2011.

<sup>4</sup> WHO. SAGE tracking sheet. [http://www.who.int/immunization/sage/2\\_Tracking\\_report.pdf](http://www.who.int/immunization/sage/2_Tracking_report.pdf). Published October 22, 2010. Accessed January 12, 2011.

for Hib, pneumococcal conjugate, rotavirus, and human papilloma virus. With its findings, the study identified practical interventions at three levels—global, regional, and country—to address the issues uncovered.

## Methods

The study employed both qualitative and quantitative analyses and benefited from the participation of stakeholders at the global, regional, and country levels. Data collection included semistructured in-depth interviews with 20 global vaccine experts; 23 representatives of 10 vaccine manufacturers (5 multinational corporations [MNCs] and 5 developing country manufacturers [DCMs]); and key informants from the public, private, and nonprofit sectors in 15 case-study countries (11 LMICs and 4 UMICs). The study's quantitative component analyzed the effects of quantitatively measurable factors on the historical adoption of the hepatitis B (Hep B) and Hib vaccines among LMICs and UMICs (see Section 2 and Annexes A, B, and D for more on the study's methods).

## Decision-Making Process in LMICs

Overall, LMICs try to take a systematic approach to deciding whether and when to adopt a new vaccine, but there are holes and weaknesses in their systems. Nearly every country studied has a National Immunization Technical Advisory Group (NITAG) or an equivalent body of national vaccine and vaccination experts that recommends vaccines for adoption, with the ministries of health (MoH) and finance (MoF) making final decisions, including budgetary allocations to ensure sustainability.

The deliberations often begin by noting the WHO recommendation concerning a vaccine. They then focus on the efficacy, cost, safety, and applicability of the vaccines to the burden of disease (BOD) in the specific country. Weaknesses to the approach include uneven access to national BOD data; variable ability to accurately interpret epidemiological data, including global estimates of BOD; and lack of skills and data to estimate and interpret cost-effectiveness ratios.

Once the NITAGs recommend a new vaccine for adoption, the decision of whether to accept the recommendation is also subject to difficulties. MoHs must balance the new vaccines against other priorities, which often involve a growing burden and visibility of noncommunicable diseases; a perception that high child mortality has already been solved; and health system issues, such as increased coverage by health insurance schemes. In addition, the consideration that MoHs and MoFs must give to costs and financing is beset by imperfections in the available information concerning prices, sources of supply, procurement options, and market dynamics for new vaccines.

The external partners (such as WHO and bilateral donors) that assist LICs with these issues through their in-country offices often do not focus on immunizations in non-GAVI LMICs. Thus they are of limited help, despite global and regional recommendations and advocacy for new vaccines by WHO and others.

The result of the systematic decision-making approach is a good intention to account for vaccine characteristics as compared with national BOD, cost-effectiveness relative to alternative uses of resources, and consideration for long-term financial sustainability. Unfortunately, flawed implementation of this intent often has the consequence of delays or misinformed decisions concerning adoption.

## Factors Influencing Decisions

The study collected data in the case-study countries on factors that have been hypothesized to influence vaccine decision making. The results fell into four categories: (1) factors important in every country studied, (2) factors important in many countries, (3) factors important in a limited number of countries, and (4) factors that were hypothesized to be important *ex ante* but found to be of limited importance.

As would be expected given the decision-making processes described previously, the study team found that BOD information, cost considerations (including price, cost-effectiveness, etc.), and WHO estimations of BOD and recommendations for use were important factors in every country studied (Section 4.1).

Other factors important in many countries (Section 4.2) included the following:

- Policies and engagement of global or regional bodies
- Procurement mechanisms
- Experiences of neighboring countries
- Strength of the existing routine immunization program

Factors that the study found to be important in a limited number of countries (Section 4.3) included the following:

- Local vaccine production (in countries with production capacity)
- Precipitating local events (such as outbreaks of vaccine-preventable diseases)
- Perception of vaccine safety
- Leadership by local champions and advocacy by other influential parties
- Experience of the private-sector vaccine market
- Progress toward the Millennium Development Goals

Factors that the study found to be of limited importance (Section 4.4) included the following:

- Vaccine characteristics (including presentation, cold chain, and other infrastructure requirements, as well as less traditional characteristics, including the injection schedule and location of production)
- Media influence

In addition to the information collected in the case-study countries, an analysis of the influence of variables that could be measured quantitatively regarding the adoption of Hep B and Hib showed the following to be positive influences in multiple analyses (see Annex D for details):

- Adoption by neighboring countries (Hep B adoption)
- Stronger basic NIPs (higher coverage)
- Being in the Americas Region
- Being in the Western Pacific Region (Hep B and Hib)

Other positive influences indicated in the quantitative analysis, but only in single analyses, were the following:

- GNI per capita (Hep B)
- Having a budget line item for vaccination (Hep B)
- Being in the Eastern Mediterranean Region (Hib)

## Manufacturer Views

The interviews conducted with vaccine manufacturers revealed some not-surprising and other apparently new attitudes concerning LMICs as markets. Manufacturers view LMICs as attractive markets, though manufacturers are organized to target marketing by geography rather than by income levels. Although the size of the LMIC market makes them attractive, manufacturers do not see a capacity problem in supplying them, as long as there is advance forecasting of when adoption will take place. According to the manufacturers, GAVI's success in "creating a market" is based in its strong procurement practices, including accurate demand forecasting, multiyear contracting, and assured funding.

An apparently new attitude is the support by manufacturers for pooled procurement by LMICs. DCMs see pooled procurement as giving them access to markets (just as GAVI's procurement through the UNICEF [United Nations Children's Fund] Supply Division has done), and MNCs appreciate the likely ease of procurement and forecasting that results from pools, as well as the ability for MNCs to maintain their tiered pricing approach. DCMs view themselves as disadvantaged when compared with MNCs in terms of the ability to produce and market new vaccines. DCMs are eager to see more technology-transfer agreements between themselves and biotechnology companies (biotechs), public health institutes, and MNCs. In addition, MNCs are interested in technology transfers with DCMs, provided that the agreements are based on "economics" (in terms of both a financial advantage to the MNCs and paying attention to the recipient's scale economics) and not on political factors (such as being required to transfer technology as a condition to supply a country). DCMs also see some LMICs discriminating against them in procurement by favoring longer-standing relationships with MNCs, even though the DCMs offer WHO-prequalified products.

The study team concluded from the manufacturer interviews that smaller-population LMICs are particularly structurally disadvantaged in their relations with manufacturers, since they lack bargaining power and information about prices, suppliers, and procurement options. Thus the smaller-population LMICs would be the greatest beneficiaries of joining a pooled procurement mechanism and having access to comprehensive information about vaccine markets, though pooled procurement would also be attractive to larger-population LMICs.

Many of the larger-population LMICs that have vaccine industries are likely to access new vaccines through technology-transfer arrangements with their local manufacturers. A disadvantage to technology transfers is that they take time that may delay new vaccine introduction if the countries are unwilling to source vaccines externally in the interim.

## Recommendations

The information gathered and analyzed by the study resulted in the identification of practical actions that could be taken at the country, regional, and global levels to assist LMIC immunization programs

perform to their full potential. The recommendations fell into four themes: (1) evidence and capacity building, (2) policy and advocacy, (3) financing, and (4) procurement and supply. The first theme addresses weaknesses in the NITAGs' technical assessment of the need for vaccines and in the availability of information concerning vaccine prices and markets as provided by MoHs and MoFs. The second and third themes address the priority given to immunizations at all levels and, in particular, to finding funding for them. The fourth theme takes up pooled procurement to enhance the ability of LMICs (in particular small-population LMICs) to operate in vaccine markets and to provide manufacturers with stable, predictable markets. Table 1 shows the highest-priority recommendations at each level in each theme area (see Section 7 for more information on these recommendations and for additional recommendations arising from the study). It is essential to note that funding must be provided for the implementation of all the recommendations, with external funding required particularly at the regional and global levels. Furthermore, an overall condition for the adoption of new vaccines is to ensure the basic strength of national immunization programs, thus ensuring that high coverage is attained with existing vaccines before taking on new ones.

**Table 1. Highest Priority Recommendations by Theme and Level**

<b>Priority One</b>			
<b>Theme</b>	<b>Level</b>		
	<b>Country</b>	<b>Regional</b>	<b>Global</b>
<b>Evidence and capacity building</b>	Strengthen epidemiological, surveillance, and economic analysis capacities	Actively promote and strengthen regional information sharing and joint research on burden of disease, pricing, cost-effectiveness, etc. (regional clearinghouse)	Create a technical and reliable source for global vaccine market information, including vaccine pipeline, vaccine prices, pricing policies, and procurement principles and practices
<b>Policy and advocacy</b>	Improve procurement regulation to promote competition, quality, and sustainability	Conduct advocacy to strengthen political will and support champions for new vaccines	Conduct advocacy to strengthen political will, regulation, and policy development
<b>Financing</b>	Take steps to increase domestic funding and capacities to negotiate with ministries of finance and other potential funders	Increase countries' and partners' awareness of the value of vaccination in the broader context of government investment and achievement of the Millennium Development Goals	Promote transparency and access to comparatively low and affordable vaccine prices with sustainable domestic financing
<b>Procurement and supply</b>	Consider using or joining a pooled procurement mechanism	Develop intercountry and regional processes for achieving pooled procurement (where desired by countries), vaccine quality, safety, and a diversified and sustainable base of supply	Support regional and country activities for efficient and effective procurement systems through assessment and identification of improvement to current practices and policies

## **Recommended Mechanisms for Intervention**

Among actors external to LMICs, WHO's stature and authority on health policy issues generally make it a natural key player in coordinating all three levels (country, regional, and global) of intervention, as well as in implementing many of the regional and global interventions. However, WHO should take advantage of the other actors that have comparative advantages in particular areas. Thus the study recommended that WHO facilitate and coordinate implementation through a partnership, network, or consortium of the actors best positioned to act. Most notably, individual MoHs should lead the country-level interventions. See Section 8 for detailed suggestions of implementers for each recommendation.



## Abbreviations and key terms

AEFI	adverse events following immunization
AMC	Advanced Market Commitment
ARV	antiretroviral
ASEAN	Association of Southeast Asia Nations
biotech	biotechnology (or biotechnology companies [biotechs])
BMGF	Bill and Melinda Gates Foundation
BOD	burden of disease
CDC	U.S. Centers for Disease Control and Prevention
CMR	child mortality rate
cMYP	comprehensive multiyear plan
DALY	disability-adjusted life year
DCM	developing country manufacturer (of vaccines)
DCVMN	Developing Country Vaccine Manufacturers Network
DTP	diphtheria, tetanus, and pertussis
DT	diphtheria and tetanus
EACIP	Experts Advisory Committee on Immunization Program
EMA	European Medicines Agency
EMR	Eastern Mediterranean Region
EMRO	Eastern Mediterranean Regional Office (WHO)
EPI	Expanded Program on Immunization
FCH	Family and Community Health
GAVI	GAVI Alliance (Global Alliance for Vaccines and Immunization)
GDP	gross domestic product
GNI	gross national income
GPO	government pharmaceutical organization
GPRM	Global Price Reporting Mechanism
Hep B	hepatitis B
Hib	Haemophilus influenzae type B
HIC	high-income country
HPV	human papilloma virus
IFPMA	International Federation of Pharmaceutical Manufacturers and Associations

IMR	infant mortality rate
JE	Japanese encephalitis
LIC	low-income country
LMIC	lower-middle-income country
MDG	Millennium Development Goal
MMR	measles, mumps, and rubella
MNC	multinational corporation
MoF	Ministry of Finance
MoH	Ministry of Health
NIP	National Immunization Program
NITAG	National Immunization Technical Advisory Group
NRA	National Regulatory Authority
NUV	new and underused vaccine
NVI	Netherlands Vaccine Institute
OECD	Organization for Economic Cooperation and Development
OLIVES	On-Line International Vaccine Economics and Statistics
ORT	oral rehydration therapy
PAHO	Pan American Health Organization
PATH	Program for Appropriate Technology in Health
Pneumo	pneumococcal conjugate
QALY	quality-adjusted life year
R&D	research and development
R4D	the Results for Development Institute
Rota	rotavirus
SAGE	Strategic Advisory Group of Experts on Immunization
SARS	severe acute respiratory syndrome
SIVAC	Supporting National Independent Immunization and Vaccine Advisory Committees
TD	tetanus and diphtheria
UMIC	upper-middle-income country
UNICEF	United Nations Children's Fund
USFDA	US Food and Drug Administration
VPD	vaccine-preventable disease
WAP	weighted average price
WHO	UN World Health Organization

# 1. Purpose

Although efforts by the international community, particularly through the GAVI Alliance, have led to more rapid introduction of new and underused vaccines in low-income countries (LICs), recent analyses indicate that lower-middle-income countries (LMICs)—with some exceptions in Latin America—are now lagging behind LICs in adopting newer vaccines.<sup>1</sup> Although LMICs have more resources, presumably enough to afford even the newer vaccines (given that they obtain attractive prices), they have received limited technical and financial support. There is concern that issues constraining LMICs may differ from those in GAVI countries and that an analytic and structured approach to cataloging and prioritizing those constraints is needed in order to provide a common basis for action (see Figure 1-1 for GAVI support among LMICs).

To help address this issue, the Bill and Melinda Gates Foundation, in collaboration with the World Health Organization (WHO), awarded a grant to the Results for Development Institute (R4D) to conduct a study to enhance global knowledge and understanding of the challenges that LMICs face as they explore adoption of new vaccines. The purpose of this study is to identify factors that play an important role in the decision-making process and outcomes for adopting new and underused vaccines in LMICs. These factors include constraints, as well as enabling factors and notable practices.<sup>2</sup> The goal is to identify practical interventions that address the issues uncovered and to suggest concrete strategies that can be taken at the global, regional, and country levels to implement the interventions in order to positively affect new vaccine adoption in LMICs. This is comparable to what GAVI has done for LICs but with less emphasis on direct financial assistance.

According to 2009 World Bank figures, the 54 LMICs hold about 55% (3.8 billion) of the world's population and have a combined annual birth cohort of 79 million. Excluding China and India, which account for more than half of this population, the remaining 52 countries still have a population and birth cohort of 1.3 billion and 35 million, respectively. All LMICs have adopted hepatitis B vaccine. In addition, by 2010, 44 countries had introduced *Haemophilus influenzae* type B (Hib) vaccine, 7 had introduced pneumococcal conjugate (Pneumo) vaccine, 6 had introduced rotavirus vaccine (Rota), and 4 had introduced human papilloma virus (HPV) vaccine.<sup>3,4</sup>

Correspondingly, WHO estimated that in 2000 (in 2004 for Rota), these countries had an estimated 5,576,912 cases of Hib (1,817,793 for the 10 countries yet to introduce Hib vaccine); 1,929,576 cases of *Streptococcus pneumoniae*; and 285,725 deaths due to Rota in the child (under 5 years of age) population. Recent global under-5 mortality for these diseases is 386,000 due to Hib; 826,000 due to Pneumo;<sup>5</sup> more

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<sup>1</sup> Hib Initiative. Update and transition plans. GAVI Alliance. NUVI Retreat; June 2009; Montreux, Switzerland.

<sup>2</sup> We use the term *notable practice* deliberately to indicate a practice that the authors think is useful for others to note, usually because it is a practice that produces desirable results. We do not use the term *best practice*, because we are not able to definitively state that the practice is better than all others.

<sup>3</sup> WHO. WHO Statistical Information System (WHOSIS). <http://www.who.int/whosis/en/>. Updated February 6, 2009. Cited December 9, 2009.

<sup>4</sup> WHO. Vaccine preventable disease monitoring system.

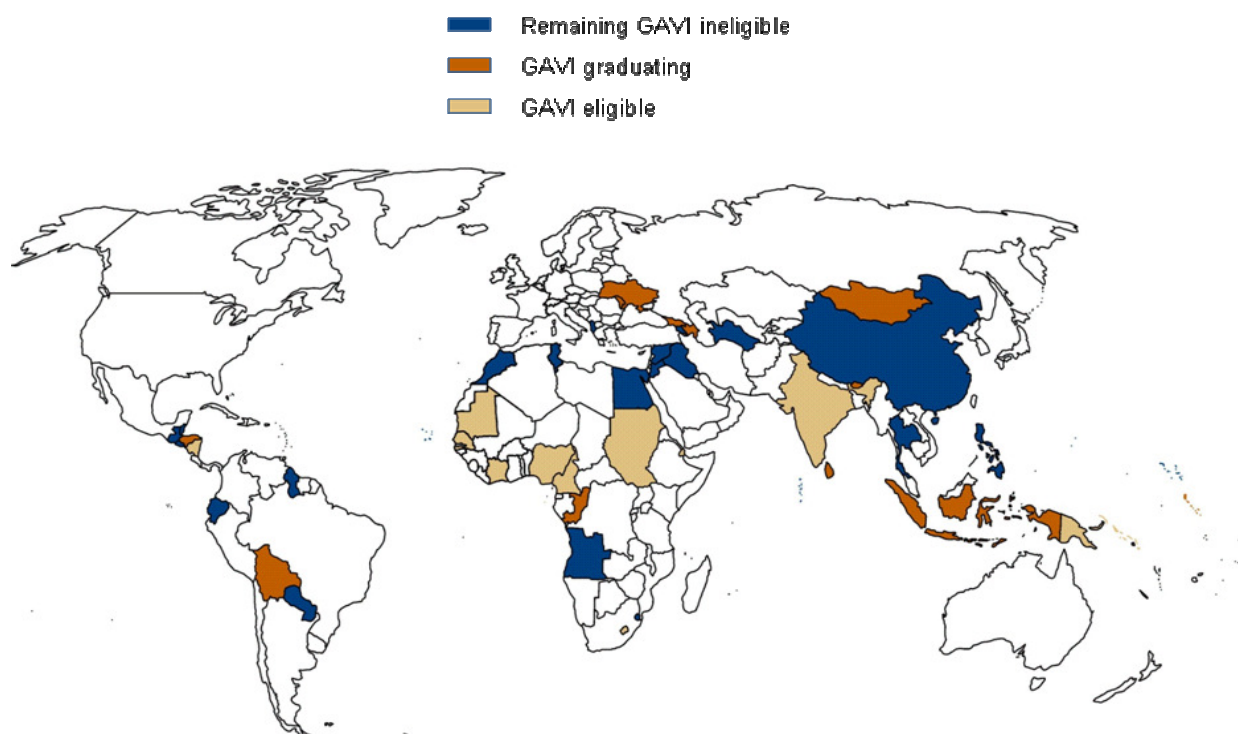
[http://apps.who.int/immunization\\_monitoring/en/globalsummary/scheduleselect.cfm](http://apps.who.int/immunization_monitoring/en/globalsummary/scheduleselect.cfm). Updated September 11, 2010. Cited October 5, 2010.

<sup>5</sup> WHO. Immunization surveillance, assessment, and monitoring: Estimated Hib and pneumococcal deaths for children under 5 years of age, 2000.

[http://www.who.int/immunization\\_monitoring/burden/Pneumo\\_hib\\_estimates/en/index.html](http://www.who.int/immunization_monitoring/burden/Pneumo_hib_estimates/en/index.html). Accessed August 10, 2010.

than 500,000 due to Rota;<sup>6</sup> and 288,000 due to cervical cancer resulting from HPV, with 80–90% of these deaths occurring in developing countries.<sup>7</sup> Although LMICs have reduced mortality as compared with LICs, the former does comprise most of the developing country population and is a large part of the potential impact for new and underused vaccines.

**Figure 1-1. GAVI Eligibility Among 2008 LMICs, 2011**



## 2. Methods

The narrative that follows uses the definitions below to categorize countries as lower-middle-income, upper-middle-income, and GAVI eligible.

Definitions of countries (2011)<sup>8</sup>:

1. World Bank lower-middle-income country (LMIC): 2009 gross national income (GNI) per capita (Atlas method<sup>9</sup>) of \$996–\$3,945.

<sup>6</sup> WHO. Immunization surveillance, assessment, and monitoring.: Estimated rotavirus deaths for children under 5 years of age, 2004; 527,000. [http://www.who.int/immunization\\_monitoring/burden/rotavirus\\_estimates/en/index.html](http://www.who.int/immunization_monitoring/burden/rotavirus_estimates/en/index.html). Accessed August 10, 2010.

<sup>7</sup> WHO. Human papilloma virus infection and cervical cancer. [http://www.who.int/vaccine\\_research/diseases/hpv/en/](http://www.who.int/vaccine_research/diseases/hpv/en/). Accessed August 10, 2010.

<sup>8</sup> World Bank. How we classify countries. <http://data.worldbank.org/about/country-classifications>. Accessed August 20, 2010.

<sup>9</sup> World Bank. World Bank Atlas Method. <http://data.worldbank.org/about/country-classifications/world-bank-atlas-method>. Accessed August 20, 2010.

2. World Bank upper-middle-income country (UMIC): 2009 GNI per capita (Atlas method) of \$3,946–\$12,195
3. GAVI eligible: GNI per capita (Atlas method) of less than \$1,500. Because of the overlap between LMIC classification and GAVI eligibility, 16 of the 56 countries that are eligible for new GAVI assistance in 2011 are LMICs. It should be noted that GAVI eligibility was reassessed on January 1, 2011. Before that date, the economic growth of some countries since the most recent evaluation of GAVI eligibility (in 2006) meant that 31 of the 72 GAVI-eligible countries were LMICs or UMICs.

Given these definitions, this study focused on LMICs that were not GAVI ineligible in 2010 and those that began graduating from GAVI support on January 1, 2011. Note that GAVI's policy is to honor multiyear commitments to countries that might extend beyond the date at which they lost their eligibility (for additional GAVI assistance). The study gave specific attention to those GAVI graduating countries.

## 2.1. Contributors

The study was conducted by a group from the Results for Development Institute (R4D), a nonprofit organization in Washington, DC, along with consultants and members of the Advisory Group (see below). Marty Makinen, principal and managing director, was the study director, while consultant Piers Whitehead and R4D principal and managing director Rob Hecht provided significant guidance to the project's design and implementation. Grace Chee and Farzana Muhib, both program officers at R4D, and Andy Tucker, a consultant, served as study coordinators at different times. Consultant Vivikka Moldrem conducted many of the country studies and drafted much of the synthesis report. Advisory Group members Rana Hajjeh and Miloud Kaddar contributed to country studies as well. Amrita Palriwala, program officer at R4D, conducted country studies and supported the broader study throughout. Consultants Sarah Schmitt, Sarah Goltz, Kun Zhao, and Julie Milstein, as well as R4D program associate Maria Belenky, also conducted country studies. Consultant Ken Carlson conducted the quantitative analysis, with supervision from Andy Tucker and Marty Makinen. Jessica Shearer reviewed the quantitative analysis. Kira Thorien and Lara Wilson, senior program associate and program associate at R4D, respectively, provided research and administrative support to the study at different times.

The R4D study was guided by an Advisory Group that consulted and provided critical feedback on the study protocol and recommendations. The Advisory Group had representatives from the following:

- Bill and Melinda Gates Foundation
- World Health Organization (WHO) headquarters
- GAVI Alliance
- Pan American Health Organization
- WHO: Eastern Mediterranean Regional Office
- UNICEF Supply Division
- Netherlands Vaccine Institute
- US Centers for Disease Control and Prevention
- International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)
- Developing Country Vaccine Manufacturers Network (DCVMN)

Annex A contains the full, original study protocol agreed upon with the Advisory Group. Some variances from the study protocol occurred during implementation—primarily in countries to be studied or visited—as circumstances dictated, with consensus of the Advisory Group.

## 2.2. Focus of the Study

The new and underused vaccines (NUVs) of primary interest to this study were for *Haemophilus influenzae* type B (Hib), pneumococcal conjugate, rotavirus, and human papilloma virus, though other new vaccines of specific interest in the case-study countries were also included. The study also looked at the experience of recent adoption of NUVs, specifically for hepatitis B (Hep B) and Hib, in countries, as well as other changes to the vaccine schedule. Although the study inquired about new vaccines in the private markets, this was primarily for the purpose of understanding any influence those markets played in the decision making and uptake of new vaccines in National Immunization Programs, which was the focus of the study.

## 2.3. Study Components

The study combined both qualitative and quantitative analyses, as outlined below.

### 2.3.1. Qualitative Analysis

The study primarily consisted of conducting in-depth interviews with the following (individuals interviewed are listed in Annex B):

- 20 global vaccine leaders and experts
- 23 representatives of vaccine manufacturers, both IFPMA and DCVMN members<sup>10</sup>
- Key informants in 15 country case studies (11 LMICs and 4 UMICs)

Of the 15 country case studies, 9 were in-country studies by R4D teams, which conducted face-to-face interviews with more than 10 key informants over 3–6 days. The R4D team conducted remote studies for the other 6 countries, targeting 4–6 key informants in each to interview by phone. The countries represent all regions and were selected to provide a picture of and examples from the variety of situations in LMICs, as well as examples and lessons learned in UMICs. Annex C provides available demographic, economic, and new vaccine information on all LMICs, with the studied countries (including the UMICs of Turkey, Panama, and South Africa) highlighted.

#### In-Country Studies

Armenia\*  
China  
Ecuador  
Egypt  
Indonesia\*  
Morocco  
Panama (UMIC)  
Thailand

#### Remote Country Studies

Albania (UMIC)\*\*  
Cape Verde  
Philippines  
South Africa (UMIC)  
Syria  
Tunisia

<sup>10</sup> IFPMA: Crucell, GlaxoSmithKline, Merck, Pfizer, Sanofi Pasteur; DCVMN: Bio Farma, Panacea, Serum Institute of India, Sinopharm

## Turkey (UMIC)

\* GAVI graduating country as of January 1, 2011.

\*\* Albania became a UMIC according to 2009 World Bank data. This ranking was finalized in July 2010 after the selection and completion of this study. Albania graduated from GAVI support in 2006, though it currently receives GAVI funding through a multiyear GAVI commitment from 2006.

The study team reviewed the reports from the interviews and case studies in order to develop the key findings (Sections 3–6), formulate recommendations for interventions (Section 7), and determine mechanisms for implementation (Section 8).

### 2.3.2. Quantitative Analysis

In addition, the study conducted a quantitative analysis that employed Kaplan-Meier curves and Cox proportional-hazards regressions. The Kaplan-Meier curves compare adoption of Hep B and Hib vaccines among low-income countries (LICs), LMICs, and UMICs, as well as across WHO regions. The Cox regressions employ time-to-vaccine-introduction for Hep B and Hib as the dependent variables and measurable factors hypothesized to influence adoption as independent variables. The independent variables include those grouped under the following headings: (1) economic, (2) programmatic/evidence based, and (3) social/contextual. The regressions were performed on data from (1) LICs and middle-income countries (MICs) together and (2) only MICs. Annex D provides a detailed explanation of this analysis, as well as the results, limitations, and practical implications.

## 3. Decision-Making Processes for New Vaccine Adoption

In the countries studied, one or more separate divisions within the Ministry of Health (MoH) is responsible for the national immunization program (NIP). However, at the service-delivery level, the program is integrated into primary health-care service delivery facilities that provide other services in addition to immunization.

Six of the countries studied have undertaken health-sector reforms within the past decade, and three have done so quite recently, all with the objectives of improving equality of access to basic health services, especially getting services into remote rural areas; enhancing the role of primary and preventive health care vis-à-vis tertiary care and specialized medicine; in some cases, decentralizing implementation responsibility to the district level and below; and in a few cases, initiating or expanding health insurance programs. In the countries that have decentralized systems, the central level maintains responsibility for determining vaccine policy, including the vaccine schedule; arranging financing and procurement; ensuring vaccine safety; and conducting awareness campaigns. Eight of the study countries<sup>11</sup> have or are developing national health insurance programs; however, only in Thailand has this significantly affected vaccine decision making.

Lower-middle-income countries (LMICs) face health problems characteristic of both developing and developed nations. Although mortality from communicable diseases has decreased dramatically—likely thanks to immunization, primary care improvements, improved water and sanitation, better overall nutritional status, and lower fertility—rates of chronic lifestyle diseases are on the rise. Childhood diseases are still important in these countries, and there is attention to achieving Millennium

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<sup>11</sup> China, Ecuador, Egypt, Indonesia, Panama, Philippines, Thailand, Turkey

Development Goal 4.<sup>12</sup> However, these health issues must now compete with heart disease, diabetes, hypertension, and cancer. The NIP's priority may be viewed as lower in LMICs than it is in low-income countries (LICs), where vaccine-preventable diseases are responsible for more child mortality and where access to donor assistance for immunization may provide significant resources and impetus for new vaccine adoption. In some ways, NIPs are victims of their own success, because they have made major contributions to solving a major portion of child mortality and morbidity issues.

The NIPs achieve generally high levels of coverage of the birth cohort (see Figure 4-1 for LMIC DTP3 coverage rates and a discussion of the exceptions). The programs have strong managerial capacity and perform in a predictable and sustainable fashion. When NIPs add new vaccines to the schedule, it is usually done without major disruption or problems (again, see Figure 4-1 for information on some exceptions).

In the countries studied, the minister of health plays a critical role. Sometimes the minister initiates consideration of a vaccine, while other times he or she responds to recommendations from experts within or independent of the ministry. The minister's role as advocate is very important in obtaining agreement from the ministries of finance and planning in order to plan and budget for the costs of adding new vaccines. The minister's background and interests, persuasiveness, and access to advocacy tools and information vary from country to country, which has an effect on vaccine decision making.

*"Ministries of Finance (MoF) are important actors to engage with and convince. If you have MoF support, then new vaccine adoption can be quick. Often the MoFs . . . are quicker to understand the cost-effective logic of preventions like vaccines."* —Marc La Force, interview with study team

The Ministry of Finance (MoF), or equivalent, buy-in is often crucial to ensure budget availability, though in many cases the MoH can make adjustments within its own budget to accommodate greater spending on vaccines and the NIP. In the cases of Panama and Ecuador, vaccine laws make mandatory the allocation of funds to support new vaccine adoption once recommended. As members of the Pan American Health Organization's (PAHO's) revolving fund, these two countries can count on obtaining competitive and stable prices. Informants indicate that MoF officials can be persuaded by strong burden of disease and cost-effectiveness information, as well as by solid documentation that shows the positive impact of previous immunization decisions. Planning for new vaccines up to 2 years or more in advance, so that they can be accounted for in government multiyear plans and budgets, including medium-term expenditure frameworks, may be helpful in obtaining budgetary resources and commitment.

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<sup>12</sup> United Nations. Millennium Development Goal 4 (MDG 4): Reduce child mortality (Target: Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate.) <http://www.un.org/millenniumgoals/childhealth.shtml>. Accessed August 20, 2010.



**Box 3-1. Notable Practice: Morocco's Early Engagement of Ministries of Finance and Planning**

Morocco's decision to introduce pneumococcal conjugate and rotavirus vaccines in 2010 was made possible largely because of the championing of the new vaccines by Her Royal Highness Princess Lalla Salma, who was partly motivated by the desire to meet the Millennium Development Goals. However, another contributing factor was an early and in-depth discussion between the Ministry of Health (MoH) and the Ministry of Finance (MoF), which concluded that the economic justification for the vaccines was solid. A key step was inclusion of these vaccines in the 2008–2012 National Health Plan. The MoH developed advocacy documents that showed graphically the burden of disease for the two diseases locally and regionally, the savings obtainable through prevention, and the projected cost for the vaccines. Although the study team found some flaws in the analysis, including absence of a cost-benefit study, the presentations were convincing enough to ensure first-year funding. The MoF and the Ministry of Planning (MoP) will need information on actual experience of vaccine introduction before making longer-term decisions. But in this case, the early, detailed, and continuous involvement of the MoF and the MoP expedited Morocco's new vaccine adoption.

Although the study countries' legislatures approve overall budgets for MoHs and often have committees that review budget proposals, they generally do not appear to have a significant decision-making role in new vaccine adoption. Instead, they rely on the government's technical expertise to determine priorities within overall budget approvals. In some cases, they have enacted legislation that ensures long-term sustainability of NIPs by making universal access to immunizations a mandatory obligation of government. In Latin America, where access to PAHO's Revolving Fund requires countries to have vaccine line items in their budgets, both Panama (2007) and Ecuador (1997) enacted national vaccine laws (as did a total of 20 countries in the Americas) to secure funding for Expanded Program on Immunization vaccines.

**Box 3-2. Notable Practice: Ecuador's Legal and Political Framework for Immunization**

Two key factors have contributed to the strength and stability of vaccine decision making in Ecuador: the 1997 Vaccine Law and the National Immunization Committee. The Vaccine Law guarantees the allocation of financial resources for the purchase of vaccines and stipulates that all imported Expanded Program on Immunization (EPI) vaccines be purchased through the Pan American Health Organization's Revolving Fund. This has allowed steady financial expansion of the program, despite political instability and changes in the national currency, thus ensuring sufficient resources and a transparent, secure mechanism for vaccine purchase. The National Immunization Committee was established in 2003 to bolster support for expansion of the routine immunization program and to engage former Ministry of Health leaders and key civil society groups in the decisions and execution of EPI. The committee has been an important source of political support for EPI in the recent, rapid introduction of new vaccines.

**Box 3-3. Notable Practice: Panama's National Vaccine Law**

Panama's National Assembly unanimously passed a national vaccine law (Number 48) on December 5, 2007. The law mandates that all new vaccines introduced in the vaccine schedule be universally available and mandatory for citizens to receive all their required vaccines. The law guarantees universal and free access through the Expanded Program on Immunization (EPI), mandates public-sector procurement through the Pan American Health Organization's Revolving Fund (with some exceptions), ensures public-sector support for cold chain and vaccine delivery programs, and prevents sale of EPI vaccines at a profit in the private sector. To ensure appropriate use of government resources, the law established and empowered a national vaccine advisory group (CONAPI) to evaluate new vaccines and to make transparent, evidence-based recommendations to the government.

In nearly every country studied, some kind of formal vaccine advisory group plays an influential role in vaccine decision making. Since 2008, the World Health Organization's effort to encourage countries to establish National Immunization Technical Advisory Groups (NITAGs) has begun to have an influence on these advisory groups. The aim is to make existing advisory groups stronger by making them independent and thus free from conflict of interest; officially recognizing them by decree or equivalent; increasing the depth and breadth of expertise in their membership; assigning them only an advisory role; and developing written defined roles, responsibilities, and operating procedures. Some, but not yet all, of the countries studied have NITAGs that meet these aims. Although a minister may decide not to proceed with a vaccine that has a positive recommendation from the advisory group, he or she will rarely decide to introduce a vaccine without the advisory group's recommendation. (In two countries, a new and underused vaccine was adopted prior to the creation of an immunization-specific advisory group—*Haemophilus influenzae* type B vaccine in Armenia, which used the ICC [Inter-Agency Coordinating Committee] as its advisory group, and rotavirus [Rota] vaccine in Panama, which made a political decision to be the first country to announce adoption of a Rota vaccine. However, both countries subsequently created advisory groups.)

These advisory groups have considerably more resources than analogous groups in LICs. They also have well-established mandates about how to make evidence-based decisions on new vaccine adoption. These decisions are often based on country-generated burden of disease and cost-effectiveness data, which is rarely available in LICs. Yet, unlike in upper-middle-income countries, LMIC surveillance systems are often of questionable quality and may mislead decision makers about the burden of disease (as is believed to have happened in Egypt).

Each vaccine advisory group in the study countries has the following characteristics:

- It is appointed and convened by the MoH and consists of experts in immunization, epidemiology, pediatrics, maternal and child health, infectious diseases, and logistics, who are from within the government and from the private sector, such as universities, hospitals, and other research organizations. Sometimes, other government departments, such as the National Regulatory Authority and the MoF, are included.
- It is tasked with making recommendations on new vaccines based on epidemiological considerations, particularly burden of disease, vaccine effectiveness and safety, and program feasibility. It may also make recommendations on the vaccine schedule and other programmatic issues.

- Table 3-1 summarizes the advisory groups that are in place in the study countries. Some of the vaccine advisory groups in the study countries have the characteristics shown in Table 3-2.

**Table 3-1 Applicability of General Advisory Group Characteristics to Study Countries**

Country	Name of Advisory Group	Description/Composition
Albania	Interagency Coordinating Committee	Ministry of Health (MoH), Ministry of Finance (MoF), Institute of Public Health, Pediatric Association, and other civil society organizations
Armenia	National Advisory Committee on Immunization	Researchers, academics, officials from MoH with technical expertise and representative of regulatory authority
Cape Verde	Immunization task force	Technical and decision-making personnel from government and hospitals; not an official, structured body with regular meetings; convened only when a vaccine is under consideration
China	Expert Advisory Committee on Immunization Program	Academics and researchers, representatives of China's Food and Drug Administration, selected because of their epidemiological expertise; provided strong support by MoH; lacks representation from health insurance
Ecuador	National Immunization Committee	Stakeholders from different sectors, including former ministers of health and civil society; emphasis has been on building political support for new vaccine introduction. As the National Immunization Program has solidified and expanded, membership is shifting to include greater technical expertise
Egypt	National Supreme Committee on Immunization	Diverse government representatives, including ministries of defense, interior, and finance; national regulatory authority; leading academic institutions, VacSera (vaccine producer)
Indonesia	Technical Advisory Group	MoH and physicians and researchers from around the country with epidemiological and pediatric expertise
Morocco	Comite National Technique et Scientifique de Vaccination	Composition is in transition
Panama	National Advisory Committee on Immunization Practices	MoH departments, including vaccine safety and school health, national health insurance, medical associations, national research institutes and hospitals, school of public health, Pan American Health Organization
Philippines	National Immunization Committee	Various departments in MoH, other federal and local governments, medical associations, other interest groups, World Health Organization (WHO), and UNICEF
South Africa	National Advisory Group on Immunization	Academic and research experts, ex officio representatives from MoH, WHO, and UNICEF
Syria	National Immunization Technical Advisory Group	Representatives from the government, universities, and the private sector, with varying expertise including Expanded Program on Immunization, laboratory analysis, regulatory affairs, pediatrics, and infectious disease
Thailand	Advisory Committee on Immunization Practice	Representatives from MoH and other government agencies, research and academic institutions, and individual nongovernmental experts
Tunisia	Comité Technique de Vaccination	Representatives from MoH, vaccination and pediatrics experts, and academics
Turkey	Immunization Advisory Committee	Infectious disease and pediatric experts from MoH, universities, and other institutions

**Table 3-2. Summary of Advisory Groups in Study Countries**

Country	It has resources to gather research and to commission research when local data are not available.	It has local cost-effectiveness data and members with economics skills.	International organizations, such as WHO and UNICEF, are formal members
Albania	X	X	X
Armenia	X	X	–
Cape Verde	–	–	X
China	X	–	–
Ecuador	X	X	X
Egypt	–	–	–
Indonesia	X	X	–
Morocco	X	–	X
Panama	X	X	X
Philippines	–	–	X
South Africa	X	–	X
Syria	X	–	–
Thailand	X	X	–
Tunisia	X	–	–
Turkey	X	X	–

X : The statement applies to the country

– : The statement does not apply to the country

#### **Box 3-4. Notable Practice: China Expert Advisory Committee's Evidence-Based Approach**

China's Experts Advisory Committee on Immunization Program (EACIP) uses a well-organized, thoroughly evidence-based approach to considering new vaccines. Because the committee is made up of experts from research and development in vaccine development, pediatrics, infectious diseases, immunology, health policy, statistics, and health law and ethics, not all committee members are aware of the full range of research results available for decision making. Prior to their meetings, the Ministry of Health's Communicable Disease Control Directorate supports members in developing a comprehensive compilation of the epidemiological research available on the vaccine to be considered. For example, before the 2008 decision to expand the routine immunization program, EACIP members identified more than 16,623 papers and documents related to vaccines against measles, mumps, rubella, meningococcal meningitis, Japanese encephalitis, and hepatitis A. Through a systematic review process and meta-analysis, 1,550 papers were selected according to predefined criteria, and 202 papers were analyzed in detail. Using these data, the EACIP analyzed the disease burden, epidemiologic characteristics, biological characteristics of the target vaccines, and supply and availability of vaccines. Data on disease-associated morbidity, mortality, disability, socioeconomic distribution, and public health burden were analyzed to facilitate prioritization of diseases and potential vaccines. This evidence-based exercise enabled the EACIP to identify the most important diseases and to prioritize vaccines to be added to the immunization schedule.

"The Role of the China Experts Advisory Group on Immunization Program," Zheng J, Zhou Y, Wang H, Liang X, National Immunization Program Department, Chinese Center for Disease Control and Prevention.

## 4. Factors Affecting Vaccine Adoption

This section discusses the factors that influence country decisions on vaccine adoption in order of priority, starting with broadly important factors critical in all countries; moving onto factors that are of strong importance in many, but not all, countries; then, other factors that play a role in many countries' decision making but that are more important in some than in others; and finally, factors that do not seem to be very important in any of the countries studied.

Lower-middle-income countries (LMICs) have been very successful in adopting *Haemophilus influenzae* type B (Hib) (45 out of 55 LMICs have adopted Hib), likely because of its convenient pentavalent presentation and the number of years that it has been available. Pneumococcal conjugate (Pneumo), rotavirus (Rota), and human papilloma virus (HPV) vaccines have been adopted by a smaller number of LMICs (7, 6, and 4, respectively). Table 4-1 summarizes the vaccines that study countries have adopted or are scheduled to adopt.

**Table 4-1. Year of (Projected) Uptake of Target Vaccines in Study Countries**

Country	Year of (Projected) Uptake			
	Hib	Pneumo	Rota	HPV
Albania	2009 (GAVI)	2010	Not under consideration	Will not be considered until after 2015
Armenia	2009 (GAVI)	Not under consideration	2012 (GAVI)	Not under consideration
Cape Verde	2011	Under consideration	Under consideration	Not under consideration
China	(some provinces)	Not under consideration	(some areas before 2000)	Not under consideration
Ecuador	2003	2010	2007	Under consideration
Egypt	Recommended but not funded	Not under consideration	Not under consideration	Not under consideration
Indonesia	2011	2013 (GAVI)	2014–2015	Not under consideration
Morocco	2007	2010–2011	2010–2011	2015
Panama	2000	2009	2006	2008
Philippines	2010	Not under consideration	Not under consideration	Not under consideration
South Africa	2008	2008	2008	Under consideration
Syria	2001	Under consideration	Not under consideration	Under consideration
Thailand	Decided against introduction	Not under consideration	Under consideration	Decided against introduction
Tunisia	2002–2005, 2011	Plan to introduce, though not scheduled	Plan to introduce, though not scheduled	Plan to introduce, though not scheduled
Turkey	2006	2008	Not under consideration	Not under consideration

The procedure used by the study team to categorize factors was as follows: First, a list was made of all hypothesized factors; other factors that arose in the course of conducting the country case studies and in the global expert interviews were later added to this list.<sup>13</sup> Second, the findings from the countries that fell under each factor were noted. If a factor showed up as important in nearly all of the countries (at least 11), it was put in the “broadly important” category. If a factor showed up as important in only a few of the countries, it was put in the “not very important” category. (See Table 4-2 for a representation of this categorization process.) In addition, the analysis of the hypothesized factors found in the qualitative

<sup>13</sup> The factors that arose in the course of the country studies were local events and MDG 4 progress. Both came up spontaneously from interviewees in some, but not all, countries in response to questions about factors influencing decision making.

country studies was cross-checked with the quantitative analyses performed. In many cases, the quantitative analysis tended to confirm the qualitative findings.

The study team found that given the information and budgetary resources available to LMICs, their decision making is deliberate and rational. Key decision makers are open-minded and ready to be persuaded. If they have not adopted new vaccines, it is because they do not have or are not allocating the resources required by the new vaccines. The team found only one country (Thailand) that had determined that a new vaccine (Hib) was not appropriate, and this decision was based on data and analysis of burden of disease (BOD), costs, and alternatives. (The team considered Thailand's analytical process a notable practice and have described it further in Box 4-2) Other countries have decided to introduce several years in the future (Morocco plans to introduce the HPV vaccine in 2015) or dependent upon confirmation of local BOD and financial sustainability (Armenia may introduce the Rota vaccine in 2012). Because of information gaps, LMICs would benefit from resources, tools, and information to help them obtain the data they need to make decisions, including cost-effectiveness data. Efforts should not be focused on one particular vaccine but on all major vaccine-preventable diseases so that LMICs can accurately prioritize their own needs.

*"We should be changing the framework for our work so that we are helping countries get the vaccines that they want, not promoting vaccines that we think they need."* —Richard Mahoney, interview with study team

**Table 4-2. Summary of Key Factors Affecting Study Country Decision Making by Country**

Country	Broadly Important Factors			Factors Important in Multiple Countries			Other Factors					
	Epidemiology	Cost-Related Concerns	WHO BOD			Engagement	NIP	Local production	Local	Perceived	MDG	Private

		Cost-effectiveness	Budget resources devoted to vaccines	Price		Neighbors' experience	UNICEF, PAHO, or GAVI procurement		Champions						
Albania	X	X	X		X		X	X		X					
Armenia	X	X	X	X	X	X	X						X		X
Cape Verde	X		X	X	X	X	X	X		X		X		X	
China	X	X	X	X	X	X					X	X	X		
Ecuador	X		X		X		X	X							
Egypt	X	X	X	X							X				
Indonesia	X	X	X		X						X				
Morocco	X			X	X			X	X					X	
Panama	X	X			X	X	X		X						
Philippines	X	X	X	X	X		X								
South Africa	X	X	X		X	X			X	X		X		X	X
Syria	X	X	X	X	X	X		X							
Thailand	X	X		X	X										
Tunisia	X			X	X										
Turkey	X	X	X		X	X			X				X		
Total X's	15	11	11	9	14	7	6	5	4	3	3	3	3	3	2

Note: Factors that the study team found to be of little importance (vaccine characteristics and role of media) are not included. For countries with a strong preference for procuring vaccines from local production (China, Indonesia, Egypt), both cost and local production are checked, though local production enables them to control costs to some extent.

## 4.1. Broadly Important Factors

From the country studies, three factors arose as highly important in the decision-making process of most (at least 11) countries studied: (1) epidemiological considerations, including burden of disease and vaccine effectiveness; (2) cost-related concerns; and (3) World Health Organization (WHO) findings on the global BOD and recommendations. From the quantitative analysis, one other factor is notable in its association with earlier adoption of hepatitis B (Hep B), but not Hib, adoption: gross nation income (GNI) per capita. In other words, higher income per capita was statistically associated with more rapid adoption of Hep B.



#### 4.1.1. Epidemiological Factors: Burden of Disease and Vaccine Effectiveness

The findings from the country studies and expert interviews indicate that decision makers give primary importance to BOD considerations.<sup>14</sup> Evidence of strong BOD and the potential impact of immunization is the first factor an immunization advisory committee needs to assess, before examining cost and programmatic issues. A recent study by the Sabin Vaccine Institute regarding Rota vaccine adoption in three countries reinforced this finding. The Sabin study concluded that “disease surveillance is key to defining severity of illness and mortality, and encouraging demand for the introduction of a vaccine.” In addition, “clinical trials in the local setting are an important means of defining the value of the vaccine and encouraging local support and demand for it.”<sup>15</sup> It must be noted, however, that epidemiological factors alone are rarely enough to ensure vaccine introduction (for example, financial considerations often weigh in). In addition, it is crucial to ensure that surveillance studies are well conducted and have adequate laboratory support; otherwise, they can result in low estimates that will lead to a perceived low BOD at the country level.

If convincing BOD data from country-level studies or from neighboring countries are lacking, immunization advisory groups generally withhold their recommendations. This does not appear to be a delay tactic. Rather, it seems to reflect legitimate questions that technical experts raise about the disease and the potential vaccine’s effectiveness.

Large-population countries and those with strong academic and research communities are more likely to have access to country-specific studies than are small-population countries.

- South Africa (an upper-middle-income country [UMIC]) has a wealth of data from its many high-quality research and medical institutions and therefore has no difficulty obtaining BOD data. In particular, it hosted a pivotal trial that produced overwhelming BOD data that supported the decision to adopt the Pneumo vaccine.
- Chinese researchers and institutions, including government agencies and vaccine manufacturers, conduct ongoing research on all the focus vaccines of this study, though they are not always aware of each other’s work. (Lack of knowledge of the range of research taking place may be an issue in other countries as well.)
- Turkey (a UMIC) has some in-country studies available, and vaccine manufacturers are willing to fund BOD research. Although the vaccine manufacturer’s funding can be valuable, it comes with a perception that the research might not be impartial.
- Indonesia is able to call on its donor partners to fund BOD studies and, as a matter of course, undertakes a pilot study of any vaccine being considered for introduction before its technical advisory group will make a positive recommendation.
- Thailand has multiple well-regarded research universities, and the Ministry of Health (MoH) has developed and now funds its own capacity in-house with the Health Intervention and

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<sup>14</sup> The regression analyses showed no significant relationship between having burden of disease (BOD) information and Hib or Hep B vaccine adoption, however.

<sup>15</sup> Walsh J, Mitu A. The critical path for vaccine introduction: an analysis based upon the rapid introduction of rotavirus vaccines into Mexico and Brazil. Report for the Sabin Vaccine Institute; November 2006; Berkeley: University of California. It is notable that Mexico received support from the US Centers for Disease Control and Prevention (CDC) for development of its surveillance system. This is a valuable resource that the CDC provides globally, though there are other sources of technical support, and some LMICs can conduct adequate surveillance and related epidemiological studies on their own.

Technology Assessment Program. The MoH also helps find additional outside funding and partners.

- Panama (a UMIC) and Ecuador both generate their own BOD relevant to decision making and have benefitted from support by the US Centers for Disease Control and Prevention (CDC) for laboratory surveillance on serotyping. Panama has also hosted vaccine trials for Rota and HPV vaccines.

Smaller countries and countries with fewer research institutions and resources to draw on may have to rely on BOD information and studies from neighboring countries when country-specific epidemiological data are not available.

- Armenia seeks BOD and vaccine effectiveness information from both Western European and former Soviet countries.
- Cape Verde has limited access to BOD data from neighboring countries and relies on WHO recommendations.

#### **4.1.2. Cost-Related Issues**

The prices of new vaccines are, not surprisingly, important to the decision to adopt. However, it is not a simple question of the price per dose or vaccine cost per fully immunized child. Rather, prices enter into decision making in a multiplicity of interrelated ways (see Table 4-2 for a summary of how the countries studied use price and cost data). The following points (each of which is elaborated upon later in the section) illustrate the many issues related to prices and decision making:

- Price of new vaccines relative to the prices that countries are used to paying for other vaccines
- Uncertainty and speculation about the future level of prices (e.g., “We expect the price to be lower in a few years.” or “We are unsure whether the price we get this year will be similar to the prices we’ll get over the next few years.”)
- The price available to the country versus the price paid by GAVI (e.g., “We would like to be able to pay a price similar to that paid by GAVI (not the price GAVI countries pay through cofinancing.”)
- How a country would know whether it is getting a “good” price compared with other countries
- Price in how it makes the vaccination intervention compare with other interventions (i.e., through explicit or implicit cost-effectiveness analysis, with comparisons to costs of treatment, cost-effectiveness of other vaccines, or cost-effectiveness relative to other health spending)
- How adding the vaccine to the current set of vaccines would change the National Immunization Program (NIP) budget
- Whether securing funding to meet the current price would be able to be sustained
- Price per dose compared with price per course and related costs

The new vaccines are all considered (correctly) to be more expensive (that is, to have higher prices) than those already in the NIP schedules. However, many of the countries have neither accurate price information nor reliable sources to obtain such information. Thus some countries are operating under mistaken assumptions about what prices (both higher and lower) are possible to obtain.

Some countries think that the prices of new vaccines will fall substantially if they wait a few years, while others believe that prices will remain about where they are. Still others are concerned that the prices they will be able to obtain will vary considerably (both down and up), such that the budgetary requirements

will vary considerably. A number of the countries studied said that they hope to be able to obtain prices for new vaccines that are close to the prices paid by GAVI (through UNICEF's Supply Division) for the vaccines that GAVI supplies to countries that it supports (with cofinancing from those countries). This hope was expressed as a desire to pay "GAVI-like" prices; the notion is that GAVI probably pays the lowest prices available, so that a price close to that paid by GAVI would allow the country to pay only a small amount above the lowest possible.

Larger and more-experienced (in terms of procuring vaccines) countries are confident that they can and do obtain low prices for their vaccine purchases on the world market. Other countries—usually those that are smaller and less experienced—worry that they do not know how to obtain favorable prices and thus would like to be able to use a procurement mechanism, such as the UNICEF Supply Division, the Pan American Health Organization's (PAHO's) Revolving Fund, or a similar mechanism, to be sure they are getting appropriate information, quality products, and good prices. Countries that are members of the PAHO Revolving Fund or that work with UNICEF Supply Division feel comfortable that they are getting good prices.

Many of the study countries responded that they would like to have cost-effectiveness data or be able to do locally specific cost-effectiveness analyses. Thailand stands out as a country that has a substantial national capacity to conduct cost-effectiveness and related analyses that are used explicitly in decision making for new vaccine adoption.<sup>16</sup> Although many interviewees in other countries expressed a wish for cost-effectiveness data for decision making, few could articulate how these analyses might be used. There appears to be an awareness that cost-effectiveness data could be helpful in making a case with decision makers and those holding budgets; however, for many, the specifics of how cost-effectiveness analyses are done—as well as the alternative methods for such an analysis (such as including or excluding indirect costs and cost savings) and the different kinds of questions (comparisons among vaccines, comparisons with other health interventions) that the alternatives can answer—are still hazy. This is mirrored by the uneven inclusion of people with analytic cost-analysis skills on immunization advisory committees. The finding that many countries see the epidemiological burden being more morbidity than mortality for the diseases prevented by Pneumo, Rota, and Hib vaccines indicates the potential importance for the immunization costs (including vaccine prices) to be compared with costs of treatment in the analyses performed. For example, Tunisia benefited from a cost-effectiveness analysis, conducted with UNICEF and WHO assistance that compared Pneumo, Rota, and HPV vaccines; the result was a strong consensus around the priority order for the adoption of the vaccines. Panama, however, is an exception to the desire for cost-effectiveness data as a part of decision making. Panama informants consider epidemiological data and cost data to be sufficient, without more sophisticated analysis. One interviewee responded, "We don't believe in paralysis through analysis."

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<sup>16</sup> Thailand uses a threshold of less than 1 gross domestic product (GDP) per capita per disability-adjusted life year (DALY) to judge whether any health intervention should be funded. It is the only one of the studied countries to report a specific cost-effectiveness threshold.

**Box 4-1. Notable Practice: Thailand's Use of BOD and Cost-effectiveness Data for Rational Vaccine Decisions**

A strong, evidence-based decision-making process may lead a country to determine that a new vaccine, even one recommended by the World Health Organization (WHO), may not be appropriate.

Thailand bases its vaccine adoption decisions on careful deliberation by the Department of Disease Control, through its Advisory Committee on Immunization Practice. These deliberations are based primarily on technical factors and, secondarily, on cost issues. After review, Thailand decided not to introduce the *Haemophilus influenzae* type B (Hib) vaccine in 2008, despite the 2006 WHO/Strategic Advisory Group of Experts on Immunization's universal recommendation, because rates of invasive Hib disease were much lower locally than in global and regional estimates (3.8 per 100,000 as opposed to the 40–50 per 100,000 estimated by WHO). Thus the rates did not justify the intervention, particularly considering the availability of relatively cheap treatment for most Hib disease.

Similarly, a recent study of rotavirus (Rota) in Thailand found that mortality is quite low compared with WHO estimates. Cost utility has also been studied with an outcome in the range of 1–3 gross domestic product (GDP) per capita per disability-adjusted life year (DALY) from a social perspective. (Generally, Thailand considers less than 1 GDP per capita/DALY to be cost effective.) This has convinced some, but not all, about adopting the Rota vaccine, especially since oral rehydration therapy and other clinical care have reduced mortality to such a low level.

Since the prices of the new vaccines are substantially higher than those already in NIPs, the impact of adding the new vaccines to the programs in terms of percentage increases in budgets is often great. Many of the countries studied said that this type of comparison is often made: “The budget would have to increase by 40%!” However, it is rare to nonexistent for decision makers to compare the changes in vaccine spending with the overall health budget, and even rarer for fiscal space analysis to be conducted.

**Box 4-2. Notable Practice: Thailand's Incorporation of Immunization Program Into National Health Insurance**

Thailand has achieved universal health coverage through three national insurance programs—the civil servant benefit scheme; the social security scheme, in which government, companies, and employees share the cost of premiums; and the national health insurance plan, which covers all others and is run by the National Health Security Office (NHSO). Individuals' vaccine costs (both routine immunization and epidemic-related, such as flu) are covered by their insurance plans. The Ministry of Health recommends and obtains budget approval for new vaccines; however, since the entire Expanded Program on Immunization's (EPI's) vaccine budget is included in the NHSO's budget, ultimately NHSO approval is needed to implement. NHSO approval requires that a convincing case be made for vaccines as a good investment and use of limited resources. Although this process complicates decision making, it strengthens sustainability.

Related to the issue of a change in the NIP budget required by adding new vaccines is the question of the sustainability of financial support. Because NIPs frequently receive their funding on an annual basis,

there is some worry that even if funding is found for the first year or two of a new vaccine, the ability to sustain the increased funding would be uncertain. Countries that have either budget line items for their immunization programs or an immunization law (such as in many of the countries in the Americas) feel more confident about sustainability. The regression analysis showed a significant relationship between budget line items and adoption of Hep B (but not Hib) in middle-income countries (MICs). In the case of Cape Verde, a smaller country at lower GNI per capita, it was proposed that external financial support be offered to introduce a new vaccine on a declining basis for a few years, so that national funding could be increased gradually to attain full national funding and then be sustained. However, the more common assumption is that all vaccines will be purchased from domestic resources, as are all of the vaccines currently in the NIP. Even those countries whose GAVI funding will decrease dramatically between now and 2015 (such as Albania and graduating Armenia and Indonesia) are already self-financing the majority of their programs.

In addition to how the new vaccines directly add to the NIP budget<sup>17</sup> is the question of nonvaccine costs associated with the adoption of new vaccines. For example, in Panama, the NIP spent the past 3 years trying to find US\$20 million for cold chain improvements, finally seeking donations from manufacturers to support this and promotion campaigns.

In some countries, all vaccine needs, both short- or long-term, must be met from the same budget. This situation forces some trade-offs within NIPs when outbreaks or threats of outbreaks crop up. For example, in Cape Verde, although the adoption of both Pneumo and Rota vaccines is planned, the threat of yellow fever spreading from neighboring countries is a more immediate concern that may delay their introduction. In Tunisia, in order to stockpile Tamiflu in preparation for a potential epidemic, the MoH took the funds from what had been budgeted for the Hib vaccine.<sup>18</sup>

To sum up, price is an important factor in a variety of ways. Countries want to know what prices are available; they want to be sure they are getting competitive prices; they would like to have a better idea of future price paths; they want prices to be predictable; and they feel that participating in international procurement efforts would give them predictability. They would also like to be able to better analyze cost-effectiveness and use the results of the analyses in decision making and advocacy; however, they do not fully grasp what this means in all cases. They tend to compare the resources needed to purchase new vaccines with NIP budgets rather than with MoH budgets, or to analyze the resources in terms of overall fiscal space; they are sometimes forced to meet short-term needs and delay longer-term adoption decisions; and they are concerned about the sustainability of financing.

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<sup>17</sup> One way to minimize the impact of a new vaccine on the National Immunization Program (NIP) budget is to get another source of funding to pay for it. A few of the countries studied have arranged to have health insurance programs make the costs of some vaccines reimbursable (see Box 4-2). For example, China has experimented with providing insurance coverage for influenza vaccination.

<sup>18</sup> Information from study team interview with global expert Rana Hajjeh, February 16, 2010. Since Tunisia used monovalent Hib, this was relatively easy to do.

### Box 4-3. Vaccine Prices

Vaccine prices are one of several factors influencing the decision to adopt. Other factors include burden of disease (BOD), presence of an influential champion for adoption, experiences of neighboring countries, budget availability, reliability of supply, and costs of treatment. Prices rank with the BOD as the most important influences on adoption, though the adoption decision is made in the context of the interaction of all the factors. For example, if the BOD is high—in particular the mortality burden—then price becomes less important. If government funding or funding for the health sector becomes relatively plentiful, then price is less important. Domestic production, which ensures the reliability of supply, can also make price less important for large-population countries. Low mortality burden and low cost of treatment can make price a more important factor, since the cost-effectiveness ratio is less favorable. The presence of a strong champion can make price less important.

The prices for vaccines available to lower-middle-income countries (LMICs) are the result of a complex set of factors, including the number of qualified manufacturers offering the vaccine and factors related to the country's procurement practices, birth cohort size, and per capita income.

For a given vaccine, the more acceptable manufacturers that are available and the greater their capacity to produce, the lower the prices in the marketplace will be. The entry of additional developing country manufacturers (DCMs) of hepatitis B (Hep B) vaccine and the widening of the market for Hep B through GAVI purchases for low-income countries significantly lowered its price in the mid-1990s, from about US\$7 to about US\$0.30 per dose.<sup>1</sup> The entry of a second industrialized country manufacturer in 2007 and two DCMs in 2008 into the production of the *Haemophilus influenzae* type B (Hib) vaccine started a downward path for the price paid by UNICEF Supply Division for GAVI after several years of relative stability. The weighted average price paid by UNICEF Supply Division for Hib-containing pentavalent vaccine was close to US\$3.50 per dose throughout 2001–2009, and then fell to US\$2.97 per dose in 2010. GAVI estimates that the cost will be US\$2.58 per dose in 2011.<sup>1</sup> The limited number of manufacturers of rotavirus, pneumococcal conjugate, and human papilloma virus vaccines are likely to keep the prices available for those vaccines relatively high until there are new entrants. This supply situation limits LMIC negotiating power and places a premium on strong planning and procurement practices to maximize the bargaining power that remains.

Given the above and the general landscape for prices that is set by the number and production capacity of prequalified producers, other factors also influence the prices available to LMICs. Countries that use predictable, transparent, longer-term, and well-informed procurement practices (see Box 4-4) improve their chances of obtaining more favorable prices. Countries that have bigger birth cohorts can use their purchasing power to obtain discounts. Smaller birth cohort countries can join pooled procurement mechanisms to obtain volume discounts. The willingness of vaccine manufacturers to tier prices should allow countries with lower per capita incomes to obtain lower prices for vaccines than those that prevail in rich countries.

#### **Box 4-4. Examples of Favorable Procurement Practices**

Countries using predictable, transparent, longer-term, and well-informed procurement practices can obtain the most favorable prices for new vaccines. Following are the recommended practices in each of these categories.

##### **Predictable procurement:**

- In cases where vaccine prices are not expected to rapidly decline due to greater supply, make, implement consistently, and update regularly multiyear plans for the national adoption and routine use of vaccines (use the WHO-UNICEF comprehensive multiyear plan template or a similar approach)
- Plan for, purchase, and maintain a buffer stock of vaccines to smooth out variations in the number of doses used and procured
- Use standard vaccine schedules, presentations, and vial sizes

##### **Transparent procurement:**

- Publish multiyear plans, updates, and immunization program performance information
- Share information concerning vaccine prices, contract length and terms, and other procurement information with other countries regionally and globally
- Make vaccine registration transparent, rapid, and as easy as possible to ensure quality and safety (consider a “fast track” registration for WHO prequalified vaccines)
- Open procurement to all manufacturers of registered WHO prequalified vaccines (that is, do not require an in-country presence)
- Allow sufficient time between the call for tenders and the due date so that manufacturers have time to prepare their bids

##### **Longer-term procurement:**

- Consider entering into multiyear procurement contracts with manufacturers in return for discounted prices
- Consider asking for bids for 1-, 2-, and 3-year contracts (with discounts for the longer terms) so that the trade-offs can be compared; similarly, consider offering different volume commitments (shares of the market), again so that trade-offs can be compared

##### **Well-informed procurement:**

- Gather information about the prices and contract conditions (length of contract, options for purchasing more or less than the base number of doses, presentations and vial sizes, other services included in the contract, etc.) obtained for the same vaccine by other countries of similar size of birth cohort and per capita income level
- Gather information concerning which manufacturers are prequalified and when others can be expected to enter the market
- Gather information about the availability and cost of alternative sources for any technical assistance needed for new vaccine introduction, outside of the assistance offered by vaccine manufacturers
- Ensure that procurement staff have training and skills in working in vaccine markets or obtain needed training from UNICEF Supply Division or WHO
- Use the information gathered to negotiate the best arrangement in terms of price, reliability, and safety

**Table 4-3. Study Country Use of Price and Cost Analysis**

Country	How price and cost data are used in decision making
Albania	Reviews price data; decision makers were aware of a cost-effectiveness analysis for <i>Haemophilus influenzae</i> vaccine.
Armenia	Price and affordability are reviewed; cost-effectiveness data are not available.
Cape Verde	Price and related increase in the immunization budget for adding a new vaccine are considered; use United National Children's Fund (UNICEF) procurement services.
China	Price is reviewed; cost-effectiveness is reviewed if data are available.
Ecuador	Price is not an issue if the vaccine is determined to be needed; access to Pan American Health Organization (PAHO) Revolving Fund ensures price stability.
Egypt	Price is important (but accurate information on prices is not available); cost-effectiveness is also considered. Ministry of Finance (MoF) is represented on immunization advisory committee.
Indonesia	Cost-effectiveness analysis is standard practice. Price is controlled through purchase only from local manufacturer at agreed-upon prices.
Morocco	Price and budgetary impact are considered within Ministry of Health and when negotiating with MoF. Use UNICEF procurement service.
Panama	Price is considered (availability through PAHO Revolving Fund); cost-effectiveness is not generally a factor.
Philippines	Price is considered; use UNICEF procurement service .
South Africa	Considers cost-effectiveness and has ample access to cost-effectiveness data.
Thailand	Uses cost studies; considers cost utility and cost-effectiveness.
Tunisia	Cost-effectiveness analysis is an important factor in setting priorities.
Turkey	Price and budgetary impact are reviewed.

#### 4.1.3.WHO Estimation of Global BOD and Recommendations on Use

All countries take notice of WHO's estimates of global BOD for communicable diseases and its recommendations. Although WHO's recommendations alone are not sufficient to convince LMICs to adopt new vaccines, they do provide the impetus for further consideration. Countries that do not have access to local BOD studies rely heavily on WHO recommendations. Most study countries require in-country studies, or at least strong evidence from similar neighbors, before making a positive recommendation on a new vaccine, and this is especially true with Pneumo and Rota vaccines, for which the WHO recommendations are qualified, depending on local BOD. One country expressed the view that WHO recommendations are becoming complex to understand and implement.

## 4.2. Factors Important in Multiple Countries

This section discusses factors that considered by many countries but that for most countries are not as critical as those discussed in Section 4.1.

#### 4.2.1. Engagement by Global and Regional Bodies

Global and regional bodies play a more important role in some countries than in others. Their influence is greater in countries and regions where they undertake strong advocacy efforts, especially if these efforts are accompanied by technical assistance and financial resources.



- PAHO has a large influence on vaccine adoption in Latin American countries such as Ecuador because it provides invaluable technical, pricing, and logistical resources. The Ecuador immunization team relies solely on PAHO and the organization's regional meetings for its information and technical decision-making resources for new and existing vaccines. In addition, PAHO organizes regional advocacy events, such as "Vaccination Week in the Americas," and mobilizes high-profile people, such as heads of state, to go to isolated rural areas to emphasize the importance of reaching all children with immunizations. PAHO was also an important factor in Panama's vaccine decisions, though Panama's considerable financial resources allow it more independence. In both of the regression analyses performed on the adoption of the Hib vaccine, countries in the Americas were found to be significantly faster adopters. The Kaplan-Meier curves also showed the Americas as being significantly faster adopters of both the Hib and Hep B vaccines than other regions.
- In Morocco, WHO regional meetings, position papers, and Strategic Advisory Group of Experts on Immunization (SAGE) recommendations were key in initiating the process of considering Pneumo and Rota vaccines. One of the two regression analyses on Hib vaccine adoption showed that countries in the Eastern Mediterranean Region were significantly faster to adopt.
- In Cape Verde, WHO's regional promotion, as well as the strong in-country advocacy by WHO and UNICEF, were influential in the country's decision to introduce the Hib vaccine.
- Indonesia will likely follow the advice of WHO and international donors in introducing Hib, Rota, and Pneumo vaccines.
- WHO recommendations and strong advocacy by the Western Pacific Regional Office and WHO Philippines led to the introduction of Hep B (which had been delayed several years) and Hib vaccines. One of the two regressions analyzing Hep B adoption and, similarly, one of the two regressions on Hib adoption showed Western Pacific countries to be significantly faster to adopt.
- Armenia's decision to introduce Rota vaccine in 2012 is largely due to WHO advocacy (including WHO funding of a BOD study and hosting of a regional meeting), advocacy from the PATH (Program for Appropriate Technology in Health) Rota project, and most important availability of GAVI financing (at least until 2015).
- In Albania, UNICEF and WHO worked with the MoH to analyze 4 vaccines of interest (hepatitis A [Hep A], HPV, Pneumo, and Rota). Although not a formal economic analysis, the MoH's work helped them to prioritize Pneumo as the next vaccine to be introduced
- In Tunisia, a cost-effectiveness analysis (supported by UNICEF) of potential new vaccines is widely cited as having convinced stakeholders about the priority order of Hib, Pneumo, Rota, and HPV for new vaccine adoption.

In China, however, where limited in-country WHO advocacy occurs and no technical resources are provided, WHO and other international agencies' policies and recommendations are not very important factors in vaccine decision making.

The Sabin Vaccine Institute study cited earlier found that meetings among regulatory authorities and industry experts, especially when convened by regional or global organizations such as PAHO or WHO, are important for exchanging information and bringing together stakeholders.<sup>19</sup>

Some stakeholders in LMICs question the advice coming from international organizations. Engagement by international organizations may not always lead to the best decisions. Some Thai informants are leery of advice coming from WHO and other international organizations, believing that those organizations take a paternalistic approach and sometimes target countries unnecessarily to adopt new vaccines before the countries have the capacity to do so. The study team heard from some Armenian informants that they felt Pneumo might be a more important vaccine to introduce at this time than Rota, but due to efforts mentioned previously, Rota rather than Pneumo is the vaccine currently under discussion.

#### **Box 4-5. Notable Practice: Armenia's Multiscenario Comprehensive Multiyear Plan for Immunization**

As a (soon to graduate) GAVI country, Armenia has developed a comprehensive multiyear plan (cMYP) for 2011–2015, the final years of GAVI funding. The cMYP identifies financing gaps for the existing vaccine program in the plan's out-years and lays out a series of alternative scenarios, including how the program might proceed if financing gaps can be met and the decisions that may have to be made if the needed funds cannot be obtained. This is a valuable process that decision makers can use to understand the financial implications of achieving sustainability and the programmatic impacts that insufficient funding can have.

Some non-GAVI African countries are beginning to use cMYPs, which could be a useful process for many other lower-middle-income countries.

#### **4.2.2. Procurement Mechanisms**

Countries in this study procure in three different ways: (1) tenders issued by individual countries; (2) use of UNICEF Supply Division's procurement facility; and (3) participation in PAHO's Revolving Fund. The procurement mechanism used influences both price and, to some extent, predictability of future prices, since UNICEF and PAHO are perceived to have substantial purchasing power with manufacturers.

*"The most important thing that was done to ensure adoption and stable price and supply was the PAHO Revolving Fund... The core components were procurement centralized and free of corruption, access to better pricing and average pricing, and payment in local currency."* —Ciro de Quadros, interview with study team

Countries that procure through UNICEF (Albania, Armenia, Cape Verde, Philippines and, for its traditional vaccines, Morocco<sup>20</sup>) and PAHO (Panama and Ecuador) are able to estimate budgetary

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<sup>19</sup> Walsh J, Mitu A. The critical path for vaccine introduction: an analysis based upon the rapid introduction of rotavirus vaccines into Mexico and Brazil. Report for the Sabin Vaccine Institute; November 2006; Berkeley: University of California.

<sup>20</sup> Morocco did not procure its new vaccines through UNICEF because the new vaccines were not available through organization when the decision was made to introduce them.

requirements with confidence, which may expedite decision making. Armenia is not sure that UNICEF's prices for vaccines purchased after Armenia is no longer supported by GAVI will be near the prices at which UNICEF currently procures GAVI-supported vaccines. In addition, countries need to develop the technical capacity to conduct their own procurement. The Philippines is an example of a country that experienced stock-outs when it quickly tried to switch to self-procurement for a few years before reverting back to UNICEF, demonstrating the difficulty some countries experience with the complexities (specific market knowledge, required skills, and a favorable regulatory environment) of procuring vaccines.

Those countries that use a tender process and have done so for several years appear comfortable with this process and believe they are able to receive a fair price. Countries like South Africa consult with the UNICEF Supply Division during procurement to ensure that they receive fair prices for vaccines and services. The study was able to collect price data for national procurements from only a few countries for a few vaccines. For example, Table 4-3 shows the prices paid by a country in the Eastern Mediterranean Region (EMR) through direct procurement over the past 5 years, with UNICEF's weighted average price (WAP) shown as a reference. The EMR country paid higher prices than UNICEF's WAPs, the latter of which are dominated by procurements for GAVI countries that mainly fall into the low-income country (LIC) category and thus are close to the lowest, if not the lowest, prices available. In 2010, Tunisia paid US\$4.32 (€3.13) per dose for DTP (diphtheria, tetanus, and pertussis)/Hep B/Hib. This price is only a bit above the WAP, and Tunisia's contract included some additional services beyond the vaccines.<sup>21</sup> Albania paid a lower price than PAHO for Pneumo 7-valent vaccine in 2010 (US\$17.70, compared with US\$20.00), though this price is still much higher than the price that GAVI-eligible countries pay (US\$3.50, which is half of the overall advanced market commitment price of US\$7).

**Table 4-4. Comparison of Eastern Mediterranean Countries' Vaccine Prices With UNICEF's Weighted Averages, 2005–2009 (US\$)**

	2005		2006		2007		2008		2009	
<b>Vaccine</b>	EMR Country*	UNICEF* *	EMR Country*	UNICEF**	EMR Country*	UNICEF* *	EMR Country*	UNICEF* *	EMR Country*	UNICEF**
BCG	0.30	0.07	0.30	0.08	0.35	0.08	0.45	0.08	0.43	0.08
DTP	0.36	0.12	0.44	0.16	0.41	0.19		0.20		0.20
Measles	0.28	0.16	0.41	0.17	0.38	0.19		0.21		0.22
MMR	0.97	1.19	1.46	1.27	1.36	1.38	1.58	1.73	1.69	1.05
OPV	0.10	0.10	0.17	0.12	0.16	0.12	0.17	0.13	0.16	0.14
IPV							3.95		3.78	
Hep B	1.09	0.29	1.15	0.22	0.96	0.21	1.15	0.21	1.15	0.20
DTP-Hib	3.27	2.75	3.97	3.36	3.41	3.24	3.38	3.58		3.22
DTP-Hep B-Hib		3.62		3.61		3.61	5.12	3.50	4.57	3.39
DTP-Hib-IPV							8.06		7.53	
DT	0.30		0.41		0.37		0.44		0.49	
Td	0.36		0.42		0.41		0.50		0.56	
DT/dT		0.09		0.07		0.10		0.09		0.08

<sup>21</sup> WHO Rapid Assessment 2010.

	2005		2006		2007		2008		2009	
Vaccine	EMR Country*	UNICEF* *	EMR Country*	UNICEF**	EMR Country*	UNICEF* *	EMR Country*	UNICEF* *	EMR Country*	UNICEF**
TT	0.27	0.06	0.29	0.06	0.30	0.06	0.37	0.06	0.42	0.06
Meningitis- Tetra	5.57		5.89							

\* The EMR country data do not include the 30% markup by the local pharmaceutical stores for 2007–2009; unsure if this markup is included for 2005–2006. Prices were converted from Euros using annual midpoint (1 July) International Monetary Fund exchange rate ([http://www.imf.org/external/np/fin/data/param\\_rms\\_mth.aspx](http://www.imf.org/external/np/fin/data/param_rms_mth.aspx))

\*\* The UNICEF price is the average price per dose, calculated using total value of each vaccine (in millions of US dollars) divided by total doses for each vaccine (in millions) bought per year. Prices for diphtheria and tetanus toxoids (DT) and tetanus and diphtheria toxoids (Td) are not provided separately.

Sources: Data from WHO Assessments, 2007, 2010; UNICEF Supplies and Procurement, [http://www.unicef.org/supply/index\\_7991.html](http://www.unicef.org/supply/index_7991.html)

Only a few countries suggested on their own the participation in pooled procurement arrangements as a way to improve procurement and to obtain lower prices. Morocco, which is discussing such a mechanism with WHO's Eastern Mediterranean Regional Office, and Egypt, which is interested in participating, are two countries that raised pooled procurement prospectively. The two PAHO countries visited were pleased with the results they get from being part of the PAHO Revolving Fund. Other countries mentioned a desire to have assistance with procurement or to work with UNICEF Supply Division to procure for them.

#### Box 4-6. Special Cases: The Impact of GAVI Funding

Albania (already graduated) and Armenia (about to graduate) currently still receive GAVI support, though they know that it will end after 2015. Indonesia is eligible for GAVI funding, has used it in the past, and plans to apply for new vaccine funding. Although conclusions can be drawn for this limited data set, they should only be cautiously applied to other situations.

Albania (currently receiving funding for pentavalent *Haemophilus influenzae* type B [Hib] vaccine with no copay) and Armenia (currently receiving funding for Hib vaccine and may request support for rotavirus vaccine introduction) should both be in a financial position to pay for these vaccines when GAVI funding ends. However, informants expressed concern about sustainability, because in both cases, health expenditures are not rising and the costs to fully fund the vaccines are seen as substantial, especially for Albania. Some of the fears about affordability might be related to uncertainty about the prices the countries will face when they are out of the GAVI system.

Indonesia has no current new vaccine support from GAVI, though GAVI assistance does partially finance the costs of its immunization advisory committee. Local production capacity seems to be a greater issue for potential introduction of Hib and pneumococcal conjugate vaccines than does access to GAVI funds.

One important benefit from GAVI in all three cases is development or improvement of each country's decision-making process for new vaccines through the use of immunization advisory groups or technical groups associated with their Inter-Agency Coordinating Committee (ICC). It is important that these groups be institutionalized so that they remain functional after GAVI support ends.

A government may negotiate prices with bidders by using benchmark prices (based on recent procurements in nearby countries or on UNICEF prices). A government may also negotiate “bundling” of other needed services (training, equipment, supplies) along with vaccines in order to get a better price. There are pros and cons to bundling: It may produce better overall prices and simplify procurement, but it may also build a dependency on the winning company, a concern of the study team in Panama. The larger countries that procure vaccines internationally consider the size of their orders big enough to give them bargaining power, but it is not clear that these individual procurements enable countries to receive competitive prices, because information about these countries’ prices was not readily available during the country studies. Informants in these larger countries did not express a view that procurement issues influenced their decisions to adopt new vaccines one way or the other. (China and Indonesia are exceptions, in that their routine immunization program indicates the price range that local manufacturers may set for vaccines.)

#### 4.2.3. Experience in Neighboring Countries

When considering a new vaccine, the findings from the country studies show that most countries take into consideration whether other countries in their region have adopted the vaccine and what the experience of those other countries with the vaccine. Note that this is of greater importance to some countries than to others. A recent quantitative study of the factors influencing Hib adoption found that the presence of two or more neighboring country adopters was a significant factor.<sup>22</sup> However, in this study’s quantitative analyses, neighboring adopters were significantly associated with Hep B adoption but not with Hib adoption (see Annex D for more on the quantitative analyses).

For countries with limited ability to obtain local epidemiological data, the experience of neighboring countries can be an important factor in decision making. This experience includes documentation of the vaccine’s actual effectiveness in reducing disease and its positive economic impact.

- Armenia considers the experiences of both Western European and newly independent states. In addition, many of its technical experts and medical practitioners find Russian experience and attitudes about new vaccines to be especially important.
- A key factor in Cape Verde’s decision to adopt Hib was that nearly all of its neighbor Sub-Saharan African countries had done so with good results.
- Turkey was one of the last countries in the WHO European Region to adopt Hib, which had some influence on the country’s decision. Turkey sees itself equally as a part of the broader international community, in terms of having a very strong NIP, and is concerned that too rapid introduction of new vaccines can have an adverse impact on national programs. As an example, Turkey points to the polio outbreak in Tajikistan.

For some of the larger countries, the desire to maintain their positions as regional leaders factor into their decisions.

- Morocco is an “early adopter” and takes pride in its standing in the region.
- One of several factors (along with the clinical trials data mentioned earlier) influencing South Africa’s adoption of the Pneumo vaccine earlier than originally planned was that neighboring

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<sup>22</sup> Shearer JC, Stack ML, Richmond MR, Bear AP, Hajjeh RA, Bishai DM. Accelerating policy decisions to adopt *Haemophilus Influenzae* type B vaccine: a global , multivariable analysis. *PLoS Medicine*. 2010;7(3).

countries were applying to GAVI for its introduction, and South Africa did not want to fall behind.

- Panama wanted to be the first to introduce the Rota vaccine and did so rapidly, introducing one day prior to Brazil.

For other larger countries studied (Egypt, Indonesia, China), the experience of neighboring countries did not have significant influence. Egypt has been the only Arab nation that has not adopted Hib for a few years, despite its own advisory panel's recommendation. Only recently does it seem to be moving toward adoption.

Many country informants expressed interest in sharing vaccine experiences with other countries in the region. WHO, GAVI, and other international organizations have funded such activities in the past and can take the lead in doing so in the future.

- Turkish informants noted the value of a 2007 regional new and underutilized vaccines conference that was sponsored jointly by WHO and the International Children's Center (an international nongovernmental organization headquartered in Turkey).
- Moroccan informants noted that the consideration of new vaccines often is initiated because of regional meetings, which were particularly important in the decision to adopt HPV.
- In Panama, recent regional meetings organized by PAHO and the Sabin Vaccine Institute appear to have informed vaccine researchers, managers, and planners about the vaccine pipeline, current vaccine recommendations, and early program strategies in other countries.

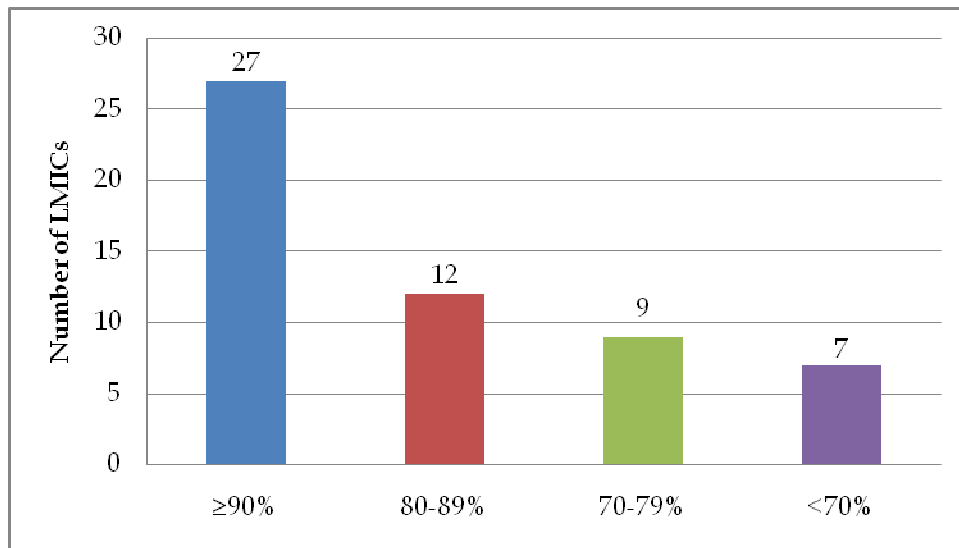
#### **4.2.4. Strength of the Existing Routine Immunization Program**

Informants in several countries expressed the strong view that the existing routine immunization program must be well-established before introducing a new vaccine—that is, personnel must be available and trained, and the needed infrastructure, including a monitoring system that enables managers to analyze vaccine effectiveness and to identify problems, must be in place. As one informant put it, “You can’t implement new things effectively on a shaky structure and expect to see results.” This view was reinforced by results of the study’s quantitative analysis, which, using DTP3 coverage as a proxy for NIP strength, found it to be related to earlier adoption of Hib and Hep B in the analyses performed on data for LICs and MICs together.

- As cited earlier, informants in Turkey and Thailand both expressed concern that too-rapid adoption of new vaccines can jeopardize the effectiveness of existing programs.
- China, South Africa, Thailand, and Turkey all shared concern about the need to strengthen their systems by increasing coverage of immunization services in remote and rural areas before introducing new vaccines.
- Morocco has delayed switching from DTP-Hib plus Hep B vaccines to pentavalent vaccines from 2010 to 2011, in order to ensure sustainability of vaccine supply until the introduction of Pneumo and Rota vaccines are completed in 2011.
- Panama and South Africa both experienced start-up challenges (e.g., in preparing their NIP staff) when decision makers moved to purchase a vaccine ahead of the original schedule (Rota in Panama; Rota and Pneumo in South Africa).

While strengthening the routine Expanded Program on Immunization (EPI) should always be a priority, these programs are generally already running well in most LMICs (see Figure 4-1).

**Figure 4-1. DTP3 Coverage Among Lower-Middle-Income Countries**



- LMICs with DTP3 coverage < 70% are Samoa, Papua New Guinea, Nigeria, Iraq, India, Republic of Congo, and Yemen.
- LMICs with DTP3 coverage 70–80% are Azerbaijan, Pakistan, Mauritania, Ecuador, Paraguay, Vanuatu, Indonesia, Federated States of Micronesia, and Timor-Leste.

Source: Data from WHO Global Health Observatory, WHO-UNICEF estimates; 2009; Geneva, Switzerland. <http://apps.who.int/ghodata/>. Cited September 2, 2010. These estimates use country-reported data that are confirmed or adjusted by survey data.

### 4.3. Other Factors

Some issues were important in a minority of the countries studied; however, in those countries, the factors had a substantial impact on new vaccine adoption.

#### 4.3.1. Local Vaccine Production Capacity

Six of the countries studied have or are developing local production capacity, as outlined in Table 4-5. Beyond these, Morocco, Syria, and Tunisia all have plans to develop vaccine production.

**Table 4-5. Local Vaccine Production Capacity by Study Country**

Country	Local Production	Vaccine Procurement	Impact on New Vaccine Adoption
China	More than 30 local manufacturers, both private and state-owned, produce all vaccines that are currently in the routine immunization program (except a portion of measles, mumps, and	<ul style="list-style-type: none"> <li>• The government sets the price range for vaccines in the routine immunization program; local manufacturers compete within the program.</li> <li>• Technology-transfer agreements with international vaccine manufacturers exist and are growing.</li> <li>• Focus is domestic, though some are</li> </ul>	Availability of local production is a major consideration in the adoption of new vaccines to ensure adequate supply.

Country	Local Production	Vaccine Procurement	Impact on New Vaccine Adoption
	rubella vaccine).	beginning to expand internationally.	
Ecuador	National Institute of Hygiene produces four vaccines and is attempting to develop its own pentavalent vaccine, with technical assistance from Cuba.	<ul style="list-style-type: none"> <li>• INH (National Institute of Hygiene) expects to meet total demand of the immunization program for four vaccines in 2010, though the Pan American Health Organization (PAHO) expressed uncertainty that this was possible.</li> <li>• Procurement of other vaccines is through the PAHO Revolving Fund.</li> </ul>	Availability of local production appears to be a consideration in the adoption of new vaccines.
Egypt	One state-owned vaccine manufacturer (VacSera)	<ul style="list-style-type: none"> <li>• Purchases in bulk for filling and packaging some vaccines for national immunization program (NIP); procures others.</li> <li>• Long-term technology-transfer agreement with GSK (GlaxoSmithKline); status is not clear.</li> <li>• VacSera's production capacity is not improving.</li> <li>• Focus is primarily on production for Egypt, though some vaccines are donated to neighboring countries.</li> </ul>	If <i>Haemophilus influenzae</i> type B (Hib) were added in pentavalent form, VacSera would lose its market for filled and packaged diphtheria, tetanus, and pertussis (DTP); some think this is a factor in the failure to adopt Hib.
Indonesia	One major state-owned vaccine manufacturer (BioFarma)	<ul style="list-style-type: none"> <li>• The government sets vaccine prices for routine immunization program and invests in research and development (R&amp;D).</li> <li>• Collaborates with industry, nongovernmental organizations, and universities on the development of platforms and antigens.</li> <li>• R&amp;D is guided by government need</li> </ul>	Ability of BioFarma to produce a new vaccine is a major factor in adoption.
South Africa	Public-private partnership for vaccine production and procurement (BioVac Institute)	<ul style="list-style-type: none"> <li>• Not yet producing; imports or formulates/fills imported vaccines for the NIP.</li> <li>• Expects to produce basic vaccines (hepatitis B, tuberculosis, DTP) by 2013.</li> <li>• Interested in eventual export in Africa.</li> </ul>	BioVac's production capacity is not a factor in vaccine adoption.
Thailand	Thai Red Cross and Government Pharmaceutical Organization (GPO)	<ul style="list-style-type: none"> <li>• NIP purchases some vaccines through GPO, some through international tenders, BCG from Thai Red Cross.</li> <li>• GPO produces some vaccines through joint ventures with international vaccine manufacturers.</li> <li>• GPO exports some vaccines.</li> <li>• GPO received prequalification in September 2011 for the measles vaccine it fills and packages from Sanofi Pasteur's bulk product.</li> </ul>	Local production capacity is not an identified factor affecting vaccine adoption.



Country	Local Production	Vaccine Procurement	Impact on New Vaccine Adoption
		<ul style="list-style-type: none"> <li>The government plans to produce flu vaccine through GPO to ensure supply for future pandemic.</li> </ul>	

In China, Egypt, and Indonesia, local production capacity is an important factor in new vaccine adoption. In all three cases, an important rationale for giving preference to local production is to promote the development of national capability, if not self-sufficiency, in the production of biological products.

China has two other reasons to favor local production: supply security, which is understandable given China's huge population (this is also an issue for Indonesia, the world's fourth-largest country), and assured quality. As is discussed later in this paper, China is very concerned about vaccine safety, so it prefers to be able to oversee every part of the production process.

China's size also makes its reliance on local supply more feasible than in smaller countries. In smaller countries that do not have multiple local manufacturers, committing to procure domestically can lower the country's vaccine supply security. Manufacturers in smaller countries may also struggle to provide vaccines for a lower price than is provided by international manufacturers, because the former do not have local competition and—at least as long as they supply only domestically—do not benefit from economies of scale.

National pride in producing and becoming self-sufficient is a strong driver of the stated desire to develop national vaccine production in Ecuador. However, although Ecuador would like to produce vaccines, it is not immediately capable of doing so. Thailand hopes to increase its local production capacity, including an ambitious goal of producing flu vaccine to ensure supply during a pandemic. Vaccine supply security is also a consideration in Ecuador, as it is concerned that its access to pandemic flu vaccine be ensured locally and not dependent on imports. Egypt's vaccine advisory committee has recommended adoption of Hib-containing pentavalent for several years, without a positive decision taken. At the same time, VacSera, Egypt's vaccine manufacturer has been working for about a decade with an international partner to obtain technical know-how that will allow it to produce pentavalent. It seems that in Egypt, a positive decision on pentavalent might be predicated on the success of the technology transfer.

#### 4.3.2. Precipitating Local Events

Occasionally, local epidemics have drawn policymakers' attention to immunization needs.

- In China, the emergence of severe acute respiratory syndrome (SARS) and then influenza A (H1N1) highlighted the importance of public health and childhood immunization. This emergence, along with rapid economic growth that made investments in vaccines more affordable, was a factor influencing the government's decision to add several new vaccines in

2008 (Hep A, Japanese encephalitis B, meningococcal meningitis A and C vaccines, among others).

- In South Africa, an alarming number of infant deaths from diarrhea and pneumonia in early 2008 led the government to introduce Pneumo and Rota vaccines earlier than planned.
- Thailand's concern about seasonal flu, which it believes could reach epidemic proportions, has led to its decision to build capacity for local production of flu vaccine within the next 5 years.

Local epidemic events can also have a negative effect on the adoption of new vaccines. As noted earlier, the need to procure vaccines for epidemic diseases like influenza, including H1N1, can absorb limited immunization resources.

- In Egypt, for the past half decade, the immunization program's focus has been on conducting polio and measles campaigns and on responding to emerging threats, including H1N1 and seasonal influenza.

#### **4.3.3. Perception of Vaccine Safety**

The perception of vaccine safety is, of course, a concern of all countries and is one of the issues considered by each country's immunization advisory group. WHO prequalification of a vaccine is considered an important guarantee of vaccine safety, and not all countries require further registration of vaccines that have received WHO prequalification. Among the study countries, Armenia, Ecuador, and Panama accept WHO prequalification for vaccines in their NIPs without further in-country registration.

Vaccine safety does not become a constraint to introduction of new vaccines, unless there have been adverse effects significant enough to gain the public's or decision makers' attention. Informants noted a couple of examples.

- China's one-child policy makes safety of all medicines particularly important, because parents will lose confidence in the system if their only child becomes ill or dies due to safety issues. In one province, nearly 100 children became ill and 4 were said to have died because improper storage of a vaccine rendered it ineffective. This incident received a great deal of news coverage, both on the Internet and in print, thus curtailing any public discussion of immunization for a time.
- Armenian informants say that both doctors and parents are skeptical of introducing new vaccines, in part due to safety concerns. Mention was made of adverse reactions thought to result from the quality of vaccines imported from developing countries and Eastern Europe.

#### **4.3.4. Leadership by Local Champions and Advocacy by Other Influential Parties**

Advocacy can lead to earlier consideration and adoption of new vaccines, if it is supported by good epidemiological and cost rationale. Particularly important is leadership by political and government figures who can keep immunization issues on the front burner over the long term.

- The wife of the King of Morocco, Her Royal Highness Princess Lalla Salma, has founded and heads a foundation dedicated to cancer prevention and treatment, which is a key advocate for HPV immunization. The foundation has done epidemiological research on HPV and is supporting the development of a large cervical cancer screening program. The foundation's work

and the princess's support have been instrumental in Morocco's decision to introduce HPV in 2015.

- Turkey's minister of health, a pediatrician with a strong interest in immunization who has held this position for 7 years, has built credibility with an ambitious health-reform program. Turkish informants consider his leadership and interest as the most important factor in maintaining the NIP's strength and in fostering the consideration and introduction of Hib and Pneumo vaccines.
- Ecuador has had the same manager for its immunization program for 10 years. Her leadership has enabled the program to grow steadily and has encouraged programmatic stability during politically insecure times. National laws and institutions that favor childhood immunization support her leadership.
- In Panama, the decisions to introduce Rota, Pneumo, and HPV vaccines benefitted from political support at the highest level during a supportive presidency (2004–2009). In addition an important factor was the leadership of two ministers of health, who saw new vaccines as an issue of national pride, regional superiority, and a means to demonstrate their commitment and political potential to the public. In fact, decisions to adopt the Rota and HPV vaccines had the backing and involvement of a former president and minister and were announced with little or no consultation with the EPI or technical experts.
- In the Philippines, a senator whose father had died of liver cancer advocated strongly for introduction of the Hep B vaccine. Despite opposition within the senate because of cost, she was able to convince the majority of the senate to secure funding.

Advocacy efforts from outside the government and political leadership can also be influential.

- An internationally acclaimed Panamanian researcher, Dr. Xavier Sáez-Llorens, has played a critical role in recent vaccine decisions. His epidemiological research and vaccine trials have engaged the most prestigious hospitals, as well as an important group of clinical researchers and providers. He has used his prestige, his column in the national newspaper, and his direct access to the highest levels of government to inform and ultimately catalyze major vaccine decisions.
- In South Africa, where HIV-affected children are at 40 times greater risk of contracting pneumonia than are non-HIV affected children,<sup>23</sup> activism by AIDS organizations helped influence the government in introducing the Pneumo vaccine.
- In Armenia, WHO and PATH advocacy for Rota vaccine have helped Armenia and its ICC edge toward the decision to request GAVI support in order to introduce the vaccine in 2012.

Advocacy from organizations without strong technical understanding of the conditions in a country, though well-meaning, may not support effective decision making.

- South African AIDS activities are now pushing for rapid introduction of HPV vaccine, though the school health system, through which the HPV vaccine would be introduced, is just now being reestablished and lacks the needed infrastructure.
- Some Armenian informants questioned introduction of Rota vaccine before Pneumo vaccine, as pneumonia may be a more important cause of childhood morbidity and mortality. However,

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<sup>23</sup> 9-valent Pneumo vaccine trials carried out in Soweto under the Pneumo Accelerated Development and Introduction Plan (ADIP), 2010

they felt that because of international advocacy for Rota vaccine and an absence of good BOD for pneumonia, the latter did not receive consideration.

Although the study team did not ask specifically, marketing by vaccine manufacturers was rarely raised by country informants as a strong influence on new vaccine adoption decisions when asked the open-ended question, “What are the major factors influencing new vaccine adoption decisions?” An indirect influence that was commonly mentioned were the BOD and vaccine effectiveness studies funded by vaccine manufacturers, which were sometimes mentioned among those factors that helped immunization advisory committees make their recommendations. However, the global expert interviews conducted suggested that vaccine manufacturers are influential through marketing and lobbying.

#### 4.3.5. Experience of the Private-Sector Vaccine Market

Some or all of the vaccines targeted in this study are available in the private market in study countries, even if they are not included in the routine immunization program. Although it is not clear whether all the countries monitor effectiveness or adverse events following immunization (AEFI) of vaccines offered in the private market,<sup>24</sup> private-sector sales do provide an indication of public acceptability of and demand for these vaccines.

In general, the private market for vaccines is relatively small in LMICs, and high prices limit their use to wealthy people. Many interviewees mentioned this fact, and Tables 4-5–4-7 support them. Table 4-5 illustrates the size and price of the private market in the countries studied, while Tables 4-6 and 4-7 illustrate UNICEF and US prices for comparison. Both Morocco and Panama (UMICs) pay prices approaching those in the US public market, whereas the Philippines and South Africa pay much lower prices, due, in part, to significant country-specific price cuts by GlaxoSmithKline during 2008.

**Table 4-6. Share and Price of Private Vaccine Sector in Country Studies (US\$)**

Country	Private Share of Vaccine Market (by volume, unless stated otherwise)		Prices in Private Sector per Dose	
	EPI vaccines	Non-EPI vaccines	EPI vaccines	Non-EPI vaccines
Albania	“Emerging”		—	—
Armenia	—		—	—
Cape Verde	“Very small”		“High” prices	
China	30% (Category 2) overall		Profit margin 30–40% for imported vaccines, 50% for locally produced vaccines	
Ecuador	5%		With 5% of market share, estimated to be worth as much as EPI’s annual budget	
Egypt	Supplies 5% of		• Meningitis AC 5 cm (2009) \$0.685	—

<sup>24</sup> The study did not ask about systematically monitoring safety and effectiveness of vaccines used only in private markets, and such monitoring was not spontaneously mentioned by respondents. Thus it is not certain to what extent safety and effectiveness monitoring are done, beyond routine reporting of adverse effects following immunization.

Country	Private Share of Vaccine Market (by volume, unless stated otherwise)		Prices in Private Sector per Dose	
	EPI vaccines	Non-EPI vaccines	EPI vaccines	Non-EPI vaccines
	birth cohort overall		• Typhoid + tetanus 10 cm (2009) \$0.5125	
Indonesia	10–12%		—	—
Morocco	Vaccinates 1/3 of birth cohort overall		<ul style="list-style-type: none"> <li>• 7-valent Pneumo (Feb 2010 approximate) \$110</li> <li>• Rota (Feb 2010 approximate) \$73</li> </ul>	—
Panama	—	—	<ul style="list-style-type: none"> <li>• 7-valent Pneumo (June 2010 approximate) \$69.50 to the physician, \$100–120 to the user</li> <li>• Rota (2009 approximate) \$45 to the physician, \$70 to the user</li> <li>• Quadrivalent HPV (2010 approximate) \$98 to the physician, \$120 to the user</li> </ul>	—
Philippines	10%		—	<ul style="list-style-type: none"> <li>• Rota (June 2010) \$30–\$40</li> <li>• Pneumo (June 2010) \$30–\$50</li> <li>• HPV (2010) \$35</li> </ul>
South Africa	28% (2006)		—	• HPV (December 2008) \$43
Syria	5%, mainly vaccines not available through public market		—	—
Thailand	< 5%	—	—	—
Tunisia	< 5%	—	<ul style="list-style-type: none"> <li>• DTP-Hib-IPV (2009) \$18.86* purchase price</li> <li>• Pneumo 7-valent (2009) \$40 purchase price</li> </ul>	—
Turkey	1%	10%	—	—

\* Price converted from Euros using exchange rate on July 1, 2010, from oanda.com.

Sources: Data from Dr. Sáez-Llorens, interview with study team, Panama City, Panama, July 1, 2010; Tunisian Directorate of Pharmaceuticals and Drugs, 2010; Stakeholder opinions: vaccines in emerging markets (Asia) – Opportunities in China, India, Taiwan and South Korea, *Datamonitor*, October 2009; BioPharm International, 2007; Zero2IPOCapital, Competition and development momentum of the Chinese vaccine industry, 2009, <http://www.zero2ipo.com.cn/en/n/2009—12—31/20091231104458.shtml>, 2009; Wentzel L, Frost, Sullivan, South African vaccines manufacturing unit, <http://www.frost.com/prod/servlet/market-insight-top.pag?docid=111145268>, published November 6, 2007; Advisory Board Company, GlaxoSmithKline to reduce price of HPV vaccine Cervarix in South Africa, December 5, 2008, <http://www.medicalnewstoday.com/articles/131918.php>.

In Table 4-7, important differences between the UNICEF and the US and PAHO prices require caution in terms of direct comparisons. UNICEF procures from multiple manufacturers and reports weighted average prices (WAPs) that are an average for many suppliers and for vaccines going to countries of varying sizes and income levels. In comparison, the US and PAHO prices are specific to one manufacturer, because the United States displays prices by company and PAHO procures from only one manufacturer per vaccine. Although PAHO procures for many countries, it pays one price for a vaccine for all of its member countries.

**Table 4-7. US, UNICEF, and PAHO Prices, 2006-2010**

Vaccine	Year	United States			UNICEF for GAVI	PAHO
		Manufacturer (where relevant)	Public (CDC)	Private	WAP	
<b>Hep B recombinant pediatric 1 dose, liquid</b>	2006	GSK*	\$9.10	\$21.37	–	\$0.20
	2007	GSK	\$9.10	\$21.37	–	\$0.23
	2008	GSK	\$9.50	\$21.37	\$0.27	\$0.25
	2009	GSK	\$9.75	\$21.37	\$0.27	\$0.27
	2010	GSK	\$10.25	\$21.37	–	\$0.28
<b>DTP-Hep B-Hib 1 dose, liquid</b>	2006	–	–	–	–	\$3.99
	2007	–	–	–	–	\$3.95
	2008	–	–	–	\$3.53	\$3.95
	2009	–	–	–	\$3.60	\$3.55
	2010	–	–	–	\$3.00	\$3.20
<b>Hib 1 dose + diluent, lyophilized</b>	2006	Merck	\$10.62	\$22.77	–	\$3.10
	2007	Merck	\$10.83	\$22.77	–	\$3.15
	2008	Merck	\$11.26	\$22.77	\$3.35	\$3.35
	2009	Merck	\$11.29	\$22.77	\$3.40	\$3.45
	2010	Merck	\$11.51	\$22.77	\$3.40	\$2.25
<b>Pneumococcal 7-valent</b>	2006	–	\$57.59	\$73.70	–	\$53.0
	2007	–	\$62.14	\$79.19	–	–
	2008	–	\$66.44	\$83.88	–	–
	2009	–	\$71.04	\$83.88	–	\$21.75
	2010	–	–	–	–	\$20.00
<b>Pneumococcal 13-valent</b>	2010	–	\$91.75	\$108.75	\$7.00**	–
<b>Rotavirus 1 dose, liquid</b>	2006	Merck	\$52.00	\$63.25	–	–
	2007	Merck	\$55.05	\$66.94	–	–
	2008	Merck	\$57.20	\$69.59	–	\$7.50
	2009	Merck	\$57.20	\$69.59	–	\$5.50
	2010	Merck	\$59.18	\$69.59	–	\$5.15
<b>HPV Quadrivalent</b>	2006	–	\$96.00	\$119.75	–	–
	2007	–	\$96.75	\$120.50	–	–

Vaccine	Year	United States			UNICEF for GAVI	PAHO
		Manufacturer (where relevant)	Public (CDC)	Private	WAP	
	2008	–	\$100.59	\$125.29	–	–
	2009	–	\$105.58	\$130.27	–	–
	2010	–	\$108.72	\$130.27	–	\$32.00

\* GlaxoSmithKline

\*\* The price to countries is \$3.50.

– Not available or not relevant

Sources: UNICEF product menu for vaccines supplied by UNICEF for the Global Alliance for Vaccines and Immunization (GAVI), 2008, 2010; PAHO *Immunization Newsletter*, 2006–2010, No. 1; CDC vaccine price list, September/October 2006–2010.

Regardless of the small size and high prices of LMIC private markets, the availability of vaccines in the private sector can inform and influence new vaccine decision making and was said to do so in a few countries.

- In China, government health facilities administer vaccines that are included in the routine immunization program (free) and those that are not (at market prices). Therefore, the government has access to information about demand, effectiveness, and AEFI, though currently these data are not aggregated to the national level.
- In Turkey, the national immunization program rushed to adopt measles, mumps, and rubella (MMR) vaccine when it reached 20% private-market penetration, because of concerns about increasing congenital rubella syndrome.
- In South Africa, because of its concern with equitable access to health services, when an important vaccine such as Rota is available through the private market but not in the routine immunization program, this is perceived as allowing a dual system; as such, it factors into the government's decision making.<sup>25</sup>
- In Panama and Ecuador, health services—including vaccines—are legally considered a right of each citizen. Thus as new vaccines become available in the private sector, there is considerable pressure on the government to stand by its commitment to equity and provide them, though the usual decision-making process ultimately decides.

International vaccine manufacturers are interested in having new vaccines adopted for routine immunization programs, even though those companies would be likely to receive a much lower price than they would through private-market sales. Table 4-8 shows evidence of this, with only one exception (Egypt's typhoid+tetanus) from country studies. The public market volume, however, is many times greater than the private market in all countries studied.

<sup>25</sup> The importance of the availability of vaccines in private markets came up as a factor in the interviews conducted. However, the study did not collect data on prices of vaccines in South Africa.

**Table 4-8. Comparison of Public- and Private-Sector Vaccine Prices by Study Country**

Country	Vaccine/Indicator	Price Indicator (Prices are to the physician, unless stated otherwise.)	
		Private Market	Public Market
Albania	Pneumo 10-valent	—	\$17.70 (2010)
Armenia	—	—	—
Cape Verde	Overall price	“High”	—
China	Profit margin	30–40% for imported vaccines, 50% for locally produced vaccines	“Thin”
Ecuador	—	With 5% of market share, private market is estimated to be worth as much as EPI’s annual budget	
Egypt	Meningitis AC 5 cm	\$0.685 (2009)	\$0.80 (2009)
	Typhoid + tetanus 10 cm*	\$0.5125 (2009)*	\$0.58 (2009)*
Indonesia	—	—	—
Morocco	7-valent Pneumo	\$110 (Feb 2010 approximate), 900 MAD	—
	Rota	\$73 (Feb 2010 approximate), 600 MAD	—
	DTP-Hib	—	\$3.60 (2007)
Panama	7-valent Pneumo	\$69.50 to the physician, \$100–120 to the user (2010 approximate)	\$21 (2008)
	Rota	\$45 to the physician, \$70 to the user (2009 approximate)	—
	Quadrivalent HPV	\$98 to the physician, \$120 to the user (2010 approximate)	—
Philippines	DTP-Hep B-Hib	—	\$3.50 (2010)
	Rota	\$30–40 (June 2010)	—
	Pneumo	\$30–50 (June 2010)	—
	HPV	\$35 (2010)	—
South Africa	Bivalent HPV	\$43 (2008)	—
Syria	—	—	—
Thailand	—	—	—
Tunisia	7-valent Pneumo	\$40 (2009)	—
	DTP-Hep B-Hib	—	\$4.32 (2010), €3.13
Turkey	—	—	—

\* Unique example in study of a lower vaccine price in the private market than in the public market.

Egypt’s VacSera has a near-exclusive supply relationship with the public sector but faces competition for private sales.

Sources: Data from Dr. Sáez-Llorens, interview with study team, Panama City, Panama, July 1, 2010;

Tunisian Directorate of Pharmaceuticals and Drugs, 2010; Stakeholder opinions: Vaccines in emerging



markets (Asia) – Opportunities in China, India, Taiwan and South Korea, *Datamonitor*, October 2009; BioPharm.

#### **4.3.6. Progress Toward Millennium Development Goals**

All countries are motivated by the drive to reduce infant and child mortality, but surprisingly few countries mentioned the specific desire to achieve MDG child mortality rate (CMR) goals as a factor for new vaccine adoption. Although the study team did not query informants as to the reasons for this, we surmise that vaccines already included in the program have resulted in dramatic declines in the CMR. Because of the widespread availability of antibiotics and ORS (oral rehydration salts), the benefits of new vaccines addressing Hib, Pneumo, and Rota may be considered greater for reductions in morbidity than in mortality. This, in turn, lowers their relevance to an MDG related to CMR.

- In Morocco, new vaccine adoption is an explicit part of the effort to achieve MDG 4. To help achieve this goal, Morocco's current health plan calls for a reduction of infant mortality rate (IMR) from the current 34 per thousand to 15 per thousand in 2012. The MoH has determined that the addition of Pneumo and Rota vaccines are among the most effective ways to accomplish this goal.
- South Africa's lack of progress on reducing IMR and planned discussions of MDG 4 at the 2008 World Health Assembly factored into the Minister of Health's decision to move up the introduction dates for Pneumo and Rota vaccines.

#### **4.4. Potential Factors of Limited Importance**

From the country studies, the study team found that several hypothesized factors had limited importance in vaccine decisions. In addition, the regression analyses found no statistically significant relationship between Hib and Hep B adoption and some hypothesized independent variables.

##### **4.4.1. Vaccine Characteristics**

Typical vaccine characteristics include the presentation of the vaccine and cold chain and other infrastructure requirements, as well as less traditional characteristics, such as the injection schedule and location of production. The perception of vaccine safety was considered separately (see Section 4.3). The study team found that although countries consider these factors, they are more likely to delay introduction of a vaccine until solutions can be found than they are to prevent vaccine adoption.<sup>26</sup> Informants did not cite vaccine characteristics as an important constraint.

- In Armenia, informants had concerns about where the vaccine was produced, with an apparent preference for vaccines produced in the United States or Western Europe, as opposed to Developing Country Vaccine Manufacturers Network (DCVMN) products. It was noted that Hib vaccine produced in Bulgaria caused unexpected side effects.

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<sup>26</sup> In Brazil, the vaccine schedule that required children to receive many injections at a single immunization session met with resistance.

- South Africa's National Advisory Group on Immunization recommended a deviation from WHO's recommended vaccination schedule on introduction of Pneumo vaccine, for local disease and programmatic reasons.<sup>27</sup>

#### 4.4.2. Media

The influence of the media in vaccine decisions is quite limited and was rarely mentioned in the country interviews, although governments use media outlets to inform and motivate the public about new vaccines.

When the media plays a role, it is as monitor rather than as advocate.

- Ecuador's media announces new vaccines and when and where they can be obtained. It also publishes articles about vaccine stock-outs and calls on the government for a quick response. Chinese online media publicized the safety issues raised by handling a vaccine in one province (see Section 4.3).
- Antivaccination sentiment is spreading through Web sites from other countries in Armenia, Ecuador, Indonesia, and Turkey. The EPIs in Ecuador and Indonesia have responded to this sentiment through outreach campaigns, while in Armenia the sentiment seems to be contributing to skeptical attitudes toward new vaccines within the medical community.
- In Thailand, the MoH occasionally uses the media to advocate with the government and to apply public pressure for funding programs, which could be used for future vaccine decisions.

#### 4.4.3. Insignificant Independent Variables in Regressions

The variables related to government spending on health and on the immunization program did not show statistically significant relationships to the adoption of either Hep B or Hib in any of the regression analyses performed. In the regression analyses, similar statistically insignificant results were found for the variables indicating BOD (both indicators of the existence of "good" and "some" BOD evidence and the estimated number of disability-adjusted life years [DALYs] accounted for by the diseases addressed by the vaccines).

## 5. How These Factors Affect Adoption of Four New and Underused Vaccines

Just as the factors cited in Section 4 have varying degrees of influence on decision making in lower-middle-income countries (LMICs), there are also considerations specific to each of the four new and underused pediatric vaccines that are the focus of the study and that are now being considered by these countries. It is also important for the vaccines to be considered together so the countries can prioritize the order of introduction. Whereas some countries (Panama, Morocco) have already approved all 4 vaccines, many other countries will introduce them one at a time. Only in some cases (see below some examples) has an objective analysis been conducted, comparing the burden of disease (BOD), cost utility (using disability-adjusted life years [DALYs] and quality-adjusted life years [QALYs] to compare vaccine-preventable diseases [VPDs]), and other factors in order to prioritize.

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<sup>27</sup> Schoub B, Ngcobo NJ, Madhi S. National Advisory Group on Immunization of South Africa. *Vaccine*. 2010; 28S.

- Despite limited local data, Tunisia conducted such an analysis with UNICEF technical assistance. All informants readily cited the order of priority for vaccine adoption coming from the analysis: *Haemophilus influenzae* type B (Hib), pneumococcal conjugate (Pneumo), rotavirus (Rota), and human papilloma virus (HPV).
- Albania also conducted an analysis with technical assistance from UNICEF and the World Health Organization (WHO) to give priority to adopting Pneumo over hepatitis A (Hep A), HPV, and Rota. In Thailand, several Ministry of Health (MoH) informants felt that development of both a methodology and an analysis was needed prior to further new vaccine adoption, while others within Thailand are advocating moving forward with adopting Rota based on a positive cost-effectiveness study.
- As previously mentioned, other factors may influence Armenia in introducing Rota, when some feel that Pneumo may be a higher priority.

## 5.1. Hib Vaccine

Over the past few years, Hib adoption increased significantly due to a number of factors, including the launch of the Hib Initiative in 2005, a clear universal WHO/Strategic Advisory Group of Experts on Immunization (SAGE) recommendation for Hib vaccine in 2006, GAVI's continued support and approach to sustainability, and the vaccine's presentation in combined vaccines that are programmatically easy to use. Most countries have now adopted Hib into their vaccination schedule. The notable exception is Thailand (previously mentioned), where the decision not to adopt was based on low BOD data.

The important barriers to Hib adoption also apply to Pneumo. These barriers include weak laboratory infrastructures, the widespread availability of inexpensive antibiotics, and the vaccines' ability to prevent only some serotypes of pneumonia and meningitis.

The process for laboratory diagnosis of Hib-specific disease, as well as the most serious diseases caused by pneumococcus (pneumonia, meningitis, bacteremia), has stringent technical requirements that complicate countries' efforts to include them in routine surveillance or even in studies to determine local BOD. Improved laboratory-based surveillance for invasive bacterial diseases will be critical to better estimate BOD for Hib and pneumococcal disease, as well as for better monitoring of the impact of vaccines.

The widespread use of antibiotics significantly reduces the mortality of both of these vaccines' target diseases. Combined with generally good access to care, the cost-effectiveness equations in LMICs can be less favorable than global studies that are based on the economics and cost structure of more developed countries, particularly when there is a different price level for the new vaccines. Especially in LMICs with better access to care, this can cause countries to hesitate to use the vaccines. In addition, even if vaccine adoption is considered cost effective, countries may be more focused on addressing priorities in mortality than morbidity.

## 5.2. Pneumococcal Conjugate Vaccine

The market for Pneumo vaccines has become much more favorable to LMICs recently through more competition, better supply, and lower prices. The Pneumo market, which had been dominated by one product for a decade, has, for the past year, included 2 companies and 2 second-line vaccines of higher

valency.<sup>28</sup> Many other manufacturers, including those in emerging economies, are in the process of developing pneumococcal conjugate vaccines. PATH has entered partnerships to support the development of alternate vaccines (e.g. common protein vaccine) that may be easier and more economical to produce. The Pneumo Advanced Market Commitment (AMC), launched in 2009, aims to stimulate research and development for Pneumo vaccines by ensuring large contracts for manufacturers to supply Pneumo vaccines to low-income countries (LICs) at a fixed low price (currently US\$7, about half of the Pan American Health Organization's [PAHO's] 2011 price). This has enabled at least one manufacturer to make the large investments in research and production capacity that allow it to provide large volumes of vaccines at prices that are accessible to LICs.<sup>29</sup> Although the AMC's low price is not available to most LMICs, it is hoped that LMICs will benefit through economies of scale.

See the discussion of obstacles to both Hib and Pneumo adoption in Section 5.1.

### 5.3. Rotavirus Vaccine

In addition to respiratory diseases, diarrheal diseases are still a major cause of childhood illness in LMICs, and Rota causes more severe (30–50%) diarrhea<sup>30,31,32</sup> in children than any other etiological agent. However, as with pneumococcal disease, good health-care access and a very cheap treatment—in this case, oral rehydration therapy (ORT)—has greatly reduced the mortality due to Rota and made it a morbidity problem.

Some countries have expressed concern about determining predominant serotypes as part of establishing BOD. Because the current vaccines seem to have good cross-protection, better documentation of the cross-protection and appropriate communication to policymakers will be important.

Again, issues of different cost structures, new vaccine prices, competing problems of mortality, and difficulty in communicating that most diarrhea will not be prevented may be barriers to vaccine adoption.

### 5.4. Human Papilloma Virus Vaccine

The first obstacle that HPV vaccines face is a poor understanding of the epidemiology of cervical cancer. Globally, it is estimated to be the 5th most common cancer in terms of mortality,<sup>33</sup> and the 2nd most common cancer in women—though it may be less common in some countries. (Turkey estimates it is the 8th leading cause of cancer deaths in women.) Second, and related to the epidemiology, the vaccines do

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<sup>28</sup> GlaxoSmithKline. Synflorix™, GlaxoSmithKline's pneumococcal vaccine, receives European authorization [press Release]. [http://www.gsk.com/media/pressreleases/2009/2009\\_pressrelease\\_10039.htm](http://www.gsk.com/media/pressreleases/2009/2009_pressrelease_10039.htm). Published March 31, 2009.

<sup>29</sup> Jack A. GSK and Pfizer pledge vaccines. *The Financial Times*. March 24, 2010. <http://www.ft.com/cms/s/0/4793f754-36a8-11df-b810-00144feabdc0.html>.

<sup>30</sup> Brandt CD, Kim HW, Rodriguez JO, Arrobio JO, Jeffries BC, Stalling EP, Lewis C, Miles AJ, Chanock RM, Kapikian AZ, et al. Pediatric viral gastroenteritis during eight years of study. *J Clin Microbiol*. 1983;18:71-78.

<sup>31</sup> Matson DO, Estes MK. Impact of rotavirus infection at a large pediatric hospital. *J Infect Dis*. 1990;162:598-604.

<sup>32</sup> Konno T, Suzuki H, Imai A, Kutsuzawa T, Ishida N, Katsushima N, Sakamoto M, Kitaoka S, Tsuboi R, Adachi M. A long-term survey of rotavirus infection in Japanese children with acute gastroenteritis. *J Infect Dis*. 1978;138:569-576.

<sup>33</sup> WHO. Fact sheet No. 297: Cancer. <http://www.who.int/mediacentre/factsheets/fs297/en/index.html>. Published February 2006.

not protect against all cervical cancer, nor do they obviate the need for screening programs, and there is little knowledge of the prevailing serotypes in many developing countries (though there is good evidence that the available HPV vaccines include the serotypes most commonly responsible for cancer in all countries).

Third, cost-effectiveness may not be favorable because the screening programs available in some countries should not stop when vaccination begins and because there is such a long delay between vaccination (age 12–16) and incidence of disease (generally > age 40). However, this latter factor was ultimately not an issue with hepatitis B (Hep B), which has a similar profile from time of infection to development of liver cancer, particularly once the price of Hep B vaccine decreased dramatically. Price was commonly mentioned as a barrier to HPV being seriously considered for adoption in the near term. In fact, countries that do not currently have screening programs, such as Cape Verde, and thus some prevention of cervical cancer, would receive greater benefit from HPV immunization. Due to the long delay between intervention and prevention, the discount rate **used** in cost-effectiveness analyses of HPV vaccine is critical, and slight changes that rate can have large effects on the result (see Table 5-1). Given the dearth of economic expertise on advisory committees, this information may be difficult to convey.

**Table 5-1. Discount Rate Effect on Future Value of US\$100**

Time Delay	Discount Rate		
	1%	3%	5%
<b>25 Years</b>	\$77.8	\$46.7	\$27.7
<b>40 Years</b>	\$66.9	\$29.6	\$12.9

Fourth, communication, education, and advocacy will be difficult not only for the aforementioned reasons but also because the vaccine prevents a sexually transmitted disease. In some societies, it may be difficult culturally to address this issue with society and parents of preteen girls who will be targeted for vaccination.

Fifth, HPV vaccine is administered to school-aged girls, not to infants and toddlers at the same time as other childhood vaccines now on most countries' immunization schedules. This may require some countries to build their capacity to include immunization in school health programs (generally carried out through Ministries of Education rather than Ministries of Health), thus introducing additional bureaucratic, logistical and cost issues.

## 5.5. Japanese Encephalitis

Japanese encephalitis (JE) is a disease of public health concern only for the regions of south and east Asia and the western Pacific (at least half the world's population). It has been brought up in countries in this region, as new vaccines against it are becoming available. JE is responsible for a reported 50,000 cases and 10,000–15,000 deaths annually, with most of the survivors left with severe disabilities. This disease generally affects the rural poor. Because of the difficulty in conducting diagnostics and surveillance, the disease is generally underreported. In addition, because of the high mortality rate and severe morbidity of the disease, as well as with the lack of specific treatment, JE vaccination is really the only option where effective mosquito control programs are not practical.

A significant barrier for adoption had been that the supply of inactivated vaccine, made in mouse brain, was limited. With the availability of alternative vaccines, however, particularly the live attenuate vaccine, this barrier has been removed, and country adoption has increased. Though there is still no prequalified JE vaccine and production quantities are still relatively limited, countries, including, China and Thailand, have introduced universal vaccination (since 2005). Indonesia is planning a field trial, with a plan to adopt the vaccine for high-risk areas of the country.

Of the 4 countries in the study in this region, almost all had seriously considered introduction of JE vaccination (except the Philippines, primarily for lack of BOD evidence).

## **5.6. Summary**

In summary, the new vaccines under consideration by Expanded Program on Immunization (EPI) initiatives in LMICs have barriers that go well beyond price and that are generally not associated with the traditional EPI vaccines. These barriers can be categorized as follows:

- Epidemiology: serotyping, morbidity versus mortality
- Vaccine effectiveness: they only address some causes of diarrhea and cervical cancer
- Economic analysis: cost studies adjusted to local situation
- Communication: advocacy and education
- Programmatic aspects: ability of the program to implement a new vaccine, such as HPV; school vaccination programs, and so on

These additional issues magnify scrutiny of vaccines.

## **6. Manufacturer Interviews**

This section synthesizes what this study learned from its interviews with vaccine manufacturers. (See Annex E for specific questions asked.) First, we summarize what the vaccine manufacturers told the interviewers. Then, we discuss what the study team believes to be the implications for new vaccine adoption by lower-middle-income countries (LMICs).

### **6.1. Summary of Responses**

This section summarizes what the study team learned from the manufacturers interviewed for this study. We have also noted where there are differences in how the two groups of manufacturers—International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) companies (or multinational companies [MNCs]) and Developing Country Vaccine Manufacturers Network (DCVMN) members (or developing country manufacturers [DCMs])—replied to interview questions.

Both the MNCs and the DCMs see LMICs as potentially attractive markets. However, none of the companies organize their sales efforts around countries grouped by income levels; rather they are based around geographies and international tenders as a separate segment.

When asked about lessons for LMICs from GAVI, the manufacturers cited the “creation of a market” and GAVI’s implementation of strong procurement practices (using UNICEF Supply Division and the Pan

American Health Organization's [PAHO's] Revolving Fund). Manufacturers consider supply factors as only one component of a successful new vaccine introduction, and they regard the focus by others on unit price as excessive. Accurate forecasting, professional procurement practices, and multiyear contracting are supply-related factors that the manufacturers also consider important. Local requirements to customize vaccine presentations add to costs (and therefore prices), and customization can restrict competition, as some potential suppliers consider custom requirements not worth the trouble. Pooled procurement, in general, is regarded favorably by manufacturers for the standardization and visibility it brings, provided the principles of tiered pricing are respected (for MNCs); some manufacturers are critical of PAHO in this respect. The study team interpreted this importance to imply that LMICs cannot expect MNCs to offer them the "lowest price" offered to low-income countries (LICs).

Although many perspectives are common to MNCs and DCMs, the latter see themselves as disadvantaged relative to MNCs as suppliers of new vaccines: Most important, DCMs do not currently produce the new vaccines for human papilloma virus (HPV), pneumococcus (Pneumo), and rotavirus (Rota). For "newer" vaccines such as hepatitis B (Hep B) and *Haemophilus influenzae* type B (Hib), which are produced by DCMs, introduction is incomplete in LMICs, despite capacity availability and affordable pricing. DCMs also are disadvantaged relative to MNCs by the former's relative lack of export representation and, in some countries, regulatory requirements that look to MNCs' historic domestic markets for reference.

A number of technology-transfer arrangements are in hand or in negotiation between MNCs and DCMs for some of the new vaccines in several of the major LMICs. However, DCMs would like to see more such arrangements. But MNCs worry that some LMIC governments will demand technology transfers to local DCMs when this would be uneconomic otherwise.

## 6.2. Implications

The following are the study team's conclusions concerning the implications of the responses by manufacturers to the interviews in terms of the adoption of new vaccines in LMICs.

The newest vaccines (HPV, Pneumo, and Rota) are, in each case, only produced by a subset of MNCs, which is likely to remain the case for some years. Thus LMICs will face limited supply options in terms of (1) numbers of competitors and (2) manufacturers that are likely to pursue only tiered pricing approaches. However, MNCs are interested in supplying LMICs with all new vaccines. Therefore capacity to meet LMIC markets should not be an issue, especially if introduction and required volumes are accurately forecast. However, the supply offered to LMIC markets should be monitored.

Larger-population LMICs are likely to access new vaccines through technology-transfer arrangements to their own manufacturers (Rota and others in Indonesia, meningitis A and C in Egypt). Some countries might decide to wait to attain technology transfer, even though this may involve delaying introduction of the vaccines. Local supply in the larger LMICs is not the only constraint on new vaccine introduction. For example, India in particular has lagged in the introduction of Hep B and Hib, despite ample local production of assured quality for export and the domestic private sector.

Given the situation in the larger countries concerning technology transfers, there are the following outstanding issues: There appear to be some gaps in the arrangements currently coming into place concerning technology transfers—for example, for HPV in India and Indonesia. It would be optimal for the technology-transfer plans to align with stated and planned public health priorities so that rapid

domestic introduction of the new vaccine will follow the transfer. There is not, however, an explicit coordination of public health priorities with industry technology transfers in many, if any, of the LMICs. The study did not learn whether the technology-transfer arrangements permit the recipients to supply other LMICs. If the agreements do permit export, many of the LMIC manufacturers (excepting the Indian firms) do not seem to be very interested in export in the near term.

Access and supply issues around new vaccines mainly apply to smaller population LMICs. Technology transfer to smaller LMICs will not occur where there is no vaccine industry. Furthermore, technology transfer is unlikely to be economically viable in other small-population countries that have or would like to develop manufacturing capability. DCMs in larger countries often are prohibited from exporting products produced as a result of technology transfer by terms of their licenses from MNCs. The bargaining position in vaccine markets of individual small-population LMICs is weak, with limited sources of supply for vaccines of interest. Many of these LMICs also lack sufficient procurement expertise.

The key negotiating asset of the smaller-population LMICs is the opportunity to create a market for new vaccines. These countries offer MNCs opportunities for incremental growth and profit for the period during which a small number of MNCs control the supply of the new vaccines, as long as the MNCs can obtain prices that they consider adequate. The market needs to be credible to affect MNC behavior, meaning it needs to have robust introduction planning supported by appropriate budgets. Uncertainty over pricing for both buyers (“If we decide to introduce, what price can we expect?”) and sellers (“Should we offer prices closer to those in high-income countries or the price for GAVI procurements to entice LMICs into the market?”) makes creating the market an iterative process. Information about prices across countries would be important in order to give buyers leverage and to lower the risk of introduction in the developing market. Smaller LMICs would be much stronger collectively than individually, such as in a pooled procurement mechanism. For vaccines with both MNC and DCM producers, there would be benefit in each LMIC to ensure that there are no procurement practices or regulatory barriers to DCM supply.

## **7. Recommended Interventions**

The goal of the study’s recommendations is to ensure that lower-middle-income country (LMIC) national immunization programs (NIPs) perform at their highest possible level to improve and achieve public health outcomes. The objective of making recommendations is to identify practical interventions and concrete strategies at the global, regional, and country levels to affect new vaccine adoption in LMICs, comparable to what GAVI has done for low-income countries (LICs). The study identified numerous paths that could address the objective at all levels, and these recommendations fall into one or more of four main thematic categories: (1) evidence and capacity building, (2) policy and advocacy, (3) financing, and (4) procurement and supply. However, some of the recommendations arising from the study have higher priority than others. Based on a qualitative assessment of their importance, the study categorized its recommendations as either Priority One or Priority Two. These interventions are derived from suggestions by key informants to the team; notable practices that the team identified in some countries; and information or practices that, though not expressed by informants, the team determined were lacking or inadequate. (See Box 7-1 for more.)



It is essential to note that funding must be provided for the implementation of all the recommendations; in particular, external funding is required at the regional and global levels. At the country level, many LMICs can take steps to meet several of the recommendations within current program resources or with supplementary domestic funding, though external financial and technical assistance could help in many cases.

### Box 7-1. Recommendation Levels, Themes, and Priorities

#### Levels

- **Country interventions** are important because they address the specific needs and situations of individual countries and can often be accomplished within a country's own resources, with only minimal requirements for outside technical support or advocacy.
- **Regional interventions** take into account that countries (1) within a region often have similar disease characteristics, so their experiences and research are comparable; (2) look to each other for advice and healthy competition; (3) often make intracountry comparisons with regional neighbors; and (4) could undertake joint research.
- **Global interventions** address common factors affecting countries throughout the world, and encourage countries and organizations to share tools, information and practices that can have global application.

#### Themes

- The **evidence and capacity building** recommendations focus on providing fundamental information and skills needed for making good decisions.
- **Policy and advocacy** recommendations are important to ensure that data and expertise translate into government decisions and action.
- The **financing** recommendations concern making not only the necessary resources available for vaccines but also the tools and procedures necessary to ensure that resources are planned for and are used efficiently. The financing theme also includes the recommendation that resources be found to implement all of the recommendations.
- **Procurement and supply** recommendations focus on how countries, individually or collectively, can effectively and efficiently obtain vaccines once adopted.

#### Priorities

- **Priority One** recommendations are the most important to implement at each level in each of the four theme areas.
- **Priority Two** recommendations are those that are important to pursue at each level and in each theme area, but that are not as important as those in Priority One.

Box 7-2, Table 7-1 and Table 7-2 summarize the recommendations by level, category, and priority. The following pages elaborate on each recommendation.



### Box 7-2. Prerequisite: Ensure Strength of Existing Routine Immunization Program

Outside of the themes discussed on the following pages, the strength of the existing routine immunization program is considered to be a basic prerequisite to the introduction of new vaccines. This idea was highlighted by informants in several countries, as well as by the study's quantitative analysis, as a key consideration in the decision-making process. The dimensions of a strong program include attaining and sustaining high and equitable coverage of the surviving birth cohort, a history of successfully adding new vaccines, and a reputation for safety and reliability. It is important that the additional demands that will be made on the system through the introduction of a new vaccine be carefully assessed to ensure that the program does not suffer from an inadequate system. For example, if DTP3 coverage of 75% or more is used as a first proxy for strength of the program, then the following LMICs would be classified as needing program strengthening before introducing new vaccines: Azerbaijan (DTP3 coverage of 70%), India (66%), Nigeria (54%), Papua New Guinea (52%), and Samoa (46%). (See table in Annex C.) Some other countries that meet this coverage standard have significant regional disparities, and others need to expand their cold chains and other supporting infrastructure before introducing new vaccines. Informants noted such disparities in the study countries of China, Morocco, South Africa,<sup>1</sup> Turkey,<sup>1</sup> Indonesia, and the Philippines, though in all cases the governments are making efforts to reduce inequality of service delivery.

**Table 7-1. Priority One Recommendations**

Theme	Level		
	Country	Regional	Global
<b>Evidence and capacity building</b>	Strengthen epidemiological, surveillance, and economic analysis capacities	Actively promote and strengthen regional information sharing and joint research on burden of disease (BOD), pricing, cost-effectiveness, etc. (regional clearinghouse)	Create a technical and reliable source for global vaccine market information, including vaccine pipeline, vaccine prices, pricing policies, and procurement principles and practices
<b>Policy and advocacy</b>	Improve procurement regulation to promote competition, quality, and sustainability	Conduct advocacy to strengthen political will and support champions for new vaccines	Conduct advocacy to strengthen political will, regulation, and policy development
<b>Financing</b>	Take steps to increase domestic funding and capacities to negotiate with ministries of finance and other potential funders	Increase countries' and partners' awareness of the value of vaccination in the broader context of government investment and achievement of the Millennium Development Goals	Promote transparency and access to comparatively low and affordable vaccine prices with sustainable domestic financing

<b>Procurement and supply</b>	Consider using or joining a pooled procurement mechanism	Develop intercountry and regional processes for achieving pooled procurement (where desired by countries), vaccine quality, safety, and a diversified and sustainable base of supply	Support regional and country activities for efficient and effective procurement systems through assessment and identification of improvement to current practices and policies
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**Table 7-2. Priority Two Recommendations**

Theme	Level		
	Country	Regional	Global
<b>Evidence and capacity building</b>	<ul style="list-style-type: none"> <li>Strengthen National Immunization Technical Advisory Groups (NITAGs) and National Regulatory authorities (NRAs)</li> <li>Foster information sharing and use of all evidence among all concerned in-country stakeholders (Expanded Program on Immunization, Family and Community Health [FCH], planning, finance, and procurement entities)</li> <li>Consider pilot or test introduction at sub-national scale to learn about effectiveness, safety, and implementation issues</li> </ul>	<ul style="list-style-type: none"> <li>Foster joint research and surveillance among neighboring countries</li> </ul>	<ul style="list-style-type: none"> <li>Continue efforts and funding to build capacity of NITAGs and NRAs</li> </ul>
<b>Policy and advocacy</b>	<ul style="list-style-type: none"> <li>Ensure budgetary line items, policies, and practices that highlight vaccine financing</li> <li>Improve advocacy skills of new vaccine champions</li> </ul>	<ul style="list-style-type: none"> <li>Take advantage of regional networks beyond the World Health Organization (WHO), e.g., the European Union</li> </ul>	<ul style="list-style-type: none"> <li>Promote and maintain vaccines and immunization among the top priorities of the global health agenda</li> </ul>
<b>Financing</b>	<ul style="list-style-type: none"> <li>Strengthen Ministry of Health capacities to negotiate with Ministry of Finance and vaccine manufacturers</li> <li>Develop and implement</li> </ul>	<ul style="list-style-type: none"> <li>Provide technical support for country finance and budgeting activities</li> </ul>	<ul style="list-style-type: none"> <li>Provide funding to implement recommendations at regional and global levels</li> <li>Provide introductory financing to help introduce new vaccines</li> </ul>

Theme	Level		
	Country	Regional	Global
	multiyear plans that consider all potential sources of funding, including health insurance		
<b>Procurement and supply</b>	<ul style="list-style-type: none"> <li>• Consider using and benefiting from Pan American Health Organization (PAHO) and UNICEF procurement services</li> <li>• Strengthen communication with manufacturers</li> <li>• Use products of assured quality (WHO definition) as a reference</li> </ul>	<ul style="list-style-type: none"> <li>• Consolidate demand forecasting</li> <li>• Conduct regular regional vaccine market analysis and dialog on vaccine market development</li> </ul>	<ul style="list-style-type: none"> <li>• Promote active use of PAHO and UNICEF Supply Division's procurement services and references</li> <li>• Conduct regular global vaccine market analysis and dialog on vaccine security and market development</li> <li>• Help ensure better understanding and planning of the role of local production when considering new vaccine adoption</li> <li>• Encourage and support prequalification of products from additional manufacturers</li> </ul>

## 7.1. Priority One Recommendations

### 7.1.1. Country-Level Interventions

#### 1.1.1.1. Evidence and Capacity Building

##### 7.1.1.1.a. Strengthen epidemiological, surveillance, and economic analysis capacities

Lack of country-specific knowledge about burden of disease (BOD) is a major constraint to evidence-based decision making in many countries. In addition, national capabilities to assess the quality of epidemiological and economic evidence are uneven, which can lead to erroneous conclusions concerning BOD and the economic impact of vaccines. The concept of evidence-based decision making is well established in the LMICs; countries can make better decisions if they have or can collect quality data that allow them to properly assess the BOD and economic factors related to all the major diseases for which new vaccines may be considered. The countries can then establish priorities and make informed choices among potential vaccines to adopt, in line with ensuring that the LMICs are obtaining value for money.

As shown in Appendix 1, various economic analyses can be performed to shed light on the financial benefits and opportunity costs associated with the decision of whether to adopt new vaccines. Although several of the countries studied include cost-effectiveness in their analysis of potential new vaccines, not all do. Others are unable to do so, due to a lack of sufficient and accurate<sup>34</sup> country-specific information, including both cost and effectiveness data (see Section 4.1.2), to carry out the analysis. Among those

<sup>34</sup> Note that the value of cost-effectiveness analysis in making decisions is compromised if the effectiveness data, which depend on good epidemiological BOD estimates, are inaccurate.

countries that consider economic analysis, some do not have the expertise of economic analysts on their advisory committees or within the Ministry of Health. Several actions can be taken to address this issue:

- Encourage all LMIC governments, particularly those that have expressed interest in cost-effectiveness analysis, to identify and include individuals with cost-effectiveness analysis skills on their immunization advisory committees. In particular, encourage them to add participation from Ministry of Finance (MoF) experts, both to gain their expertise in carrying out the economic analysis and to obtain early MoF buy-in in the decision-making process. Likewise, health economics skills are often available in the academic sector, and such experts could be contracted by advisory committees to conduct these analyses.
- Provide technical support to local research institutions to improve their ability to carry out such analyses.
- Expand PAHO's ProVac's work on cost-effectiveness to other regions.
- Help government or research institutions to design methodologies that would enable decision makers to collect and analyze cost information, especially when there are insufficient data to undertake formal cost-effectiveness analysis.

#### **7.1.1.1.b. Improve procurement regulation to promote competition, quality, and sustainability**

Countries can modify their procurement systems to promote competition, quality, and sustainability by taking the following steps (if these procedures are not already in place):

- Ensure that all potential suppliers of World Health Organization (WHO)–prequalified vaccines are eligible to bid on tenders and that all are informed about the opportunity to bid. Identify and remove barriers to market entry for producers of vaccines of assured quality.
- Ensure that National Regulatory Authorities (NRAs) and the unit responsible for procurement are strong and work together to make sure that the maximum number of suppliers of acceptable-quality vaccines can participate in tenders.
- Do not require as a prerequisite in-country presence for suppliers of WHO-prequalified products in order to participate in tenders.
- Consider offering framework contracts for more than one year's supply when needed (as UNICEF Supply Division does).
- Use competitive contracting procedures, separate from the procurement of vaccines, for the acquisition of related services and technical assistance (to avoid conflicts of interest and to make the vaccine procurement as clear and transparent as possible).
- Use fast-track procedures to register the WHO-prequalified vaccines.

#### **7.1.1.1.c. Take steps to increase domestic funding**

In general, LMICs have the resources to finance new vaccine introductions through domestic sources. The new vaccines have costs that are higher on a per-dose or full-course basis than traditional Expanded Program on Immunization (EPI) vaccines. Thus substantial additional domestic funding must be allocated to vaccine budgets in order to accommodate the new vaccines. However, the sums necessary are often a relatively small fraction of current government spending on health. For example, a vaccine that cost US\$20 per course (3 doses plus wastage) would represent less than 5% of LMIC government health spending at the lower end of the gross nation income (GNI) per capita list (from \$1,000–\$2,000)

and less than 1% of government health spending for LMICs with GNI per capita of between \$2,000 and \$4,000.<sup>35</sup> A more-expensive vaccine that cost US\$80 per course would represent less than 5% of government spending on health for LMICs with GNI per capita of about \$2,000–\$3,000 and less than 2% of government spending on health for LMICs with GNI per capita of about \$3,000–\$4,000. It should be noted that the outlay of governments' net of cost savings (e.g., from treatment of illnesses averted) would be less than the amount paid for the vaccine alone.

#### **7.1.1.1.d. Consider using or joining a pooled procurement mechanism**

Navigating vaccine markets is challenging for all countries, but more so for smaller and lower-per-capita-income LMICs, as well as for those with little experience in vaccine procurement (such as those LMICs that have benefited from GAVI support but are now graduating from it). These LMICs should consider joining a pooled procurement mechanism, such as the Pan American Health Organization's (PAHO's) Revolving Fund or the still-developing pool in the WHO's Eastern Mediterranean Region. A pool would allow the orders from smaller birth cohort countries to be aggregated into bigger orders, with the potential to attract lower prices. Lower-per-capita-income countries often lack personnel with the skills to operate effectively in vaccine markets. By combining efforts into a pool, countries can benefit from their comparative advantages, infrastructure, and capacities and likely do a better job of negotiating overall. The countries that recently began graduating from GAVI support told this study that they are uncomfortable with and concerned about entering vaccine markets for new vaccines that have substantially higher prices than traditional vaccines. Entering into a pool mechanism would allow the GAVI graduating countries to feel more at ease about getting competitive prices for vaccines. If a country is not eligible for any pool mechanisms but finds itself in the situation described here, it might want to take up the next recommendation—using UNICEF Supply Division's procurement services.

### **1.1.1.2. Regional Interventions**

#### **7.1.1.1.e. Actively promote and strengthen regional information sharing and joint research on BOD, pricing, cost-effectiveness, and so on, through a regional clearinghouse**

LMICs are interested in the experiences of their neighbors when considering a new vaccine in order to learn more about comparative information on BOD, vaccine safety, price estimates, and cost-effectiveness. The WHO regions organize annual intercountry meetings of national EPI managers that update the managers on new technologies and innovations, with much focus during the past few years on new vaccines. The WHO regions also have organized workshops on decision making and prioritization concerning new vaccines. These meetings and information sharing are important and useful; however, more information sharing that goes beyond new technologies and innovations could help with new vaccine adoption. Information should be made available that could be accessed on an as-needed basis rather than once annually or when a workshop is scheduled. This kind of information sharing would also involve more than just EPI managers. For example, the development of regional information clearinghouses through which government officials, academics, researchers, and medical associations within a region could post and review a variety of data in an organized, user-friendly way

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<sup>35</sup> These calculations are based on the following assumptions drawn from the group of LMICs concerning government health spending: At the middle of the LMIC range (GNI per capita of US\$2,500), governments spend about US\$100 per capita on health and have a crude birth rate of 25/1,000 population. Those at the lower (upper) end of the LMIC range spend less (more) on health per capita and have higher (lower) crude birth rates.

could greatly improve the information available on new vaccines to decision makers. If possible, including information on prices (supported by information about procurement details that affect prices, such as volume, presentations, duration of tenders, special packaging, etc.) that neighboring countries have paid in recent tenders for new vaccines would help other countries in planning new vaccine introductions and in negotiating with vaccine manufacturers. It would also help indicate the likely future price offered and thus provide a possible range of prices for the analysis of cost-effectiveness. Similarly, posting the results and methodological details of BOD studies could, in some cases, be convincing that there is a similar BOD in another country, provide support for similar findings from smaller-scale studies conducted in other countries, or help guide decisions concerning methods to be used in upcoming BOD studies. This could speed up decision making by providing more confidence in otherwise limited data and help ensure that quality evidence is gathered for decision making.

The study team suggests a similar intervention—that is, a clearinghouse—at the global level (see Section 7.1.1.3.a). Decisions on the functions and purposes of such clearinghouses will determine whether separate entities are needed at regional and global levels and how they should be related.

#### **7.1.1.1.f. Conduct advocacy to strengthen political will and support champions for new vaccines**

Renowned figures who are viewed as knowledgeable and unbiased can help strengthen the efforts of country immunization programs by giving personal attention to country-level figures able to engage in advocacy for immunization. The advocacy of one vaccine champion, Dr. Ciro de Quadros's, was an important influence on new vaccine adoption in Latin America. This type of advocacy is also important on the global level (see Section 7.1.1.3.b).

#### **7.1.1.1.g. Increase awareness of the value of vaccination in the broader context of government investment**

LMIC decision makers want to be sure to obtain value for the resource allocation decisions that they make concerning new vaccines. They are spending national resources and want those resources to be used well. Hence, decision makers want to get the maximum benefit for the funds they spend. To address this issue, regional efforts should include awareness raising about the vaccines and the value represented by making an investment in health through the adoption of the vaccines. This would mean raising the relative cost-effectiveness of the vaccines (acknowledging that specific cost-effectiveness analysis calculations for the specific country circumstances, including country-specific BOD and costs, could or should be performed) compared with alternative health investments that might be considered. It is likely that the new vaccines would fare well in cost-effectiveness calculations when compared with surgeries or with the treatments of many chronic diseases that are arising on the health agendas of LMICs (for example, human papilloma virus [HPV] vaccine preventing future cervical cancer).

#### **7.1.1.1.h. Develop intercountry and regional processes for achieving vaccine quality and safety and a diversified base of supply**

Some LMICs rely on the acceptance of vaccines and pharmaceutical products by the European Medicines Agency (EMA) or the US Food and Drug Administration (USFDA). These practices could be extended to regional agencies for quality and safety assessment, or countries within a region could recognize each other's assessments (including "mutual recognition mechanisms") or collaborate on performing safety



and quality assessments. These practices would cut down on the costs for all countries, economize the skills within each country, and, in some cases, speed up adoption.

Pooled procurement carries with it advantages and disadvantages that should be weighed by each region<sup>36</sup>. A regional procurement mechanism can provide pricing stability and potentially lower prices, as well as foster improved regional information exchanges and country-level actions (such as line-item budgets and multiyear planning) to promote faster adoption. Yet pooled procurement could also result in higher prices than might otherwise be obtained for the poorest countries in the pool. Thus countries of similar levels of GNI per capita might best be suited to join in a pooled procurement mechanism. Pooling also requires that countries (1) use harmonized products to achieve economies of scale, (2) are committed to participate consistently, and (3) have trust in other pool participants and pool management.

Regional procurement mechanisms are being discussed in multiple regions, including advanced discussions of alternative setups and exchanges with the PAHO Revolving Fund and the UNICEF Supply Division in the Eastern Mediterranean Region (EMR). Informants from EMR countries have expressed interest and enthusiasm about the proposal. Pooled procurement may be useful in regions other than EMR, though it is most likely to go ahead in the short term in regions that have already begun discussions and generated interest in the topic.

The PAHO Revolving Fund offers a model for adaptation for regional pooled procurement. One way to move forward with the EMR initiative suggested by one interviewee would be to perform a pilot joint procurement of a new vaccine while also documenting the procedures used and identifying issues to resolve if the arrangement is to be taken to a greater scale.

Finally, and critically, successfully launching a pooled procurement mechanism requires significant technical and financial support in building the system, preparing countries to use the system, and raising the seed money for any revolving fund mechanism.

### **1.1.1.3. Global Interventions**

#### **7.1.1.1.i. Create a technical and reliable source for global vaccine market information (global clearinghouse)**

As stated in Section 7.1.1.2.a, LMICs are interested in the experiences of other countries, specifically their neighbors, when considering a new vaccine. This includes interest in epidemiological information as well as information concerning vaccine availability, vaccine markets, price, and procurement. Thus this study recommends making available information on these topics at both the regional and the global levels. Regions are likely the better focus for information sharing on epidemiology and experiences with vaccine availability, vaccine markets, price, and procurement, because of similar disease conditions, political and administrative systems, and common languages. Furthermore, pooled procurement systems seem to be starting regionally (e.g., the long-standing PAHO Revolving Fund and the nascent Eastern Mediterranean pooling initiative). However, to ensure that information is available that permits countries to foster maximum competition among vaccine suppliers for their tenders, it is important that vaccine availability, quality information, and experience with prices, contract terms, and so forth also be available globally. Hence, it is desirable to have both regional and global sources of vaccine market and epidemiological

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<sup>36</sup> Note that there is no strong reason for a pooled procurement arrangement to be limited to a given region. A mechanism could include countries from more than one region and not all countries in a region need join a pool.

information, with regional sources that coordinate with the global source and offer information tailored to regional needs.

Concerning the organization of the information sharing recommended above, there are a number of ideas or existing initiatives to build upon. The Center for Global Development has suggested that an “Infomediary”<sup>37</sup> be developed, where “funding agencies, procurement agents, technical agencies, global health partnerships, and national buyers” could post information about health products, including vaccines and supply information (sales, prices, plans, product quality information, etc.), with the aim to improve forecasting. When applied to vaccines, this model would also provide procuring countries and vaccine manufacturers with information about vaccine availability and presentation, pricing, and global supply. The model could be expanded to provide information about country-level BOD, research, and experiences with new vaccines. PAHO has begun to develop a basic information system, through its ProVac Initiative, known as the On-Line International Vaccine Economics and Statistics (OLIVES). This global database does not yet have data in all planned categories, but it does offer a solid start for a more comprehensive effort. In addition, the US Centers for Disease Control (CDC) publishes on its Web site the prices it pays for vaccines as well as US private-sector prices for the same vaccines (as provided by manufacturers).<sup>38</sup> PAHO publishes the prices it obtains through the Revolving Fund in its newsletter. In addition, UNICEF’s Supply Division has, for many years, published the weighted average prices it obtains for GAVI vaccine procurements, and more recently has started publishing price information per product and per manufacturer. In addition, price information on antiretroviral drugs is shared globally through the Global Price Reporting Mechanism (see Box 7-3).

### **Box 7-3. Model: Global Price Reporting Mechanism**

A model for sharing price information already exists with the Global Price Reporting Mechanism (GPRM) for antiretroviral (ARV) drugs to treat AIDS. The GPRM is a Web-based transaction database initiated by the World Health Organization’s AIDS Medicines and Diagnostics Service to monitor and share price information on ARVs and tuberculosis and malaria drugs to help countries obtain optimal pricing. Pricing information is provided by global organizations that procure drugs for different countries.

This system is described at [www.who.int/hiv/amds/gprm/en/](http://www.who.int/hiv/amds/gprm/en/)

Regarding publication of pricing information, most agreements with suppliers currently do not allow the countries to make their negotiated prices public. Because this information is out of public view, other countries tend to be more uncertain about what prices they might expect than if they could see the prices and terms actually obtained by their peers. In some cases, this tactic slows new vaccine adoption because countries are not sure what funding must be mobilized and what cost figures should be used in cost-effectiveness calculations. This has negative effects on vaccine markets by delaying vaccine introductions

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<sup>37</sup> Center for Global Development. Create an Infomediary.

[http://www.cgdev.org/section/initiatives/\\_archive/demandforecasting/dfsolutions/infomediary](http://www.cgdev.org/section/initiatives/_archive/demandforecasting/dfsolutions/infomediary). Accessed November 27, 2010.

<sup>38</sup> Centers for Disease Control. CDC Vaccine Price List. See <http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm>. Accessed October 15, 2010.

and making adoption time lines uncertain. Vaccine manufacturers frequently cite more certainty about demand as being important to their ability to plan capacity. Thus this report suggests the following actions to reduce price uncertainty: (1) publication of the tier criteria that the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) uses as their pricing strategies (if possible) and (2) publication of the prices paid for new vaccines (along with contract conditions<sup>39</sup>) on a country-by-country basis.

#### **7.1.1.1.j. Conduct advocacy to strengthen political will, regulation, and policy development**

As mentioned in Section 7.1.1.2.b, engaging renowned figures who are viewed as knowledgeable and unbiased in the advocacy for immunization can help strengthen the efforts of country immunization programs. Dr. Ciro de Quadros's advocacy was an important influence on new vaccine adoption in Latin America, and now, with the Sabin Vaccine Institute, he is an authoritative voice globally. Likewise, Ban Ki-Moon's Women's and Children's Health Initiative could be a platform to address LMIC heads of state on new vaccine adoption.

Beyond advocacy for the adoption of vaccines, there is a need for advocacy for changes in the regulatory and policy environments surrounding new vaccines, particularly as these items affect procurement and production options. Regulatory regimes and policies should ensure the safety and efficacy of vaccines, but should not unnecessarily restrict competition to supply LMIC NIPs with vaccines of assured quality. Similarly, the policy and regulatory environments should ensure that quality and safety of the national production of vaccines and, when possible, make it possible for LMIC manufacturers to attain WHO prequalification of their vaccines so that they might add to the competitive supply available on world markets.

#### **7.1.1.1.k. Promote transparency and access to comparatively low and affordable vaccine prices with sustainable domestic financing**

As discussed in Section 7.1.1.3.a, transparency about the prices paid by LMICs for vaccines would assist other LMICs considering adoption in estimating the range of prices that they might pay, as well as making them aware of all potential suppliers. This would help LMICs make adoption decisions more quickly (because it would reduce uncertainty) and assist them in making more reliable demand forecasts. All LMICs interviewed assume that they will fund vaccines from their own domestic sources, but they would like to obtain the most favorable prices possible. Being able to assess likely price levels from transparent sources on prices paid by others (and related contract details, such as duration of contracts, vaccine presentations, and volume of vaccines purchased) would encourage competitive and affordable prices and would improve program sustainability.

#### **7.1.1.1.l. Support regional and country activities for procurement systems and policies**

See Sections 7.1.1.1.d and 7.2.2.4.a on pooled procurement. Pooled procurement mechanisms do not have to be regional; rather, they could involve countries from multiple regions. In addition, the global level could facilitate learning across regions and provide technical and financial support to regional groups that are considering creating pooled procurement mechanisms.

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<sup>39</sup> Conditions would include the duration of the contract, the volume of vaccines purchased, the presentation of the vaccines, and any other goods or services provided in addition to the vaccines.

## 7.2. Priority Two Recommendations

### 7.2.1. Country-Level Interventions

#### 1.1.1.4. Evidence and Capacity Building

##### 7.2.1.1.a. Strengthen National Immunization Technical Advisory Groups and National Regulatory Authorities

National Immunization Technical Advisory Groups (NITAGs), or equivalent organizations and National Regulatory Authorities (NRAs) are already playing a pivotal role in LMICs' new vaccine decision-making processes by assembling evidence and making recommendations concerning new vaccines. NITAGs and NRAs can be strengthened by providing them with additional skills (e.g., economic analysis skills on NITAGs) and resources (e.g., for the commissioning of specific studies that fill gaps in information considered necessary to make decisions). Global support for the development of NITAGs and NRAs can complement national efforts (see Section 7.2.3.1.a).

##### 7.2.1.1.b. Foster information sharing and use of all evidence among concerned in-country stakeholders

Many factors go into the successful adoption and implementation of a new vaccine. Thus it is important that information be shared widely across the disciplines, offices, and institutions when deciding whether to recommend vaccine adoption and then making the practical decisions involved with introducing the new vaccine. In countries with a variety of medical and academic organizations that carry out epidemiological research funded from a variety of sources, the NIP's team and the NITAG may not be aware of the full range of ongoing and completed research on a particular disease. Even within government organizations, research activities may not be shared adequately. Improved collaboration among researchers can help answer important questions and identify priorities for new vaccines. The decision to adopt a new vaccine goes beyond epidemiology to ensuring the financing for the purchase of the vaccine, the preparation of the health-care system to deliver it (including having adequate cold chain facilities), and being able to procure safe and quality vaccines in global markets at attractive prices. Therefore it is important that information be shared among all the actors involved in all of the practical aspects. This includes information sharing among the planning and financial units within the Ministries of Health (MoHs), between the MoH and the Ministry of Finance (MoF), and with the units responsible for procurement. There are several ways that countries can facilitate the desired information sharing:

- Broaden membership of the advisory committee to members outside the MoH or the government in general, such as to members of pediatric associations, medical research institutes, financial and procurement agencies, and academia.
- Follow China's procedure for compiling extensive documentation for review by its advisory committee (described in "Notable Practice: Decision-Making Processes on New Vaccine Adoption").
- Provide financial resources to advisory committees so that they can commission needed research, studies, or surveillance. For example, encourage collaboration with the CDC or other well-known health research institutions (and provide travel for attendees to increase participation from outside members).
- Host national consultations to bring together all relevant information. (This can be done at the regional level as well, as noted in Section 7.1.1.2.a.)

International organizations may support LMICs by providing technical assistance to help them systematically identify and select the most important research.

**7.2.1.1.c. Consider pilot or test introduction at sub-national scale to learn about effectiveness, safety, and implementation issues**

Introduction on a small scale initially enables the Ministry of Health to treat it as a pilot project, while also addressing critical health needs. Although pilot programs can be performed in either the best-performing regions (where any disruptions caused by the introduction will be best monitored) or the most at-risk regions, it should be noted that introductions will have the greatest impact in the latter. The program can still do intensive monitoring of vaccine effectiveness and adverse effects following immunization (AEFIs) as well as identify potential implementation needs. Comments from global experts interviewed by the team support this:

*“A strategy to get Rota vaccine adopted in the National Immunization Program probably should concentrate on the underserved populations in middle-income countries.”* —John Wecker, interview with study team

*“Demonstration projects can be powerful tools when advocating for vaccine introduction in middle-income countries, and this type data was used in the introduction of Hep B vaccine. Small pilot studies helped convince policymakers that the vaccine would have a huge impact.”* —Richard Mahoney, interview with study team

**1.1.1.5. Policy and Advocacy**

**7.2.1.1.d. Ensure budgetary line items, policies, and practices that highlight vaccine financing**

Policies and practices that support vaccine financing can encourage good vaccine decision making and ensure that introductions of new vaccines are sustainable. Country studies and the quantitative analysis identified three effective measures that countries can take:

- Introduce a separate line item for immunization in the MoH budget (and, of course, ensure that it receives adequate funding to meet the needs for purchasing long-standing vaccines, new vaccines, and the needed delivery costs). This line item will make it obvious what a small percentage of the total health budget immunization represents, even after relatively costly new vaccines are included. A 2008 study of 185 WHO member countries concluded, “In many countries, the creation of a vaccine specific line item in the national health budget seems to have been a viable means of inducing greater national expenditures on vaccines and ensuring a reliable annual allocation.”<sup>40</sup> This study’s quantitative analysis, as noted earlier, found a strong relationship between the presence of a line-item budget for immunization and early adoption of new vaccines.

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<sup>40</sup> Lydon P, Beyai PL, Chaudhri I, Cakmak N, Satoulou A, Dumolard L. Government financing for health and specific budget lines: the case of vaccination and immunizations. *Vaccine*. December 2008;26(51). The authors went on to say, “Having said that, a vaccine specific line item is a necessary but not sufficient condition for vaccines and immunization financial sustainability.”

- Develop a comprehensive multiyear plan (cMYP), which is an approach to immunization planning and budgeting that was developed by WHO and UNICEF and that is widely used by LICs; however, it is hardly known or used by LMICs. Among other things, a cMYP for immunization compares the budgetary impact of alternative funding scenarios, so that decision makers can see the consequences of different budgetary options. Countries may already have other planning and analysis tools that provide comparative information on the potential impacts of alternative options for vaccine adoption. However, for those that do not, a cMYP can be a very useful method to support good decision making.
- Encourage vaccine laws, as has been widely done in the Americas, that guarantee a budget will be made available for immunization. The result of such laws has been a guarantee that budgets will provide sufficient funding for all vaccines in the NIP, thus providing assurances of long-term sustainability. Countries that examine the experiences in the Americas may be persuaded to take action, with appropriate local champions and support from international organizations. (Panama's and Ecuador's vaccine laws were described as notable practices in Section 3.)

#### **7.2.1.1.e. Improve the advocacy skills of new vaccine champions**

Convincing key officials inside and outside of the health sector, including Ministers of Planning and Finance, members of parliament, and even heads of state, that investments in new vaccines are beneficial can be important to the adoption of new vaccines. In addition, it can be helpful to provide those within the health sector, such as Ministers of Health, directors of preventive health services, EPI managers, and influential people from outside the ministry (such as well-known academics and members of the immunization advisory committee), with additional advocacy tools that they can use in the decision making. These advocacy tools could take (1) an accessible approach to making health data come alive to lay audiences or (2) the approach of calculating the costs and benefits of new vaccines in financial terms that are meaningful to decision makers in the Ministries of Planning and Finance.

#### **1.1.1.6. Financing**

##### **7.2.1.1.f. Strengthen Ministry of Health capacities to negotiate with Ministry of Finance and vaccine manufacturers**

In countries around the world, MoHs often have difficulty in negotiations with MoFs, because the former are used to focusing on health information and data and program management, while the latter are focused on achieving results related to the amount of funding allocated. LMIC MoHs are no exception to this, although they have at least some familiarity with the methods used to evaluate value for money in their programs (e.g., variations on cost-effectiveness analysis). Nonetheless, LMIC MoHs could benefit from being able to be more fluent in speaking the results- and value-oriented language and in presenting budget requests in formats that are easy for the MoFs to understand and digest. This skill is particularly important in terms of vaccines and immunizations, because they often are among the most cost-effective interventions available in the health sector and thus have a strong value-for-money case.

Many LMIC government agencies, and the personnel tasked with negotiating vaccine procurement with manufacturers, would also benefit from technical assistance and training. This would help the procurement agencies to better navigate the market (e.g., by gathering information about WHO-prequalified products, price trends, contracting and negotiating strategies of neighboring and peer countries, etc.) in order to achieve the best value in terms of prices, contract length, specific vaccine

characteristics, and needs for vaccine-related technical services. The UNICEF Supply Division and WHO offer technical assistance and training in these areas.

**7.2.1.1.g. Develop and implement multiyear plans that consider all potential sources of funding, including health insurance**

When planning their NIPs, GAVI-supported countries are required to employ the cMYP template, developed by UNICEF and WHO. The plan resulting from the use of the cMYP template includes the costs of strategic changes and program implementation, and analyzes the likelihood of financing of the costs from a variety of sources. Yet this tool is valuable to all countries. LMIC NIPs should consider using a similar approach to planning—especially, the program-financing component of the cMYP template. This spreadsheet tool helps countries quickly estimate the costs of their plans and analyze actual and potential domestic and external sources of funding. This tool allows decision makers to identify gaps in financing and to use that information for advocacy purposes in order to fill the gaps or make adjustments to program objectives so they can live within available resources. LMIC NIPs are usually funded mainly through national or decentralized budget allocations. A potential additional source of funding for NIPs that is of particular promise for some LMICs might be health insurance programs, as they should be interested in interventions that prevent illness and thus reduce claims for treatment costs. Hence, insurance programs might be interested in reimbursing immunization charges for members and in promoting the uptake of immunizations; both actions would provide additional funding, reduce costs, and increase the effectiveness of NIPs.

**1.1.1.7. Procurement and Supply**

**7.2.1.1.h. Consider using and benefiting from PAHO and UNICEF procurement services**

Some LMICs might wish to use UNICEF's procurement services for new vaccines. UNICEF already provides the procurement services of its Supply Division for vaccines for nearly all GAVI-supported countries, as well as for a few non-GAVI countries. Other countries that wish to use UNICEF Supply Division procurement services may do so. UNICEF charges a handling fee<sup>41</sup> for its services in order to cover administrative costs. For that fee, a country can obtain WHO-prequalified vaccines (where available) in specified presentations, delivered securely and purchased on global markets at competitive prices, thus supporting a vaccine security strategy.<sup>42</sup> Countries can also use this mechanism for related immunization commodities, such as injection devices, safety boxes, and cold chain equipment.

Larger and higher-per-capita-income LMICs are likely to believe that they can perform vaccine procurement themselves at a lower cost than UNICEF offers and obtain the same kinds of products. However, for those LMICs that are at the lower end of the per capita income scale, have smaller birth cohorts, or do not have pooled procurement options, UNICEF's services could be a good option.

To use UNICEF Procurement Services, a country must establish a memorandum of understanding with UNICEF via the UNICEF Country Office or contact UNICEF Procurement Services at [psid@unicef.org](mailto:psid@unicef.org).

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<sup>41</sup> Commodity-specific handling fees are available at [http://www.unicef.org/supply/index\\_faq.html#What does it cost](http://www.unicef.org/supply/index_faq.html#What does it cost)

<sup>42</sup> The objectives of UNICEF's vaccine security strategy are uninterrupted, sustainable supply; quality vaccines; multiple manufacturers per vaccine; and affordable prices.

UNICEF conducts procurement in accordance with UNICEF financial rules and regulations, which, in turn, are in accordance with public procurement principles and in support of vaccine security. The bidding modality is in accordance with these criteria and depends on the profile of the demand. UNICEF issues tenders for individual countries or a group of countries, depending on the vaccine type and the timing of the requests. If UNICEF were to receive requests from multiple countries at the same time, it would combine the forecast demand. If the request were on behalf of countries beyond those for which UNICEF normally procures, it would specify with the tender which countries were included. Further information on UNICEF procurement services is available at [http://www.unicef.org/supply/index\\_procurement\\_services.html](http://www.unicef.org/supply/index_procurement_services.html).

#### **7.2.1.1.i.Strengthen communication with manufacturers**

LMICs can contribute to “healthier” vaccine markets and to the success of their own procurements of vaccines by strengthening their communications with vaccine manufacturers. The strengthening of communications could take the following forms:

- Provide multiyear strategic forecasts of vaccine requirements for the NIP.
- Give suppliers as long lead times as possible for vaccine procurements, especially when customized presentations are requested.
- Consult with suppliers on the terms and conditions of future tenders or on competitive processes in order to identify the key areas of flexibility for both parties. This optimizes supply terms and price.<sup>43</sup> Let manufacturers know about, and invite their feedback on, regulatory requirements, such as those overseen by the NRA, keeping in mind that there must be distance between NRA and manufacturers to ensure no undue influence.

While preserving national prerogatives concerning procured vaccines, these steps could also help manufacturers better plan their production capacity, be able to respond to specific requests and requirements, ensure more competition among bidders for tenders, and ensure quality supplies while not unnecessarily burdening suppliers and purchasers.

#### **7.2.1.1.j.Use products of assured quality (WHO definition) as a reference**

WHO defines a vaccine of assured quality as “one that consistently meets appropriate levels of purity, potency, safety, and efficacy as judged through an independent review system competent to take an evidence-based decision on the product for a specified population in a specific context.”<sup>44</sup> All WHO-prequalified vaccines meet this assured quality standard, as do some vaccines only available domestically within some LMICs. LMICs should only procure vaccines of assured quality for their NIPs. They should conduct procurements, using the prices of similar presentations of assured-quality vaccines to countries of similar size and income levels as a reference, to ensure that they obtain quality vaccines at competitive prices. LMICs should make tenders open to all possible providers of assured-quality vaccines, whether domestic or external.

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<sup>43</sup> For example, issue draft tenders for comment by potential suppliers in order to solicit and use feedback to improve the quality of the final tenders.

<sup>44</sup> Milstien J, Dellepiane N, Lambert S, Belgharbi L, Rolls C, Knezevic I, Fournier-Caruana J, Wood D, Griffiths E. Vaccine quality—can a single standard be defined? *Vaccine*. January 2002;20(7-8).



## **7.2.2. Regional Interventions**

### **1.1.1.8. Evidence and Capacity Building**

#### **7.2.2.1.a. Foster joint research and surveillance among neighboring countries**

Surveillance is costly, laboratory facilities are limited, and researchers available to oversee studies are in short supply and great demand. One way to reduce costs while sharing expertise is for countries with similar population characteristics and disease profiles to carry out and fund studies jointly. Doing so can make important BOD information available more quickly and at lower costs than could be done through individual country studies. International organizations and donors can encourage and support such regional activity.

This suggestion is particularly important for small countries or those with less capacity. A study would be carried out in one country with the collaboration of researchers from multiple countries. The data would then be shared among the countries, with the visiting researchers providing advocacy to their home countries. Subsequent studies could rotate to other countries, and specific researchers or regional leaders could provide expertise and training to help build capacity in other countries.

This intervention relates to the country-level interventions in Section 7.2.1.1.a (strengthen capacity to undertake economic analysis), because joint research can transfer these skills. Joint research can also take advantage of laboratory, testing, and surveillance capacity that are not available to participating countries individually.

Governments within the region, or the regional clearinghouses, may also host regional consultations on a specific vaccine or vaccine-preventable disease, to foster a full range of information exchange and discussion. (This is similar, and relates, to the national consultations intervention described in Section 7.2.1.1.c.)

### **1.1.1.9. Policy and Advocacy**

#### **7.2.2.1.b. Take advantage of regional networks beyond WHO**

The WHO regions are key components for policy and advocacy around new vaccines. However, regional efforts in this arena should not be left to WHO alone, especially if other regional bodies might be engaged. For example, in the Eastern Mediterranean Region, the Islamic Development Bank, the Gulf Cooperation Council, the Arab League, and some local private foundations are also engaged in the area. Likewise, within the WHO European Region, the European Union might also be engaged in promoting and providing assistance with the adoption of new vaccines. The Association of Southeast Asian Nations<sup>45</sup> (ASEAN) is another regional institution that could be engaged in this field. The Joint Statement of the ASEAN+3 (China, Japan, and the Republic of Korea) Health Ministers in July 2010 called for increased coordination and collaboration on “the ‘dual burden’ of infectious diseases and chronic and lifestyle-related diseases.”<sup>46</sup>

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<sup>45</sup> Brunei, Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, the Philippines, Singapore, Thailand, Viet Nam

<sup>46</sup> Association of Southeast Asian Neighbors. Joint Statement of the 4th ASEAN+3 Health Ministers Meeting Singapore, 23 July 2010. <http://www.aseansec.org/24936.htm>. The Joint Statement goes on to say, “We support

#### 1.1.1.10. Financing

##### 7.2.2.1.c. Provide technical support for country finance and budgeting activities

Regional support efforts on new vaccine adoption should include assisting LMICs in thinking through the budgets needed to introduce and sustain new vaccines, as well as with alternatives for financing. Examples of considerations in each of these categories are listed below.

- *Budget items for new vaccine introduction:* public awareness and communications, training of delivery and supervisory personnel, creating a buffer stock, increasing cold chain capacity if needed
- *Budget items for sustaining new vaccines:* continued purchase of new vaccines and related supplies, surveillance, and so on
- *Alternatives for financing:* central and decentralized budget allocations, possible insurance reimbursement, and so on

#### 1.1.1.11. Procurement and Supply

##### 7.2.2.1.d. Consolidate demand forecasting

An important function that can be conducted at the regional level is the consolidation of forecasting the demand for new vaccines. Because the WHO regional offices are in regular touch with the region's NIPs and MoHs, they could, with relative ease, compile forecasts of when new vaccines would likely to be adopted and what volumes of vaccines would be demanded (given coverage rates, birth cohorts, and expected wastage rates), with a 3–5-year horizon. This information would be of value to vaccine manufacturers so that they could plan capacity to meet the demand.

##### 7.2.2.1.e. Conduct regular regional vaccine market analysis and dialog on vaccine market development

Just as individual LMICs can contribute to “healthier” vaccine markets by strengthening their communications with vaccine manufacturers, so too can regions. The strengthening of communications could take the following forms: providing multiyear forecasts of vaccine purchases (see Section 7.2.2.4.b); encouraging procurement practices that facilitate competitive supply while ensuring that safe, high-quality vaccines are used; helping develop pooled procurement mechanisms where relevant (see Section 7.2.2.4.a); providing vaccine market information to countries (see Section 7.1.1.2.a); and hosting and facilitating interactive sessions where representatives of LMIC decision makers, procurement staff, and NIP personnel could meet with manufacturer representatives to discuss how the regional market could improve and develop.

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the development of *collaborative networks* in the areas of health promotion; capacity building for health professionals; human resource development, *addressing infectious diseases*; developing traditional, complementary, and alternative medicine; and formulating policy coherence for health and social welfare.” [emphasis added]

## **7.2.3. Global Interventions**

### **1.1.1.12. Evidence and Capacity Building**

#### **7.2.3.1.a. Continue efforts and funding to build the capacity of National Immunization Technical Advisory Groups and National Regulatory Authorities**

The WHO recommendation that countries should create or strengthen NITAGs should be further supported. As mentioned in Section 7.2.1.1.b, having independent, technically sound, and officially recognized bodies to assemble evidence and make recommendations concerning new vaccines helps with good decision making. The SIVAC (Supporting National Independent Immunization and Vaccine Advisory Committees) project<sup>47</sup> and WHO's Eastern Mediterranean Regional Office (EMRO) are particularly active in assisting in the strengthening of NITAGs. More of this kind of work is desirable.

### **1.1.1.13. Policy and Advocacy**

#### **7.2.3.1.b. Promote and maintain vaccines and immunization among the top priorities of the global health agenda**

Bill Gates declared this 10-year period the "Decade of Vaccines." Nevertheless, it is important that additional and sustained effort be made at the global level to keep vaccines and immunizations high on the agenda, particularly in regard to LMICs. This study's findings noted that global actors, such as WHO and UNICEF, which play essential roles in supporting LIC NIPs of LICs, are inconsistent in their engagement concerning immunizations with LMICs. The LMICs themselves appear almost to take for granted the success and high performance of their NIPs and then focus on other topics, such as noncommunicable diseases and health systems issues, where there is not the perception of the same degree of success. Thus the availability of new vaccines and what they can offer to LMIC children can sometimes get lost. Keeping vaccines and immunizations high on the global health agenda will avoid the risk that the benefits of new vaccines to children in LMICs will not be attained as soon as possible.

### **1.1.1.14. Financing**

#### **7.2.3.1.c. Provide funding to implement recommendations at regional and global levels**

As suggested in Section 8, a variety of organizations could play the roles recommended at the regional and global levels. These organizations either need to allocate funding from within existing budgets to play the roles or be able to obtain external funding. Although the recommended interventions have costs, these costs are not anywhere near the costs that might be involved in large-scale subsidization of vaccine prices. (Only Section 7.2.3.3.b suggests a modest vaccine subsidy.) In addition, the costs of the recommendations made here are tiny relative to the benefit to children in LMICs of receiving the protections provided by the new vaccines.

#### **7.2.3.1.d. Provide introductory financial assistance to help introduce new vaccines**

A few of the LMICs toward the lower end of the GNI per capita scale (such as those under \$2,000) or GAVI graduating countries would benefit from limited financial assistance to help introduce new vaccines. This financial assistance could help start the introduction of new vaccines or, in the case of

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<sup>47</sup> See <http://www.sivacinitiative.org/index.php?page=HOME>.

GAVI graduating countries, ease the transition from cofinancing vaccines to paying full price.<sup>48</sup> For example, a small amount of introductory financial assistance might be allocated to help LMICs in this category defray the start-up costs of new vaccine introduction, including personnel training, cold chain and delivery system improvements, and public awareness campaigns. In addition, in certain cases, this assistance could fully or partially subsidize initial vaccine procurement. Alternatively, external funding to lower-income LMICs could support a trial or pilot activity to demonstrate to government decision makers that introducing a vaccine nationally is worthy of government backing. An introductory financial assistance program should be conditioned on strong evidence that the country has a costed plan and budget in place to ensure the availability of funds in future years.

#### **1.1.1.15. Procurement and Supply**

##### **7.2.3.1.e. Promote active use of PAHO and UNICEF Supply Division's procurement services and references**

UNICEF offices in LMICs should actively inform those countries of the available procurement services. Some countries, especially smaller ones, do not feel they have the capacity or ability to conduct a successful tender process in global vaccine markets on their own (see Section 4.2.2). Procuring through UNICEF's procurement services would assure LMICs of reasonable prices for new vaccines and enable them to estimate funding requirements and cost-effectiveness with greater certainty. UNICEF can procure on behalf of any country that has a memorandum of understanding agreement between UNICEF and the government.

In addition, LMICs that have limited capacity to tender on their own could be active in approaching UNICEF in requesting support either for developing their own procurement capacity or for UNICEF to undertake procurement on their behalf. UNICEF's procurement modality depends on the size and scope of the requested demand. UNICEF provides an overview of the profile of the demand within its bidding documents. Vaccine manufacturers then submit bids for supply contracts, using the pricing strategy of their choice, which may include tiered pricing based on the country's income.

LMICs should also be aware that UNICEF (1) charges a 3.5% fee for procurement services for new vaccines going to countries outside the "less-developed countries" category (as are most LMICs); (2) includes a 10% buffer on all transactions to cover currency and freight fluctuations (refundable if not used); and (3) requires payment in US dollars in advance of order placement. Following the finalization of each transaction, a statement of account is issued to the country, and remaining funds are returned to the country or held in a country-specific account for future transactions (if requested by the country).

##### **7.2.3.1.f. Conduct regular global vaccine market analysis and dialog on vaccine security and market development**

With an aim to achieve "healthy" vaccine markets, global actors should provide a forum for dialog on vaccine market development. The dialog should include representatives of LMICs, the agencies that support them (e.g., WHO, UNICEF), and vaccine manufacturers. The dialog should focus on topics such as demand forecasting, achieving greater choice of manufacturers offering vaccines of assured quality,

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<sup>48</sup> Note that Honduras chose not to apply for GAVI support for Pneumo since it did not want to go from the GAVI price to the open market price (or PAHO Revolving Fund price) in 2015 when Honduras would lose GAVI support.

and transparency of prices and contract terms. Information from the regional and global clearinghouses suggested by this report would form an important basis for this kind of dialog.

**7.2.3.1.g. Help ensure better understanding and planning of the role of local production when considering new vaccine adoption**

Some LMICs are likely to be able to develop local production of new vaccines, while others will not. New vaccine adoption, however, should be a separate decision from the development of local production capacity. If and when there is local production of new vaccines that is of assured quality and at competitive prices, it can provide benefits in terms of vaccine security and cost. However, children should not be denied the benefits of new vaccines while waiting for local production to develop. Thus there must be global resources available to help LMICs make good choices about whether and when to invest in developing local production. China, India, Indonesia, and others promote the local production of vaccines. Some Indian private vaccine manufacturers and the Indonesian public manufacturer are active suppliers of global markets. Chinese, Egyptian, Thai, and other LMIC manufacturers now focus mainly on domestic markets. It is likely, however, that some Chinese manufacturers will expand internationally, now that China has gained full functional NRA status, which allows its manufacturers to submit for a WHO-prequalification assessment. Some other LMICs would like to enhance or develop domestic vaccine industries. To be successful, local production would deliver assured-quality vaccines reliably at prices competitive with global markets. Low unit costs would require developing a relatively sophisticated manufacturing capability and a sufficient scale of production. Many local manufacturers are currently seeking technology transfers with multinational manufacturers or from vaccine agencies, such as the Netherlands Vaccine Institute and PATH, to learn how to produce new vaccines. Global frameworks and technical resources should be made available to countries to give them unbiased assessments of their possibilities for achieving high-quality, low-cost local production of new vaccines. When the assessment is positive and followed by implementation, the resulting production can serve the domestic market and, in some circumstances, global markets as well. In the meantime, LMICs should be encouraged to make decisions on new vaccine adoption independent of local production capacities, so that children can benefit from the new vaccines as soon as possible, regardless of where those vaccines are produced.

**7.2.3.1.h. Encourage and support prequalification of products from additional manufacturers**

“Healthy” vaccine markets offer many choices of assured-quality vaccines to purchasers. “Healthy” markets allow LMICs to be confident of vaccine supply, improve competition on prices, and offer vaccines that are highly effective and safe. Thus LMICs would benefit from developing “healthy” markets in which more manufacturers are able to offer assured-quality products globally. At the global level, quality assurance requires that products attain WHO prequalification status, which is a difficult step for many Developing Country Vaccine Manufacturers Network (DCVMN) members and which constrains their participation in the global vaccine market. Technical assistance to facilitate technology transfers and further technical help to the NRAs that oversee manufacturing would help expand the market of prequalified vaccines.

## 8. Recommended Mechanisms for Interventions

Whether aimed at country, regional, or global levels, the critical interventions suggested in this report will happen only with additional support in the form of advocacy, leadership to organize and manage the needed change, technical advice on how to do it, and/or financial assistance. This section offers some preliminary ideas about what institutional and financing mechanisms might be used to provide the needed push to implement recommended interventions. Institutions should use the prioritization of the recommendations to guide the apportioning of limited resources. The roles of the principal implementers—such as the World Health Organization (WHO) and ministries of health (MoHs)—are laid out individually at the end of this section.

The suggestions seek to make use of the comparative advantages of established entities that might play a role in implementation. The lower-middle-income countries (LMICs) themselves, and particularly the MoHs and immunization advisory committees, have a major role in implementation.

Among actors external to the LMICs, it is clear that WHO should be a key player in implementation at all three levels of intervention, though other actors have specialized skills or other comparative advantages in particular areas. WHO's overarching comparative advantage is its stature and authority on health issues in general. Thus although WHO should seek to play the roles in implementing particular interventions where it has a clear comparative advantage, it should otherwise use its stature and authority to act as a facilitator and coordinator of implementation through a partnership network or through a consortium of the actors best positioned to act.

Tables 8-1 through 8-3 show the recommended Priority One and Priority Two interventions for each level and theme area, along with implementation mechanisms proposed or suggested for each.

### Box 8-1. Ensuring Strength of Existing Immunization Programs

In Section 7, this was listed as a country-level intervention, because global experts and key informants in several countries stressed its importance. No particular mechanism for implementation is recommended here. Rather, the MoH and its immunization advisory committee should consider the strength of the existing system as part of any decision-making process for new vaccines. This recommendation is highlighted in this report as a reminder, so that countries themselves, as well as WHO, UNICEF, and other organizations active in the health sector, will examine program readiness and areas in need of attention as decisions are made.

### 8.1. Priority One Intervention Mechanisms

Table 8-1 outlines the Priority One interventions once again, with the suggested implementation mechanism bulleted beneath each intervention. The reasoning for the suggested mechanisms are expanded on in the following sections.

**Table 8-1. Priority One Implementation Mechanisms**

Theme	Level		
	Country	Regional	Global
<b>Evidence and capacity building</b>	<p>Strengthen epidemiological, surveillance, and economic analysis capacities</p> <ul style="list-style-type: none"> <li>Ministries of Health (MoHs), with encouragement and assistance from WHO country offices and technical partners; immunization advisory committees, in collaboration with Ministries of Finance (MoFs) and academic experts in economic analysis</li> </ul>	<p>Actively promote and strengthen regional information sharing and joint research on burden of disease (BOD), pricing, cost-effectiveness, etc. (regional clearinghouse)</p> <ul style="list-style-type: none"> <li>WHO regional offices and technical partners</li> </ul>	<p>Create a technical and reliable source for global vaccine market information, including vaccine pipeline, vaccine prices, pricing policies, and procurement principles and practices</p> <ul style="list-style-type: none"> <li>WHO headquarters in collaboration with WHO regions, technical partners, UNICEF Supply Division (SD), and PAHO Revolving Fund</li> </ul>
<b>Policy and advocacy</b>	<p>Improve procurement regulation to promote competition, quality, and sustainability</p> <ul style="list-style-type: none"> <li>National procurement units for vaccines</li> </ul>	<p>Conduct advocacy to strengthen political will and support champions for new vaccines</p> <ul style="list-style-type: none"> <li>WHO regional offices, UNICEF</li> </ul>	<p>Conduct advocacy to strengthen political will, regulation, and policy development</p> <ul style="list-style-type: none"> <li>WHO HQ, UNICEF, UN Secretary General's Office, Bill and Melinda Gates Foundation, bilateral donors, development banks</li> </ul>
<b>Financing</b>	<p>Take steps to increase domestic funding and capacities to negotiate with MoFs and other potential funders</p> <ul style="list-style-type: none"> <li>MoH, MoF, procurement units and parliaments taking advantage of technical assistance and training offered by UNICEF SD and WHO</li> </ul>	<p>Increase countries' and partners' awareness of the value of vaccination in the broader context of government investment and achievement of the Millennium Development Goals</p> <ul style="list-style-type: none"> <li>WHO regional offices, development banks</li> </ul>	<p>Promote transparency and access to comparatively low and affordable vaccine prices with sustainable domestic financing</p> <ul style="list-style-type: none"> <li>WHO HQ, in collaboration with UNICEF SD, IFPMA, and DCVMN</li> </ul>

<b>Procurement and supply</b>	Consider using or joining a pooled procurement mechanism <ul style="list-style-type: none"> <li>• <i>MoH</i></li> </ul>	Develop intercountry and regional processes for achieving pooled procurement (where desired by countries), vaccine quality, safety, and a diversified and sustainable base of supply <ul style="list-style-type: none"> <li>• <i>WHO regional offices, in particular PAHO and EMRO; other regional networks, such as EU and ASEAN; and WHO HQ, in collaboration with EMEA and USFDA</i></li> </ul>	Support regional and country activities for efficient and effective procurement systems through assessment and identification of improvement to current practices and policies <ul style="list-style-type: none"> <li>• <i>WHO HQ</i></li> </ul>
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The study team recommends that government bodies (including the MOH, ministry of finance [MoF], and national procurement units for vaccines) take the lead on the country recommendations. Nongovernmental partners will be key actors for many recommendations. WHO country offices should encourage and help MoHs in strengthening their epidemiological capabilities. MoHs and National Immunization Technical Advisory Groups (NITAGs) should reach out to MoFs and to the academic sector in order to conduct and interpret more comprehensive economic analyses, to help ensure that new vaccine adoptions provide value for money. The units responsible for procurement should examine their approaches to ensure that their procedures favor receiving competitive prices for high-quality vaccines and promote healthy vaccine markets. Ministries of Finance and Health and the parliaments of LMICs should collaborate to ensure that budget line items for vaccines and the other costs of immunization programs are adequately funded. MoHs and the units responsible for vaccine procurement can benefit by requesting assistance from WHO and UNICEF to strengthen their capacity to work in global vaccine markets and to negotiate with both vaccine suppliers (over specific vaccine purchases) and their own MoFs (on allocations of resources)

WHO should play a major role in moving both the regional and the global recommendations forward. WHO regional offices and WHO headquarters are best positioned to coordinate efforts on the regional and global recommendations, respectively. It should be noted that in almost every case, this study recommends that WHO work with specialized partners to implement the recommendations.

WHO regional offices might be the conveners and brokers of processes to create regional clearinghouses, thus providing a basis for discussions on topics such as demand forecasting, price and availability trends, contracting methods and innovations, and so forth. This clearinghouse would require the cooperation of technical partners. WHO regional offices might also convene discussions to increase regional cooperation on vaccine quality and safety. These discussions could benefit from inputs from agencies such as the European Medicines Agency (EMA, a regional collaboration that might be a model) and the US Food and Drug Administration (USFDA), which has long experience with quality and safety regulation. In terms of procurement and supply, the Pan American Health Organization (PAHO) has been a global leader in developing its long-standing Revolving Fund and can offer experience and technical assistance to other regions. PAHO is already doing so by supporting the Eastern Mediterranean Regional Office's (EMRO's) efforts to develop a regional pooled procurement mechanism. Other WHO regional offices



interested in regional pooled procurement might seek similar support from PAHO and learn from EMRO's experience so far.

WHO headquarters is the natural global counterpart to the WHO regional offices in terms of developing and implementing a global information clearinghouse. As noted in the discussion of this intervention in Section 7, the global clearinghouse would focus relatively more on vaccine market, pricing, and procurement information and less on epidemiology as compared with the regional clearinghouses.

WHO and others—including UNICEF, the United Nations Secretary General's office (which coordinates implementation of the Global Strategy for Women's and Children's Health, announced by Ban Ki-Moon in September 2010), the Bill and Melinda Gates Foundation (BMGF), bilateral donors that focus on child health, and development banks—all have a role to play in advocating the building of additional political will to address preventable disease through childhood immunizations. Again, WHO can coordinate among these actors, each of which has advantages and disadvantages in addressing specific political leaders.

WHO can also collaborate with the UNICEF Supply Division and multinational and developing country vaccine manufacturers to promote transparency and access to competitive vaccine prices for LMICs. They can do so through the active maintenance and dissemination of clearinghouse databases and through openness about pricing strategies by manufacturers, such as providing the criteria for tiered prices and making public the nonproprietary details (e.g., duration, volumes, presentations, other items included beyond vaccines) of contracts.

Finally, WHO headquarters should continue to support and ensure information sharing among regions and countries on procurement systems and policies.

#### **8.1.1. Country-Level Interventions**

Table 8-2 covers the Priority Two country-level interventions and suggested implementation mechanisms.

**Table 8-2. Country-level Priority Two implementation mechanisms**

		Country	Implementation Mechanisms
Theme	Evidence and capacity building	<ol style="list-style-type: none"> <li>1. Strengthen NITAGs and NRAs</li> <li>2. Foster information sharing and use of all evidence among all concerned in-country stakeholders (EPI, FCH, planning, finance, and procurement entities)</li> <li>3. Consider pilot or test introduction at sub-national scale to learn about effectiveness, safety, and implementation issues</li> </ol>	<ol style="list-style-type: none"> <li>1. Ministries of Health, with encouragement and assistance from WHO country offices; assistance from SIVAC and collaboration with vaccine institutions such as CDC and NVI</li> <li>2. Ministries of Health and immunization advisory committees</li> <li>3. Ministries of Health</li> </ol>
	Policy and advocacy	<ol style="list-style-type: none"> <li>1. Ensure a budgetary line item for vaccines</li> <li>2. Improve advocacy skills of new vaccine champions</li> </ol>	<ol style="list-style-type: none"> <li>1. Ministries of Health and parliaments</li> <li>2. Ministries of Health</li> </ol>
	Financing	<ol style="list-style-type: none"> <li>1. Strengthen MoH capacities to negotiate with MoF and vaccine manufacturers</li> <li>2. Develop and implement multiyear plans that consider all potential sources of funding, including health insurance</li> </ol>	<ol style="list-style-type: none"> <li>1. Ministries of Health, with encouragement and assistance from UNICEF SD</li> <li>2. National Immunization Programs, in collaboration with Ministries of Health</li> </ol>
	Procurement and supply	<ol style="list-style-type: none"> <li>1. Consider actively using UNICEF procurement services</li> <li>2. Strengthen communication with manufacturers</li> <li>3. Use products of assured quality (WHO definition) as a reference</li> </ol>	<ol style="list-style-type: none"> <li>1. Ministries of Health</li> <li>2. Ministries of Health</li> <li>3. Ministries of Health and national procurement units for vaccines</li> </ol>

For evidence and capacity building, this report suggests that the LMIC MoHs take the lead on all of the recommended interventions. For the first two interventions, however, it does not suggest that the MoHs act alone; rather, they should collaborate with other national or external bodies. WHO country offices should encourage and help MoHs to strengthen NITAGs and National Regulatory Authorities (NRAs). They should also help broker relationships between MoHs, NITAGs, and NRAs and external projects or agencies that can provide technical assistance, training, and technology transfer. MoHs, with their NITAGs, must make a stronger effort to share information among stakeholders and to seek out and critically evaluate information to ensure that the best and most complete information is used in decision making. Finally, MoHs should consider introducing vaccines on a small scale so to learn about the effectiveness, safety, and implementation issues to be mitigated when they scale up.

For policy and advocacy, this report suggests that national institutions take the lead on both interventions. MoHs and parliaments should work together to put in place line items in health budgets for vaccines. MoHs should look both within and outside their organizations for champions of new vaccines and should provide those champions with advocacy information and skills to ensure that their voices are heard.

To address financing, National Immunization Programs (NIPs) can help improve the prospects for new vaccine financing by adopting and adapting the multiyear planning approach (cMYP) now used by all GAVI-supported countries.

### 8.1.2. Regional Interventions

Table 8-3 shows suggested implementation mechanisms for the regional-level recommended interventions.

**Table 8-3. Regional Implementation Mechanisms**

		Regional	Implementation Mechanisms
Theme	Evidence and capacity building	1. Foster joint research and surveillance among neighboring countries	1. WHO regional offices
	Policy and advocacy	1. Take advantage of regional networks beyond WHO	1. Other regional networks, such as the European Union and ASEAN
	Financing	1. Provide technical support for country finance and budgeting activities	1. WHO regional offices, bilateral donors, development banks
	Procurement and supply	1. Consolidate demand forecasting 2. Conduct regular regional vaccine market analysis and dialog on vaccine market development	1. WHO Regional offices 2. WHO Regional offices, UNICEF SD, IFPMA, and DCVMN

The WHO regions could convene sessions for more open and transparent dialog between countries and vaccine manufacturers, while inviting UNICEF Supply Division to join in as well. The information from the clearinghouse (Priority One) would provide a basis for discussions on topics such as demand forecasting, price and availability trends, and contracting methods and innovations. For the policy and advocacy recommendation in particular, it will be important to take advantage of regional networks beyond WHO. For example, the European Union (EU) and the Association of Southeast Asian Nations (ASEAN) might be interested in being partners with WHO or be willing to lead on the topic of pooled procurement in their regions.

The WHO regional offices seem to be the clear choice to take the lead on consolidating regional demand forecasting, particularly if they lead the information clearinghouse.

### 8.1.3. Global Interventions

Table 8-4 shows the mechanisms suggested for the global recommended interventions.

**Table 8-4. Global Implementation Mechanisms**

		<b>Global</b>	<b>Implementation Mechanisms</b>
<b>Theme</b>	<b>Evidence and capacity building</b>	1. Continue efforts and funding to build capacity of NITAGs and NRAs	1. WHO HQ
	<b>Policy and advocacy</b>	1. Promote and maintain vaccines and immunization among the top priorities of the global health agenda	1. WHO HQ, UNICEF, the UN Secretary General's Office, BMGF, bilateral donors, and development banks
	<b>Financing</b>	1. Provide funding to implement recommendations at regional and global levels  2. Provide introductory financing to help introduce new vaccines	1. WHO HQ, UNICEF, BMGF, bilateral donors, other networks such as EU and ASEAN 2. GAVI, bilateral donors, development banks
	<b>Procurement and supply</b>	1. Promote active use of PAHO and UNICEF Supply Division's procurement services and references 2. Conduct regular global vaccine market analysis and dialog on vaccine security and market development 3. Help ensure better understanding and planning of the role of local production when considering new vaccine adoption 4. Encourage and support prequalification of products from additional manufacturers	1. UNICEF SD, WHO HQ 2. WHO HQ, UNICEF SD, IFPMA, and DCVMN 3. WHO HQ, development banks 4. WHO HQ, in collaboration with NVI, EMEA, US FDA

WHO started the initiative to promote and assist with the development of NITAGs and should continue this effort in support of the work done by its regional offices.

The funding to make possible all the recommended interventions should come from a variety of sources. As a technical agency, WHO does not command major resources. Nonetheless, it can meet some of the funding needs of the interventions by reorienting some of its resources to focus more on immunizations and vaccines in LMICs (these items have been largely “off the table” in recent years because LMIC NIPs have achieved high levels of coverage with traditional vaccines, child mortality has dropped and remained low, and noncommunicable diseases have risen in relative importance). Bilateral donors, BMGF, and regional bodies, such as the EU and ASEAN, might provide additional resources to help WHO and others play the roles suggested.

Financial support for the initial introduction of new vaccines in GAVI graduating countries and countries at the lower end of the LMIC income spectrum might come from GAVI or bilateral donors interested in the specific countries concerned, possibly with the help of loans from development banks.

The UNICEF Supply Division should become more proactive with LMICs regarding the possibility of using its procurement services. It is clear that the division's mandate allows this, but many LMICs do not know about it. If they did know about, some would be likely to take advantage of the offer. WHO

regional and country offices could also play a role in making sure that LMICs know about UNICEF Supply Division services.

As was suggested earlier, WHO could organize and coordinate a dialog on vaccine markets at the global level, perhaps by convening a session on this topic every other year in conjunction with the Strategic Advisory Group of Experts on Immunizations (SAGE) meeting. A similar set of topics could be taken up as at the regional level, including demand forecasts, vaccine availability (numbers of manufacturers and capacities) and price trends, and contracting methods and innovations, including pooling and multiyear purchases. Participants should include UNICEF Supply Division, the PAHO Revolving Fund, analysts from the clearinghouse staff, others doing analysis and research on vaccine markets, and representatives of the two manufacturer groups (International Federation of Pharmaceutical Manufacturers and Associations [IFPMA] and Developing Country Vaccine Manufacturers Network [DCVMN]).

In addition, WHO could coordinate with development banks to help countries that wish to develop or improve their domestic vaccine industries. This help could take the form of providing objective assessments of the prospect for successful development of manufacturers or products (attaining assured quality, reliable production, and competitive costs) and assisting with financing and technology transfers where prospects are good. WHO should help countries separate the goals of developing manufacturing capacity from the new vaccine adoption question to ensure that the benefits of the vaccines are attained as soon as possible.

Finally, WHO could help broker technology transfers from entities like the Netherlands Vaccine Institute (NVI) and the strengthening of NRAs (which is necessary to achieve prequalified products for export) through exchanges with entities like EMEA and USFDA.

## **8.2. Institutional Roles in Implementation**

Tables 8-5 and 8-6 show the role that the lead institutions (WHO and MoHs) can play in implementing the study recommendations. Priority One interventions are italicized.

Table 8-5. WHO Role in Implementing Recommendations

		Level		
		Country (WHO Country Offices)	Regional (WHO Regional Offices)	Global (WHO Headquarters)
Theme	Evidence and capacity building	<ul style="list-style-type: none"> <li>Strengthen epidemiological, surveillance, and economic analysis capacities</li> </ul>	<ul style="list-style-type: none"> <li>Actively promote and strengthen regional information sharing and joint research on BOD, pricing, cost-effectiveness, and so on (regional clearinghouse)</li> <li>Foster joint research and surveillance among neighboring countries</li> </ul>	<ul style="list-style-type: none"> <li>Create a technical and reliable source for global vaccine market information, including vaccine pipeline, vaccine prices, pricing policies, and procurement principles and practices</li> <li>Collaborate with SIVAC and others to continue efforts and funding to build the capacity of NITAGs and NRAs</li> </ul>
	Policy and advocacy		<ul style="list-style-type: none"> <li>Conduct advocacy to strengthen political will and support champions for new vaccines</li> <li>Coordinate with MoHs to help the ministries take advantage of other regional networks (e.g., EU, ASEAN)</li> </ul>	<ul style="list-style-type: none"> <li>Coordinate with UNICEF, the UN Secretary General's Office, BMGF, bilateral donors, and development banks to conduct advocacy to strengthen political will, regulation, and policy development</li> </ul>
	Financing	<ul style="list-style-type: none"> <li>Take steps to increase domestic funding and capacities to negotiate with Ministries of Finance and other potential funders</li> </ul>	<ul style="list-style-type: none"> <li>In collaboration with development banks, increase countries' and partners' awareness of the value of vaccination in the broader context of government investment and achievement of the MDGs</li> <li>In collaboration with development banks and bilaterals, support country finance and budgeting activities</li> </ul>	<ul style="list-style-type: none"> <li>Collaborate with UNICEF SD, IFPMA, and DCVMN to promote transparency and access to comparatively low and affordable vaccine prices with sustainable domestic financing</li> <li>Reallocate funding and personnel resources to help implement recommendations at country, regional, and global levels</li> </ul>
	Procurement and supply		<ul style="list-style-type: none"> <li>Work with EMEA and USFDA to develop intercountry and regional processes for achieving pooled procurement (where desired by countries), vaccine quality, safety, and a diversified and sustainable base of supply</li> <li>Consolidate demand forecasting</li> <li>Organize forums involving countries, manufacturers, and UNICEF Supply Division to broaden the dialog on vaccine market development</li> </ul>	<ul style="list-style-type: none"> <li>Support regional and country activities for efficient and effective procurement systems through assessment and identification of improvement to current practices and policies</li> <li>Organize global forums on vaccine market development, in collaboration with UNICEF SD, IFPMA, and DCVMN</li> <li>Collaborate and coordinate with development banks to help countries better understand the role of local production related to vaccine adoption</li> <li>Collaborate and coordinate on technology transfer (e.g., with NVI) and on NRA organization and operation (e.g., EMEA and USFDA) to support prequalification of products from additional manufacturers</li> </ul>

**Table 8-6. Ministries of Health Role in Implementing Recommendations**

		Country Level
Theme	Evidence and capacity building	<ul style="list-style-type: none"> <li>• With encouragement and assistance from WHO, strengthen epidemiological capacities, especially to estimate BOD and evaluate quality of evidence</li> <li>• With encouragement and assistance from WHO, strengthen NITAGs and NRAs Collaborate with immunization advisory committees to foster information sharing and evidence-based decision making</li> <li>• Consider pilot or test introduction at sub-national scale to learn about effectiveness, safety, and implementation issues</li> </ul>
	Policy and advocacy	<ul style="list-style-type: none"> <li>• Work with parliaments to ensure a budgetary line item for vaccines</li> <li>• Improve advocacy skills of new vaccine champions</li> </ul>
	Financing	<ul style="list-style-type: none"> <li>• Support MoF-led effort to work with parliaments to increase domestic funding for vaccines</li> <li>• Work with national vaccine procurement units to strengthen MoH capacities to negotiate with MoF and vaccine manufacturers</li> <li>• Support NIP-led work to develop and implement multiyear plans that consider all potential sources of funding, including health insurance</li> </ul>
	Procurement and supply	<ul style="list-style-type: none"> <li>• Consider joining a pooled procurement mechanism</li> <li>• Consider actively using UNICEF procurement services</li> <li>• Strengthen communication with manufacturers</li> <li>• Work with national vaccine procurement unit to ensure use of products of assured quality</li> </ul>

## **Annex A. Study Protocol**

# **Constraints to Vaccine Adoption in Lower-Middle-Income Countries Results for Development Country Research Guide, February 2010**

## **Introduction**

The Results for Development Institute (R4D) was awarded a grant from the Bill and Melinda Gates Foundation and the World Health Organization (WHO) to conduct a study to enhance global knowledge and understanding of the challenges that lower-middle-income countries (LMICs) face as they explore potential adoption of new vaccines. Some key areas the study will address are: What are the barriers/challenges that limit the rate of new vaccine adoption by LMICs? What are the potential options to address these rate-limiting constraints? And what are the likely costs, benefits, and implications of various options for supporting countries to address identified rate-limiting constraints? Based upon these analyses, the study will develop prioritized strategies and suggest practical measures at the global, regional, and national levels to support LMICs in their decisions to adopt new vaccines.

The overall goals of the project are to:

- Identify the constraints that limit LMICs from introducing new vaccines as close to product licensure/prequalification and WHO recommendation as possible, and to identify the factors that enable quick decisions to introduce new vaccines.
- Propose solutions to the constraints faced by LMICs. Special attention will be paid to successful lessons learned from upper-middle-income countries (UMICs) and to solutions that could also benefit GAVI-eligible countries.
- With the study's Advisory Group (AG), identify strategies with high public health value at the lowest cost that could be used to improve the rate of sustainable uptake of relevant new vaccines in LMICs.

One component of data collection is an in-depth study of eight countries to examine (1) the relative importance of hypothesized constraints, (2) critical factors that lead to new vaccine introductions, as well as (3) critical factors that have caused some countries to delay introduction of *Haemophilus influenzae* type B (Hib) vaccine many years after a WHO global recommendation. This document provides guidance for the country case studies. We will evaluate and may revise this research guide if necessary based on experiences in earlier study countries.

## **Previsit Planning and Data Collection**

The case study visits are to be conducted in one week in country by a team of 2 researchers. Significant preparation in advance of the visit is conducted to make best use of the researchers' time. The study team works closely with WHO headquarters and regional offices to plan the in-country work. The previsit activities include:



- Briefing with WHO regional officials regarding health system performance and challenges, constraining and enabling factors affecting vaccine adoption in the region, and specific conditions and issues in the countries selected for study
- Identification and review of key documents and data related to immunization challenges and policy and vaccine adoption in study countries
- Communications with the National Immunization Program (NIP) manager or designate to plan the schedule for the visit
- Working with NIP manager and other country and regional advisers to identify key informants involved in decision making related to most recent new vaccine introduced
- Working with NIP manager and other country and regional advisers to identify current decision makers
- Team planning meeting with country researchers to brief them on approach and specific country conditions

The country researchers receive a briefing packet with notes from discussions with regional and country officials (and often will have participated in the discussions themselves), relevant documentation, a tentative list of key informants, and tentative schedule prior to departure.

## Key Informants

Key informants are identified in each country with input from the NIP director, and regional and in-country immunization and health advisers of international agencies (WHO, PAHO, UNICEF, etc.).

Key informants may include:

- NIP Director
- Director General–level official within the Ministry of Health (MoH) overseeing NIP
- Director General–level official of the Ministry of Finance (MoF) overseeing social services or planning and budgeting
- UNICEF and WHO advisers
- Other members of the NIP technical advisory group (pediatrician associations, public health institutes, bilateral partners), if available
- Parliament members (members of health or social program committees), if appropriate
- National regulatory authority
- Local vaccine manufacturers and suppliers , if appropriate
- Local champions, academics, local and regional scientific experts, if appropriate
- Local journalists who are opinion leaders in health issues, if appropriate
- Other entities (health insurance plans, funders, NGOs, etc.), if appropriate

The key informants include both current actors and individuals who previously held these positions and who played a role in vaccine-adoption decisions. Data are collected from these informants using open- and close-ended questions, employing a common scale for informants to rate the importance of various factors. Country teams aim to contact 10–15 key informants in each case-study country—as many as possible in person, though some contacts may take place by phone or e-mail given informants’ availability. For both the last vaccine adopted and a current vaccine under consideration, the teams target

at least 5 respondents of varying backgrounds (technical, political, etc.) to rate the importance of different decision-making factors.

## Interview Guides

To begin all interviews:

- Provide brief introduction to the objectives and approach of the study, using the 1-page summary description, if appropriate. This description may also be sent out in advance to informants.
- Offer the interviewee anonymity in his or her responses (his or her responses will not be attributed specifically to him or her but will be used in the reporting of the study) or, if the interviewee wishes, note his or her waiver of anonymity.
- “What is your name, title, and organization affiliation? How long have you been in this position?”
- “Have you held other positions where you participated in decisions on new vaccine adoption? If so, please provide position, dates held, and organization.”
- “How would you describe your influence in vaccine adoption decisions? (adviser trying to influence decision makers, one of many decision makers, one of 2–3 decision makers, the ultimate decision maker)”
- Record the date, time, and place of the interview. Make notes of any references to written strategy or plans and try to obtain documents in country.

### **Interview Guide for Technical Staff (NIP Manager, WHO/UNICEF officials, National Immunization Technical Advisory Group (NITAG) members, medical associations, others)**

1. “What are 3–5 major health priorities in the country today? How does that compare with 10 years ago? What are the health system performance, challenges, and priorities?”
2. “How does the immunization program fit into those priorities? What are the priorities within the immunization programs (new vaccines or other program goals)?”
3. “What are the vaccines of priority interest today (both those vaccines for which there is a certified product and those under development)? Are there specific plans to introduce new vaccines? Which ones and when?”
4. “What vaccines were introduced into the NIP in the past 10–15 years?”
5. *For each vaccine for which there was a positive decision:* “Please describe the decision-making process around the introduction of each of those vaccines. Did the process vary much from one vaccine to another? Who was involved in the decision-making process (please specify name and title)? How were you involved in these decisions? Who was influential in driving the decision?” (Prompt for technical, political, and financial actors inside or outside of government.) “Who was the ultimate decision maker? What were some of the final hurdles in the decision? What were the most important factors influencing the decision to adopt?” (If necessary, prompt issues related to burden of disease data, vaccine effectiveness, and financing.)
6. *For a vaccine for which no positive decision has been taken:* “Is the current decision-making process and persons involved the same? If not, how is it different? What are the major obstacles to introduction? What 1–2 factors would be most important in expediting the decision? Who are the champions?” (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
7. Go through the rating scale, if appropriate.

### **Interview Guide for Senior Decision Makers (parliamentarians, senior MoH and MoF officials, others)**

1. “What are 3–5 major health priorities in the country today? How does that compare with 10 years ago? What are the health system performance, challenges, and priorities?”
2. “How does the immunization program fit into those priorities?”
3. “Is the general public aware of the new vaccines? What is their perception? Is there general interest and demand?”
4. Are there specific interest groups (physicians associations, media, consumer groups) interested in and focused on new vaccines?”
5. *For a vaccine for which there was a positive decision:* “Please describe how you were involved in the decision-making process to introduce the vaccine (which vaccine)? Who was involved in the decision-making process (please specify name and title)? Who was influential in driving the decision?” (Prompt for technical, political, and financial actors inside or outside of government.) “Who was the ultimate decision maker? What were the most important factors that you personally considered?” (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
6. *For a vaccine for which no positive decision has been taken:* “Is the current decision-making process and persons involved the same? If not, how is it different? Who are the champions? What are the major obstacles to introduction? What 1–2 factors would be most important in expediting the decision?” (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
7. Go through the rating scale, if appropriate.

### **Interview Guide for Supply-Side Informants (regulatory authority, local manufacturers, agents, distributors, others)**

1. “Please describe the structure of the vaccine industry in this country.”
  - a. local production or imported products
  - b. number of producers
  - c. public or private producers
  - d. types of vaccines (licensed or home-grown technology)
  - e. adult or pediatric market
  - f. for local use or export
  - g. public- or private-sector distribution
  - h. market segmentation by income or socioeconomic status
2. “Please describe the marketing and distribution channels for vaccines (players, steps, regulation, functions and roles, performance, issues and challenges, etc).”
3. “Do international manufacturers generally rely on local agents for marketing and sales, or do they set up local offices for these functions? Do they enter partnerships with local firms?”
4. “How large is the market (what segment—percentage or description, such as urban middle class—of the total population) for private-sector sales of pediatric vaccines prior to national adoption? What vaccines have been first introduced in this way? How successful is this (volume sales, coverage rate)? What is the price charged to consumers and paid by providers for this vaccine (per dose)?”
5. “What is the price structure for vaccines? What is the pricing strategy of the manufacturers? Is there any regulatory policy related to vaccine price? What are the effective practices?”

6. "Who pays for vaccines in the private sector (social insurance, private insurance, out of pocket, government subsidies, etc.)?"
7. "Does this private-sector market influence national adoption of the vaccine?"
8. "How does integration into the NIP affect private-sector sales and total sales (by value)? Do you have data from earlier experiences?"
9. "What agency has oversight and regulatory authority over vaccines? What has it done in terms of oversight and regulation? Does it encompass the distribution process and vaccine handling?"
10. What is the licensing and approval process for a new product? How does it differ for imported versus locally manufactured product?"
11. "What has been the experience with technology licensing and technology transfer for vaccine production? Is there interest in these arrangements in the future?"
12. "Were you involved in current or past decisions to introduce new vaccines?" (If so, continue; if not, then no other questions.)
13. *For each vaccine for which there was a positive decision:* "Please describe the decision-making process around the introduction of each of those vaccines. Did the process vary much from one vaccine to another? Who was involved in the decision-making process (please specify name and title)? How were you involved in these decisions? Who was influential in driving the decision?" (Prompt for technical, political, and financial actors inside and outside of government.) "Who was the ultimate decision maker? What were some of the final hurdles in the decision? What were the most important factors influencing the decision to adopt?" (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
14. *For a vaccine for which no positive decision has been taken:* "Is the current decision-making process and persons involved the same? If not, how is it different? What are the major obstacles to introduction? What 1–2 factors would be most important in expediting the decision? Who are the champions?" (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
15. Go through the rating scale, if appropriate.

#### **Interview Guide for Funders (development agencies, NGOs, insurers, others)**

1. "What are 3–5 major health priorities in the country today? How does that compare with your own assessment and with your organization's priorities?"
2. "How does the immunization program fit into those priorities?"
3. "Has your organization historically supported or provided immunization services? Do you see that changing in the future?"
4. "Are/were you involved in current/past decisions to introduce new vaccines?" (If so, continue; if not, then no other questions.)
5. *For each vaccine for which there was a positive decision:* "Please describe the decision-making process around the introduction of each of those vaccines. Did the process vary much from one vaccine to another? Who was involved in the decision-making process (please specify name and title)? How were you involved in these decisions? Who was influential in driving the decision?" (Prompt for technical, political, and financial actors inside or outside of government.) "Who was the ultimate decision maker? What were some of the final hurdles in the decision? What were the most important factors influencing the decision to adopt?" (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)

6. *For a vaccine for which no positive decision has been taken:* Is the current decision-making process and persons involved the same? If not, how is it different? What are the major obstacles to introduction? What 1–2 factors would be most important in expediting the decision? Who are the champions?" (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
7. Go through the rating scale, if appropriate.

#### **Interview Guide for Other Informants (local champions, journalists, others)**

1. "What are 3–5 major health priorities in the country today? How does that compare with 10 years ago? How does immunization fit into those priorities?"
2. "How long have you had a personal/professional interest in health issues? What lead you to focus specifically on vaccines?"
3. "How would you describe the general public interest in health issues and new vaccines? Is there strong awareness of the benefits from new vaccines? Where does the public get its information? Is there demand for these vaccines?"
4. *For a vaccine for which there was a positive decision:* "Please describe how you were involved in the discussion to introduce the vaccine (which vaccine)? Who was involved in the decision-making process (please specify name and title)? Who was influential in driving the decision?" (Prompt for technical, political, and financial actors inside or outside of government.) "Who was the ultimate decision maker? What were the most important factors that you personally considered?" (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
5. *For a vaccine for which no positive decision has been taken:* "Is the current decision-making process and persons involved the same? If not, how is it different? Who are the champions? What are the major obstacles to introduction? What 1–2 factors would be most important in expediting the decision?" (If necessary, prompt for issues related to burden of disease data, vaccine effectiveness, and financing.)
6. Go through the rating scale, if appropriate.

#### **To end all interviews:**

- Thank the informant for his or her contributions to the study by answering our questions. Then ask one last question: "Do you have any recommendations that you would like to make to enable more rapid uptake of new vaccines by LMICs?"

## **Rating Factors Influencing Vaccine Adoption Decision**

A consistent scale for rating the importance of various factors affecting adoption decisions (see below) is used in all study countries for comparability. Informants are asked to focus on one specified vaccine when rating the importance of these factors. For comparability across informants and across countries, the country team limits the focus vaccines to 2–3 in each country, including (1) a new vaccine recently adopted and (2) a vaccine not yet adopted (this may include a vaccine carefully considered but rejected). The study AG identified Hib, pneumococcus (Pneumo), rotavirus (Rota), and human papilloma virus (HPV) as among the most important newer vaccines, though it is important to incorporate vaccines of interest to the informants. In general, the focus vaccines are preselected (the last new vaccine introduced

and a priority vaccine under discussion), but might also include a third vaccine that is commonly mentioned by informants in the study country as a priority.

Not all informants are asked to rate the importance of these vaccine adoption factors. Only informants who have some depth of knowledge about the decision-making process are selected, even though they might not have technical expertise or might not have been part of the decision making (e.g., journalists). This sometimes includes informants who are technical implementers (NIP manager) as well as politicians or other local champions. We aim to have at least 5 informants of different backgrounds rating the last vaccine introduced and 5 informants rating a vaccine not yet introduced.

*Please have 15–20 copies of the rating scale available for use in-country.*

Name \_\_\_\_\_ Title/Organization \_\_\_\_\_

Which vaccine? \_\_\_\_\_ Adopted? (Y/N) \_\_\_\_\_ If yes, what year? \_\_\_\_\_

Factor (follow up questions when factor rated important or critically important)	Not available or not considered	Not important	A bit important	Important	Critically important
<b>Information on Vaccine Characteristics and Vaccine Introduction</b>					
1. Knowing the burden of disease (Where did the information come from?)					
2. Knowing vaccine's characteristics (Which ones were important to know?)					
3. Knowing that the vaccine is WHO prequalified					
4. Information concerning the cost-effectiveness of the vaccine and potential impact (Where did that information come from?)					
<b>Vaccine Introduction Readiness</b>					
5. Information on how to introduce the vaccine (Where did it come from? What form did it take?)					
6. Knowing whether the vaccine could be included in current health service delivery system					
7. Support for training on vaccine introduction (From what source?)					
8. Knowing whether vaccine can be accommodated by cold chain (Does it require cold chain expansion?)					
<b>Advocacy and Endorsements</b>					
9. Materials on advocacy for vaccine introduction (From what source? Which ones?)					
10. High-level visit by int'l representative to political decision makers to promote vaccine introduction (Who visited? Who did the visitor meet with? When?)					
11. Regional meeting to discuss vaccine introduction (When was this?)					
12. Vaccine recommended by WHO or PAHO or another international expert organization (Which one?)					
13. Experience of peer countries with the vaccine (Which ones?)					
14. Endorsement of the vaccine by national group of experts (Who? Name, position, organization)					
<b>Vaccine Supply and Pricing</b>					

Factor (follow up questions when factor rated important or critically important)	Not available or not considered	Not important	A bit important	Important	Critically important
15. Assured supply of the vaccine (How is the supply assured?)					
16. Access to a pooled purchasing mechanism (Which one?)					
17. Price of the vaccine (What was the price at the time of adoption? Has it changed?)					
<b>Financial Considerations</b>					
18. Assured financial support for vaccine introduction (Source?)					
19. Assured financial support for recurrent purchase of the vaccine (What form of assurance?)					
20. Assured financing for expansion of cold chain to accommodate new vaccine (Source?)					
<b>Other</b>					
21. Experience with the vaccine in the country's private sector (Describe this experience—esp. percent of population using vaccine from private sector.)					
22. Possibility of vaccine production in country (Describe production capabilities.)					

## Report Outline

The country research team submits its report of findings and conclusions within 2 weeks of departure, following the outline below.

### I. Country Context<sup>1</sup>

- Economic situation—income and population trends
- Health system performance and challenges
- Immunization program—coverage rates, trends, challenges
- History of new vaccines introduced
- Financing of vaccines
- Health priorities and role of immunization and vaccines

### II. Factors Influencing New Vaccine Adoption (combined presentation of information provided about adopted and not-yet-adopted vaccines)

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<sup>1</sup> Much of this information is assembled by the study team in advance of the country visit and provided to the country team. The country team validates the information during their visit, noting any discrepancies.



- Decision-making process—technical advisory group or other organization responsible for technical recommendation, persons and organizations involved, procedures/processes, speed of decision process
- Burden of disease—sources of data, timing of data availability, ongoing surveillance systems, monitoring impact of vaccines
- Vaccine characteristics—vaccine presentation, information on safety and effectiveness, introduction hurdles, impact on cold chain, etc.
- Advocacy—global and regional advocacy, local champions, pharmaceutical company marketing, local demand and awareness, social values and representations, etc.
- Vaccine supply—private-sector market, procurement and supply issues, local production and sourcing
- Sustainability—price of vaccine, funding for introduction costs, national budget line for vaccines, external funding sources, donor/NGO interest in immunization, inclusion of immunization or specific vaccines in national health strategies/plans
- Rating scale of importance of various factors—factors identified as critically important and important, contradictions with open-ended responses

### III. Conclusions (These are not sections, but just ideas for discussion.)

- Most important factors influencing decision
- Most important actors in decision making
- Differences by type of informant
- Differences by type of vaccine
- Potential sources of support

### IV. Recommendations concerning practical steps that might be taken to influence this country concerning new vaccine adoption

## Factors Affecting Adoption of New Vaccines in Lower-Middle-Income Countries

### Introduction for Country Informants

In October 2009, the Results for Development Institute (R4D) of Washington, DC, USA, was awarded a grant from the Bill and Melinda Gates Foundation and the World Health Organization to conduct a study to enhance global knowledge and understanding of the enabling factors and challenges faced by lower-middle-income countries (LMICs) as they explore potential adoption of new vaccines. As part of this effort, the study team is interviewing vaccine and immunization experts, development organizations, vaccine manufacturers, and procurement agencies. We are also conducting statistical analysis to identify factors that are correlated with earlier adoption of new vaccines. Additionally, we are conducting visits to 8 countries to obtain information from their implementers and decision makers. We are here with you as a part of one of our country studies. The key study questions are:

- What are the factors that constrain and enable new vaccine adoption by LMICs?
- What are the potential options to address the constraints and enable decision making?
- What are the likely costs, benefits, and implications of various options for supporting countries?

Based upon these analyses, the study will develop prioritized strategies and suggest practical measures at the global, regional, and national levels to support LMICs in their decisions to adopt new vaccines.

We want to capture both lessons learned about how countries have overcome challenges, as well as continuing constraints that are difficult to resolve and gaps in support to LMICs. Your responses to our questions will not be reported individually, and we encourage you to be open and honest.

Do you have any questions before we begin the interview?

## Research Guide for Remote Study Countries

The remote study countries were generally selected because specific issues or experiences lend themselves to providing insights and lessons, such as:

- positive and negative outcomes of apparently politically driven decisions (South Africa and Tunisia)
- vaccine procurement issues in very-small-population countries (Cape Verde)
- engagement with countries after a decision-making process with a negative outcome (Thailand)

The research questions in remote study countries are generally the same as in case study countries. The primary difference will be that remote study countries would focus only on 1 or 2 areas of specific interest, and only 1 vaccine of interest.<sup>2</sup> In understanding the issues of interest, the researchers will require general information on the immunization program and the key actors; however, this information may not be comprehensive. Instead, we would only focus on acquiring sufficient background information in order to understand the issue of interest. Further, additional relevant issues may be identified in the course of research, which researchers would selectively pursue.

The table outlines areas of interest in each country, and the focus vaccine.

Country	Areas of Interest	Focus Vaccine
Syria	<ul style="list-style-type: none"> <li>• Factors influencing consideration of Pneumo or Rota</li> </ul>	Pneumo/Rota(?)
Tunisia	<ul style="list-style-type: none"> <li>• Decision regarding suspension of Hib vaccine</li> <li>• Current factors influencing reintroduction of Hib</li> </ul>	Hib
Albania	<ul style="list-style-type: none"> <li>• Factors influencing introduction of Hib (2009)</li> </ul>	Hib
Cape Verde	<ul style="list-style-type: none"> <li>• Constraints to Hib adoption in small-population country</li> <li>• Procurement issues</li> </ul>	Hib
South Africa	<ul style="list-style-type: none"> <li>• Factors influencing Pneumo introduction (2009); factors influencing political process</li> <li>• Public-private partnership for local production project?</li> <li>• Consideration of HPV?</li> </ul>	Pneumo/HPV
Thailand	<ul style="list-style-type: none"> <li>• Factors influencing decision not to introduce Hib</li> <li>• Consideration of HPV</li> </ul>	Hib/HPV

<sup>2</sup> The approach for India is an exception. For India, we will focus on compiling more comprehensively the findings of previous work to examine factors affecting vaccine adoption.

	<ul style="list-style-type: none"> <li>• Local production and regulation issues</li> </ul>	
India	<ul style="list-style-type: none"> <li>• Factors influencing introduction of Hib (planned for 2009, not implemented) absent financing constraints (GAVI)</li> <li>• Stakeholder analysis by Hib Initiative</li> <li>• Influence of local production</li> </ul>	Hib

As in the case study countries, the study team would work closely with WHO regional and country officials to understand specific conditions and issues of interest, to identify key documents of interest, and to facilitate access to the NIP manager and to the decision makers. The study team would work with the NIP manager and WHO and UNICEF to identify appropriate key informants for the areas of interest.

The study team would contact 4–6 key informants in each of the remote study countries—it is likely that more senior government officials and politicians may be less accessible, and our informants would tend to have more technical interests. Interviews would focus on understanding the processes around the country’s specific targeted questions and vaccine of interest. We would aim to have 2–3 informants’ responses rating the importance of factors influencing vaccine adoption decisions. The deliverables for each remote study country would be a 10–20 page note presenting findings in the areas of interest, with limited conclusions regarding the most influential factors and actors.

# Study Protocol Appendix 1

## Overview of Focus Vaccines Across Study Countries

(Additional vaccines to be added based on informants' responses.)

Country (Region)	Last Vaccine Introduced (Year)	Under Consideration	Other Information
<b>Countries to Be Visited</b>			
Egypt (EMR)	Hep B (1992)	Hib	VacSera status
Morocco (EMR)	Hib (2007)	Rota, Pneumo, HPV	UNICEF, high-level support for HPV
Ecuador (AMR)	Rota (2007)	Pneumo, HPV	
Panama (AMR)	Pneumo and HPV (2009)		Rota introduced in 2006
Philippines (WPR)	Hep B (1992)	Hib, MMR, JE	Procurement and funding issues are barriers to introduction
China (WPR)	Hep B (2002)	Hib, JE	National Hep B3 coverage rate prior to integration in NIP was 71% (1999 survey), local production, public-private partnership
Turkey (EUR)	Hib (2003)		
Armenia (EUR)	Hib (2009)	Pneumo, Rota	Transition from GAVI?
<b>Remote Study Countries (bolded vaccine is the focus vaccine)</b>			
Syria (EMR)	Hib (2001)	<b>Pneumo/Rota</b>	Supply issues
Tunisia (EMR)	<b>Hib</b>		Interrupted Hib use after 3 years
Albania (EUR)	<b>Hib</b> (2009)		Transition from GAVI, EU influence
Cape Verde (AFR)	Hep B (2002)	<b>Hib</b>	Small size
South Africa (AFR)	<b>Pneumo</b> (2009)	HPV	
Thailand (SEAR)	Hep B (1992)	<b>Hib</b>	Hib was carefully considered and not introduced; same for HPV?
India (SEAR)	<b>Hib</b> (planned in 2009, not implemented)	Pneumo, Rota	Scaling up, local production, decision-making process

## Annex B. Individuals and Companies Interviewed

### List of Tables in Annex B

Table B.1 Individuals Interviewed in In-Depth Case Studies.....	91
Table B. 2 Individuals Interviewed in Remote Case Studies .....	101
Table B. 3 Global Experts Interviewed.....	103
Table B. 4 Manufacturers Interviewed .....	104

**Table B-1. Individuals Interviewed in In-Depth Case Studies**

	Name	Organization	Position	Location
Armenia	Dr. Tigran Avagyan	WHO Armenia Country Office	National Program Coordinator for VPI	Yerevan, Armenia
	Dr. Gayane Sahakyan	Armenian Ministry of Health	National Immunization Program Manager	Yerevan, Armenia
	Dr. Haik Melik Darbinyan	Armenian Ministry of Health	First Deputy Minister	Yerevan, Armenia
	A. Vanyan	Armenian Ministry of Health	Head of State Hygiene and Anti-Epidemic Inspectorate	Yerevan, Armenia
	Avagyan Gayane	Armenian Ministry of Health, National Advisory Committee for Immunization	Chief Specialist in Obstetrics-Gynecology	Yerevan, Armenia
	Anahit Ghazaryan	Armenian Ministry of Health, National Advisory Committee for Immunization	Head Pediatrician	Yerevan, Armenia
	Mariam Ghurasyan	Armenian Ministry of Health, National Advisory Committee for Immunization	Epidemiologist and Head Specialist	Yerevan, Armenia
	Gayane Melik-Andreasyan	National Advisory Committee for Immunization	Head of Institute of Epidemiology	Yerevan, Armenia
	Anna Balyan	National Advisory Committee for Immunization	Head of University Polyclinic, Assistant of Department of Pediatrics and Pediatric Surgery	Yerevan, Armenia

	Name	Organization	Position	Location
Armenia...	Zhora Asatryan	Armenian Ministry of Finance	Head of Financial Programming of Budget Expenditure	Yerevan, Armenia
	Dr. Ara Babloyan	Armenian National Assembly	Chairman of the Standing Committee on Health Care, also former Minister of Health	Yerevan, Armenia
	Dr. Lena Nanushyan	Armenian National Assembly	Assistant to Chairman of the Standing Committee on Health Care	Yerevan, Armenia
	Lilit Ghazaryan	Armenian National Regulatory Authority	Deputy Director of the Armenian Drug and Medical Technology Scientific Expertise Center	Yerevan, Armenia
	Albert Saharkian	Armenian National Regulatory Authority	Supervising narcotics	Yerevan, Armenia
	Anahit Minasyan	Armenian National Regulatory Authority	Chief Specialist in Drug Registration Department (member of the national advisory commission on immunization)	Yerevan, Armenia
	Tigran Avagnan	WHO	CPO for VPI	Yerevan, Armenia
	Mihran Hakobyan	UNICEF	Program Assistant for Health and Nutrition Division	Yerevan, Armenia
	Dr. Narine Karakhanyan	National Center for Diseases Control and Prevention	Director	Yerevan, Armenia
	Dr. Areg Nargizian	Arabkir District Polyclinic	Director	Yerevan, Armenia
	Tigran Avagnan	WHO		Yerevan, Armenia
...China	Dr. Zhao Kun	China National Health Economics Institute	Faculty member and researcher, R4D consultant	Beijing, China
	Dr. Wang Zaoli	Center for China Cooperative Medical Scheme (CCMS)	Vice Director and Researcher, health insurance program representative	Beijing, China
	Prof. Ming Liu	Chinese Parliament; Center of AIDS Prevention and Research, Peking University School of Public Health	Member; Vice Director	Beijing, China
	Dr. Liang Xiaofeng	China Center for Disease Control and Prevention, Chinese Ministry of Health	Director, National Immunization Program	Beijing, China

	Name	Organization	Position	Location
China...	Dr. Shen Xinliang	China National Pharmaceutical Group	Director, National Research Center of Innovative Vaccine	Beijing, China
	Dr. Zhenzhong Zhang	China National Health Economics Institute	Director General	Beijing, China
	Dr. Shen Kunling	Experts Advisory Committee on Immunization Program; Beijing Children's Hospital	Member; Vice President and Professor	Beijing, China
	Representative of Regulatory Authority	State Food and Drug Administration	Director, Institute for Control of Pharmaceutical and Biological Products	Beijing, China
	Dr. Wang Long Zhu	Fuxing Hospital	Director, Station 2 (children's preventive health), Community Health Center	Beijing, China
	Dr. David Hipgrave, Dr. Xu Zhu	UNICEF China Office	Chief of Health, Nutrition and WES Section	Beijing, China
...Ecuador	Nancy Vásconez	Ministry of Health	National EPI Coordinator	Quito, Ecuador
	Maria del Carmen Grijalva Aguilar	Ministry of Health	National EPI Team	Quito, Ecuador
	Sara Naranjo,	Ministry of Health	Sub-Secretary of Planning	Quito, Ecuador
	Dr. Celia Riera	PAHO	Country Representative	Quito, Ecuador
	Laura Ramirez	PAHO	Point person on immunization	Quito, Ecuador
	Dr. Juan Vásconez	UNICEF; National Immunization Committee	Official; Member	Quito, Ecuador
	Dr. Carmen Laspina	Ministry of Health	National Health Director	Quito, Ecuador
	Pablo Torres Donsos	Merck Sharp & Dohme	Vaccine Team	Quito, Ecuador
	Dra. Leonor de Cozarelly	National Institute of Hygiene	Director, National Regulatory Authority	Guayaquil, Ecuador
	Dr. Ernesto Gutierrez	National Institute of Hygiene	Former Minister of Health, Member of the National Immunization Committee	Guayaquil, Ecuador
	Cecilia Ampuero de Mármol	National Institute of Hygiene	General Coordinator, National Vaccine Production	Guayaquil, Ecuador
	Dr. Fatima Franco	Ministry of Health	Former head of EPI Guayaquil, Current Sub-Secretary Guayaquil Region	Guayaquil, Ecuador
	Fernando Soria	Ministry of Economy and Finance	Sub-Secretary Budgeting	Quito, Ecuador

	Name	Organization	Position	Location
	Dr. Gonzalo Baquero	National Immunization Committee	Member, also Former Minister of Health	Quito, Ecuador
	Eugenia Almeida	Ministry of Health	Leader for Imports, Supply and Inventory	Quito, Ecuador

Ecuador...	Betty Garcia	Ministry of Health	Budgeting liaison within the Ministry of Health for the EPI	Quito, Ecuador
	Dr. Gonzalo Macías	Immunization Program, Province of Esmeraldas	Director	Quito, Ecuador
	Lcda. Susana Galarza	Immunization Program for Area 1 Health Services, Province of Pichincha	Director	Quito, Ecuador
...Egypt	Dr. Nasr El Said	Ministry of Health	Minister's Assistant for Primary Health Care, Preventative Medicine and Family Planning	Cairo, Egypt
	Dr. Amr Kandeel	Ministry of Health	Undersecretary of Preventative Affairs	Cairo, Egypt
	Dr. Mohamed Genaidy	Ministry of Health	Director General, Communicable Diseases Department	Cairo, Egypt
	Dr. Ibrahim Moussa	Ministry of Health	EPI Director	Cairo, Egypt
	Dr. Ashraf Bayoumi	Ministry of Health	Undersecretary of Pharmaceutical Affairs	Cairo, Egypt
	Dr. Caroline Mandouh	Ministry of Health	Head of the registration department at the Pharmaceutical Affairs department	Cairo, Egypt
	Dr. Ibrahim Gaffer	Ministry of Finance	Minister of Finance	Cairo, Egypt
	Dr. Faten Fathalla	National Organization for Research and Control of Biologicals (NRA)	Board Chairwoman	Cairo, Egypt
	Dr. Mohamed Rabie	VacSera – National Vaccine Manufacturers	Chairman and CEO	Cairo, Egypt
	Dr. Hamdallah H. Zedan	EGYVAC	Chairman and CEO	Cairo, Egypt
	Dr. Mossad M. Adley Selim	EGYVAC	Chairman of Production Board	Cairo, Egypt
	Dr. Azza Sadek	VacSera – National Vaccine Manufacturers	Public Relations, Media General Manager	Cairo, Egypt
	Dr. Hesham El Kadi	GSK	Vaccine Sales and Marketing Manager	Cairo, Egypt



	Name	Organization	Position	Location
	Dr. Tamer Saleh	Sanofi Pasteur	Medical and Marketing Director	Cairo, Egypt
	Dr. Amira Edris	National Supreme Committee Immunization/NITAG; Cairo University	Member; Professor of Pediatrics and Neonatology	Cairo, Egypt
	Dr. Hamed El Khayat	National Supreme Committee Immunization/NITAG; Ain Shams University	Member; Professor, Head of Pediatrics	Cairo, Egypt
Egypt...	Dr. Mohsen Gadallah	National Supreme Committee Immunization/NITAG; Ain Shams University	Member; Professor, Chairman Department of Community Environmental and Occupational Medicine	Cairo, Egypt
	Dr. Essam Allam	UNICEF China Country Office	Health Officer	Cairo, Egypt
	Dr. Nasr Tantawy	WHO Country Office		Cairo, Egypt
	Dr. Abdel Latif	WR Country office		Cairo, Egypt
	Dr. Ezzeddine Mohsni	WHO, EMRO		Cairo, Egypt
	Dr. Nadia Teleb	WHO Regional Office	New Vaccine surveillance	Cairo, Egypt
	Dr. Houda Langar	WHO Regional Office		Cairo, Egypt
...Indonesia	Full Committee	Technical Advisory Group (TAG)		Jakarta, Indonesia
	Dr. Vinod Bura	UNICEF	Health Specialist, EPI	Jakarta, Indonesia
	Dr. Kenny V. Peetosutan	UNICEF	Project Officer, EPI	Jakarta, Indonesia
	Dr. Bardan Jung Rana	WHO	Medical Officer, EPI	Jakarta, Indonesia
	Dr. Khanchit Limpakarnjanarat	WHO	WR	Jakarta, Indonesia
	Prof. Dr. Sri Rezeki S. Hadinegoro	Indonesian Pediatric Society (IPS); University of Indonesia; TAG	Chair, Task Force for Immunization; Chair, National AEFI Committee; Chair	Jakarta, Indonesia
	Prof. Dr. Soedjatmiko	Indonesian Pediatric Society (IPS); University of Indonesia	Secretary of IPS Task Force for Immunization; Division of Infection & Tropical Pediatrics, Dept of Child Health, Medical Faculty	Jakarta, Indonesia
	Dr. Lucky S. Slamet	National Agency for Drug and Food Control (national regulatory authority)	Deputy for Therapeutic Products, Narcotics, Psychotropic and Addictive Substance Control	Jakarta, Indonesia

	Name	Organization	Position	Location
	Dr. Iskandar	BioFarma	President Director	Bandung, Indonesia
	Elvyn Fajrul Jaya Saputra	BioFarma	Planning & Development Director	Bandung, Indonesia
	Lin Susanti	BioFarma	Pharmaceuticals, Quality Control Manager	Bandung, Indonesia
	Dr. Novilia Sjafri Bachtiar	BioFarma	Head, Product Evaluation Department	Bandung, Indonesia
	Dr. Neni Nurainy	BioFarma	Research and Development	Bandung, Indonesia

Indonesia...	Dr. Theresia Sandra	EPI/Directorate General of Disease Control & Environmental Health (DGDCEH)	EPI Manager	Jakarta, Indonesia
	Dr. Julitasari Sundoro	EPI/DGDCEH; TAG	Epidemiologist; Secretary	Jakarta, Indonesia
	Dr. Tunggul P. Sihombing	EPI/DGDCEH	Head, Program and Information Division	Jakarta, Indonesia
	S.K.M. Kuncahyo	EPI/DGDCEH	Immunization Guidance and Evaluation Section	Jakarta, Indonesia
...Morocco	Saif Eddine Senouci	Ministry of Economy and Finance	Chief of Service, Social Development and Health Service	Rabat, Morocco
	Dr. Anis El Mekaoui	Merck Sharp & Dohme S.A.	Medical Director, Northern Africa Region	Casablanca, Morocco
	Rachid Lahbabi	Merck Sharp & Dohme S.A.	Brans & Customer Manager	Casablanca, Morocco
	Abderrahmane Alaoui	Ministry of Health	Chief of the Finance Division	Rabat, Morocco
	Dr. Khalid Lahlou	Ministry of Health	Director of Population	Rabat, Morocco
	Dr. Mohammed Charradi	Ministry of Health	Chief of Maternal and Child Health	Rabat, Morocco
	Mohammed Youbi	Ministry of Health	Deputy Director	Rabat, Morocco
	Mohammed Benhafid	Ministry of Health	Manager, National Reference Laboratory for Polio and Rotavirus, INH	Rabat, Morocco
	Mme. Maella	Ministry of Health	Manager, National Reference Laboratory for Measles and Rubella, INH	Rabat, Morocco
	Omar Bouazza	Ministry of Health	Director of Drugs and Pharmacy	Rabat, Morocco

	Name	Organization	Position	Location
Morocco..	M'hamed Braikat	Ministry of Health	EPI Manager, Direction of Population	Rabat, Morocco
	Mohammed Charradi	Ministry of Health	Head of Division, Child and Maternal Health, Direction of Population	Rabat, Morocco
	Bouchra El Basri	Ministry of Health	EPI staff, Direction of Population	Rabat, Morocco
	Mme. Hakkou	Ministry of Health	Head of Service, Quality Control and Biological Testing, Direction of Drugs and Pharmacy	Rabat, Morocco
	Mme. Marzine	Ministry of Health	Head of Addictive Drugs, Direction of Drugs and Pharmacy	Rabat, Morocco
	Mme. Noussac	Ministry of Health	Epidemiologist, Service of Epidemiologic Surveillance (SES)	Rabat, Morocco
	Ahmed Rguig	Ministry of Health	Epidemiologist, SES	Rabat, Morocco
	Mr. Riatec	Ministry of Health	Head of Quality Services, Direction of Drugs and Pharmacy	Rabat, Morocco
	Dr. Rachid Bekkali	Lalla Salma Association to Fight Against Cancer	Executive Director	Rabat, Morocco
	Dr. Youssef Chami Khazraji	Lalla Salma Association to Fight Against Cancer	Coordinator of the Tobacco Control Fight	Rabat, Morocco
	Maria Bennani	Lalla Salma Association to Fight Against Cancer	Manager, International Cooperation	Rabat, Morocco
	Ahmed Zidouly	Lalla Salma Association to Fight Against Cancer	Consultant	Rabat, Morocco
	Dr. Moulay Said Afif	National College Union of Private Medical Specialists	Secretary General	Casablanca, Morocco
	Prof. Hadj Khalifa Habiba	Casablanca Children's Hospital	Chief of Pediatric Services III	Casablanca, Morocco
	Luis Alfonso Diaz	Pfizer Global Pharmaceuticals	Director General	Casablanca, Morocco
	Francoise Griguer	Sanofi-Pasteur Casablanca	Director, North Africa	Casablanca, Morocco
	Anis El Mekaoui	MSD Maroc	Medical Manager	Casablanca, Morocco
	Rachid Lahbib	MSD Maroc	Brand and Customer Manager	Casablanca, Morocco
	Moulay Said	Moroccan Society of Pediatrics	Representative, Private Practitioner	Casablanca, Morocco

	Name	Organization	Position	Location
	Khalifa Hadj	Moroccan Society of Pediatrics	President	Casablanca, Morocco
	Mostafa Benmimoun	Pfizer Global Pharmaceuticals	Medical Operations Director	Casablanca, Morocco
	Tarik Hajji	Pfizer Global Pharmaceuticals	Customer Manager	Casablanca, Morocco
	Neim Youssef	GSK Casablanca		Casablanca, Morocco
	Nail Youssef	GSK Morocco	Vaccines Key Account Manager	Casablanca, Morocco
	Khaoula Harkat	GSK Morocco	Vaccine Business Manager	Casablanca, Morocco
	Farah Hajji	ANAM	Pharmacist	Casablanca, Morocco
	Laila Ibnmakhlouf	ANAM	Pharmacist	Casablanca, Morocco
	Sanaa Mehdioui	ANAM	Pharmacist	Casablanca, Morocco
	Ahmed Laabid	UNICEF	Health Specialist	Casablanca, Morocco
	Said Salah Youssouf	WHO	Representative for Morocco	Casablanca, Morocco
Panama	Lic. Itzel de Hewitt	Ministry of Health	EPI Manager	Panama City, Panama
	Dra. Betancourt	Ministry of Health	Former Minister of Health (1982)	Panama City, Panama
	Dr. Mora	Ministry of Health	Director General of Public Health	Panama City, Panama
	Dr. Camilo Alleyne	Ministry of Health	Former Minister of Health, made decisions on Rota and HPV	Panama City, Panama
	Dr. Hugo Moreno	Parliament	President of the Public Health and Social Security Commission	Panama City, Panama
	Juan Alberto Batista	Formerly Ministry of Health; Currently Administration and Financial Management Unit (AFMU)	Formerly in the Finance Department of the MOH during decisions on Rota and HPV; Currently Executive Director at the AFMU	Panama City, Panama
	Mtger. Ivan Conte	National Directorate of Pharmacy and Drugs	Director	Panama City, Panama
	Dr. Rudy Kant	Social Security Administration; CONAPI	Director of Epidemiology at Social Security Administration; Director	Panama City, Panama
	Dr. Xavier Saez	Children's Hospital	Director of Infectology, national vaccine champion and researcher	Panama City, Panama
	Maritza Romero	PAHO	Subregional Adviser	Panama City, Panama
	Dr. Joaquin Molina	PAHO	Country Representative	Panama City, Panama

	Name	Organization	Position	Location
	Dr. Javier Nieto Guevara	Gorgas Commemorative Institute for Health Studies	Sub-Director General	Panama City, Panama
	CONAPI Representatives			Panama City, Panama
..Thailand	Dr. Passakorn Akkasewi	Bureau of Epidemiology, Department of Disease Control (DDC)	Director	Bangkok, Thailand
	Dr. Winai Swasdivorn	National Health Security Office (NHSO)	Secretary-General	Bangkok, Thailand
	Dr. Arthorn Riewpaiboon	Mahidol University	Associate Professor, Social and Administrative Pharmacy, Faculty of Pharmacy	Bangkok, Thailand
	Dr. Visith Sitprija	King Chulalongkorn Memorial Hospital; Queen Saovabha Memorial Institute, Thai Red Cross	Professor, Department of Medicine; Director	Bangkok, Thailand
Thailand...	Dr. Terapong Tantawichien	National Committee on Vaccines; Queen Saovabha Memorial Institute, Thai Red Cross Society; Chulalongkorn University Hospital	Member; Deputy Director of Clinical Services; Professor of Medicine, Division of Infectious Diseases	Bangkok, Thailand
	Prof. Sumana Khomvilai	Queen Saovabha Memorial Institute, Thai Red Cross Society	Deputy Director of Administrative Affairs	Bangkok, Thailand
	Dr. Suwit Wiboonpolprasert	Ministry of Public Health (MOPH); Benefits Committee (NHSO) and Essential Medicine Committee	Senior Advisor on Disease Control; Chair	Bangkok, Thailand
	Ms. Worasuda Yoongthong	Food and Drug Administration (FDA); Essential Medicine Committee	Senior Pharmacist, National List of Essential Medicines Office, Drug Control Division; Secretary	Bangkok, Thailand
	Mr. Vinit Usavakidviree	FDA	Director, Drug Control Division	Bangkok, Thailand
	Ms. Yupin Lawanpraset	FDA	Senior Advisor of Safety, Effectiveness and Use of Health Products	Bangkok, Thailand
	Mrs. Teeranart Jiwapaisanpong	Ministry of Public Health (MOPH)	Director, Institute of Biological Products, Department of Medical Sciences	Bangkok, Thailand
	Dr. Supachai Rerks-ngarm	DDC	Senior Expert, Preventive Medicine	Bangkok, Thailand
	Dr. Supamit Schunsuthiwat	DDC	Senior Expert, Disease Control	Bangkok, Thailand

	Name	Organization	Position	Location
	Dr. Piyanit Thamaphornpilas	DDC	EPI Manager, Bureau of General Communicable Diseases	Bangkok, Thailand
	Dr. Charung Muangchana	DDC	Director, National Vaccine Committee Office	Bangkok, Thailand
	Dr. Maureen Birmingham	WHO Thailand	Representative	Bangkok, Thailand
..Turkey	Dr. Cristina Profili	WHO Turkey Country Office	WR	Ankara, Turkey
	Mr. Y Mehmet Kontaş	WHO Turkey Country Office	Deputy Head	Ankara, Turkey
	Dr. Toker Ergüder	WHO Turkey Country Office	National Professional Officer	Ankara, Turkey
	Dr. Mehmet Ali Torunoğlu	Ministry of Health, General Directorate of Primary Health Care	Director	Ankara, Turkey
Turkey...	Dr. M. Levent Altun	General Directorate of Drugs and Pharmaceuticals (regulatory authority)	Deputy Director General	Ankara, Turkey
	Dr. Levent Akin	Immunization Advisory Committee; Hacettepe University	Member; Professor, Dept of Public Health	Ankara, Turkey
	Dr. Ufuk Beyazova	Immunization Advisory Committee; Gazi University	Member; Social Pediatrics Department, Faculty of Medicine	Ankara, Turkey
	Dr. Münevver Bertan	International Children's Center (Turkish NGO)	Professor, Executive Director	Ankara, Turkey
	Dr. Kadriye Yurdakök	International Children's Center (Turkish NGO); Hacettepe University Institute of Child Health; IAC	Deputy Executive Director; Department of Social Pediatrics; Member	Ankara, Turkey
	Dr. Dilek Haznedaroglu	International Children's Center (Turkish NGO)	Staff	Ankara, Turkey
	Senem Berpu	International Children's Center (Turkish NGO)	Staff	Ankara, Turkey
	Dr. Umit Ozdemirer	EPI Unit	Polio Eradication Program and Vaccine Preventable Diseases Surveillance	Ankara, Turkey
	Dr. Pervin Ozelci	EPI Unit	Public Health Specialist, Communicable Diseases and Outbreak Control Department	Ankara, Turkey

	Name	Organization	Position	Location
	Dr. Aslihan Coskun	EPI Unit	Public Health Specialist, Communicable Diseases and Outbreak Control Department	Ankara, Turkey
	Dr. Serap C. Coban	EPI Unit	Public Health Specialist, Communicable Diseases and Outbreak Control Department	Ankara, Turkey
	Undisclosed	International Vaccine Company	Regulatory & Public Affairs Director	Ankara, Turkey
	Undisclosed	International Vaccine Company	Medical Director	Ankara, Turkey
	Dr. Lelia Jelamschi	UNICEF	Maternal and Child Health	Ankara, Turkey

**Table B-2. Individuals Interviewed in Remote Case Studies**

	Name	Organization	Position	Location
Albania	Anshu Banerjee	WHO Albania Country Office	Head of WHO Albania Country Office	Albania
	Silvia Bino	Institute of Public Health	Head of Control of Infectious Diseases Department	Albania
	Mariana Bukli	UNICEF	Albania Health and Nutrition Officer	Albania
	Erida Nelaj	Institute of Public Health	EPI Manager	Albania
	Ivone Rizzo	GAVI Alliance Secretariat		Geneva, Switzerland
	Zhaneta Shatri	USAID	Officer	Albania
Cape Verde	Edith Santos	Cape Verdean Ministry of Public Health	Director General for Pharmaceuticals	Cape Verde
	Maria de Jesus Carvalho	Cape Verdean Ministry of Public Health	Director, National Reproductive Health Program	Cape Verde
	Paula Maximiano	UNFPA		Cape Verde
	Yolanda Estrela	WHO	Economist and Planner	Cape Verde

	Name	Organization	Position	Location
Philippines	Dr. Alexander Padilla	COBAC	Undersecretary of Health	Philippines
	Dr. Joyce Ducusin	EPI	EPI Manager	Philippines
	Dr. Lulu Bravo	Philippines Pediatric Society		Philippines
	Dr. Howard Sobel	WHO Philippines	EPI Officer	Philippines
	Dr. Marisa	UNICEF	Child Health Section	Philippines
	Dr. Eduardo Banzon	World Bank Philippines	Chief of the Health Section	Philippines
South Africa	Mr. Johan Van Den Heever	Department of Health	Deputy Director of the Child and Adolescent Health Directorate in charge of the Expanded Program on Immunization	Pretoria, South Africa
	Ms. Lindsay Botham	EPI, Department of Health	In charge of Immunization Cold Chain	South Africa
	Dr. Barry Schoub	National Advisory Group on Immunization		South Africa
	Mr. Makhoana Morena	BioVac	CEO	Pinelands, South Africa
Syria	Khaled Baradei	EPI	Manager	Syria
	Sahar Idlibib	Syrian Pediatric Association	University of Damascus Hospital; Secretary	Syria
	Hyam Bashour	Damascus University; SAGE	Chair, Department of Family and Community Medicine, Faculty of Medicine; member (2004–present)	Syria
Tunisia	Prof. Souad Bousnina	Vaccination Technical Committee (CTV) (NITAG)	Chair	Tunis, Tunisia
	Dr. Akthem Fourati	UNICEF Tunisia	Health Specialist	Tunis, Tunisia
	Dr. Mohamed Ben Ghorbal	National Immunization Program	Director	Tunis, Tunisia
	Dr. Mongi Hamrouni		Director of Primary Health Care	Tunis, Tunisia
	Dr. Zohra Ladjimi		Directorate of Pharmaceuticals and Medicines	Tunis, Tunisia



**Table B-3. Global Experts Interviewed**

Name	Organization	Position
Ciro de Quadros	Sabin Vaccine Institute; IAVI; PAHO	Executive Vice President; Member of the Polio Advisory Committee; Chairperson of the TAG on Vaccines and Immunizations
Julie Milstein	University of Maryland; Independent	Professor; Consultant with experience at the WHO
Mark Kane	Independent	Consultant with significant experience at the US CDC working in the EPI at the WHO
Stefano Malvoti	PATH; AVI Management Team	Strategic Vaccines Supply Director; Principal
Lulu Bravo	Sabin Vaccine Institute PACE Council; WHO Technical Steering Committee of the Child and Adolescent Health Department; International Society of Tropical Pediatrics; University of the Philippines Manila	Member; Member; President; Professor of Pediatric Infectious and Tropical Diseases at the College of Medicine, Vice Chancellor for Research and Executive Director of the National Institutes of Health
John Fitzsimmons	PAHO	Special Program for Vaccines and Immunization
Vivien Tsu	PATH; University of Washington School of Public Health	Associate Director of Reproductive Health; Affiliate Professor of Epidemiology
David Heymann	WHO	Assistant Director-General—Health Security and Environment Representative of the Director-General for Polio Eradication
Richard Mahoney	The Pediatric Dengue Vaccine Initiative of the International Vaccine Institute	Director of Vaccine Access
Julie Jacobsen	Bill and Melinda Gates Foundation	Senior Program Officer, focusing on neglected tropical diseases including JE
Rana Hajjeh	US CDC; Hib Initiative	Director of the Division of Bacterial Diseases in the National Center for Immunization and Respiratory Diseases; Project Director
Chris Elias	PATH	President and CEO
Jay Wenger	National Polio Surveillance Project (India)	Project Director
John Wecker	PATH	Global Program Leader, Vaccine Access and Delivery

Name	Organization	Position
Paul Fife	GAVI Board; NORAD	Member; Director
Marc La Force	PATH	Global Program Leader, Meningitis Vaccine Project
Jon Andrus	PAHO; George Washington University	Deputy Director; Professor of Global Health
Susan McKinney	GAVI Board; USAID	Member; Senior Technical Adviser for Immunization
Howard Sobel	WHO Philippines	Medical Officer
Najwa Khouri-Bulos	Jordan University Hospital	Member; Head of the Division of Infectious Disease

**Table B.-4. Manufacturers Interviewed**

	Company	Location of Headquarters
DCVMN	Fiocruz /Biomanguinhos	Rio de Janeiro, Brazil
	Panacea Biotec	New Delhi, India
	PT BioFarma	Bandung, Indonesia
	Serum Institute of India	Pune, India
	Sinopharm	Beijing, China
IFPMA	Crucell	Leiden, Netherlands
	GlaxoSmithKline	Middlesex, UK
	Merck	Whitehouse Station, USA
	Pfizer	New York City, USA
	Sanofi Pasteur	Lyon, France

## Annex C. Data on Lower-Middle-Income Countries and Selected Upper-Middle-Income Countries

According to the World Bank classification, which was used in this report, lower-middle-income countries (LMICs) are economies with a 2009 gross nation income (GNI) per capita (Atlas method, current US\$) of between \$996 and \$3,945.

### List of Tables in Annex C

Table C. 1 Basic Indicators.....	106
Table C. 2 Health Financing, 2000-2008 .....	110
Table C. 3 Target Vaccine Introduction Years and Burden of Disease Data .....	114
Table C. 4 Progress on Millennium Development Goal (MDG) #4 .....	120

The key below applies to all tables in Annex C:

In-Depth Country studies of LMICs
Remote Country studies of LMICs
In-Depth Country studies of UMICs
Remote Country studies of UMICs
– Data not available

**Table C-1. Basic Indicators**

GNI per capita decreased between 2008 and 2009
Birth cohort estimated from crude birth rate and population

Country	2009 GNI per capita (Atlas method, current US\$)	2008 Population	2008 Birth Cohort	2008 Crude Birth Rate	2008 Under-5 Mortality Rate	2008 Infant Mortality Rate	2008 DTP3 Coverage (%)
Albania <sup>a</sup>	3,950	3,143,291	46,175	15	14	13	99
Angola	3,490	18,020,668	773,231	43	220	130	81
Armenia	3,100	3,077,087	46,839	15	23	21	89
Azerbaijan	3,740	8,680,100	154,484	18	36	32	70
Belize	2,020	322,100	7,821	25	19	17	94
Bhutan	1,630	686,789	14,781	21	81	54	96
Bolivia	1,170	9,694,113	264,841	27	54	46	83
Cameroon	3,010	19,088,385	652,584	37	131	82	84
Cape Verde	3,620	498,672	12,098	24	29	24	98
China	1,830	1,324,655,000	16,026,987	12	21	18	97
Congo, Republic of	1,060	3,615,152	3,182,596	35	–	–	69
Djibouti	1,280	849,245	24,310	28	95	76	89
Ecuador	3,940	13,481,424	282,889	21	25	21	75
Egypt, Arab Republic	2,070	81,527,172	2,024,320	25	23	20	97
El Salvador	3,370	6,133,910	124,991	20	18	16	94
Georgia	2,530	4,307,011	47,097	12	30	26	92
Guatemala	2,630	13,686,128	454,690	33	34	29	85
Guyana	1,450	763,437	13,775	18	61	46	93
Honduras	1,820	7,318,789	201,900	27	31	26	93
India	1,170	1,139,964,932	26,789,176	23	69	52	66

Country	2009 GNI per capita (Atlas method, current US\$)	2008 Population	2008 Birth Cohort	2008 Crude Birth Rate	2008 Under-5 Mortality Rate	2008 Infant Mortality Rate	2008 DTP3 Coverage (%)
Indonesia	2,230	227,345,082	4,273,954	19	41	31	77
Iraq	2,210	30,711,152	958,802	31	45	36	62
Jordan	3,740	5,906,043	171,866	26	20	17	97
Kiribati	1,890	96,558	–	–	48	38	82
Kosovo	3,240	1,795,000	34,123	19	–	–	–
Lesotho	1,020	2,049,429	58,565	29	79	63	83
Maldives	3,870	305,027	7,258	19	28	24	98
Marshall Islands	3,060	59,667	–	–	36	30	93
Mauritania	960	3,215,043	104,003	34	118	75	74
Micronesia, Federated States of	2,220	110,414	2,888	25	39	32	79
Moldova	1,590	3,633,369	44,658	12	17	15	95
Mongolia	1,630	2,641,216	57,123	19	41	33	96
Morocco	2,790	31,605,616	641,318	20	36	32	99
Nicaragua	1,010	5,667,325	141,172	25	27	23	96
Nigeria	1,140	151,212,254	6,034,168	40	186	96	54
Pakistan	1,020	166,111,487	4,523,509	30	89	72	73
Panama	6,740	3,398,823	70,671	21	23	19	82
Papua New Guinea	1,180	6,576,822	190,688	31	69	53	52
Paraguay	2,280	6,237,855	154,549	25	28	24	76
Philippines	1,790	90,348,437	2,255,368	25	32	26	91
Samoa	2,840	178,869	4,477	24	26	22	46
São Tomé and Príncipe	1,140	160,174	5,215	32	97	64	99
Senegal	1,040	12,211,181	473,501	38	108	57	88
South Africa	5,770	48,687,000	1,087,814	22	67	48	67
Sri Lanka	1,990	20,156,204	382,968	19	17	13	98
Sudan	1,230	41,347,723	1,307,250	31	109	70	86

Country	2009 GNI per capita (Atlas method, current US\$)	2008 Population	2008 Birth Cohort	2008 Crude Birth Rate	2008 Under-5 Mortality Rate	2008 Infant Mortality Rate	2008 DTP3 Coverage (%)
Swaziland	2,350	1,167,834	35,051	30	83	59	95
Syrian Arab Republic	2,410	20,581,290	599,257	28	16	14	82
Thailand	3,760	67,386,383	982,291	15	14	13	99
Timor-Leste	2,460	1,098,386	44,156	40	93	75	79
Tonga	3,260	103,566	2,917	28	19	17	99
Tunisia	3,720	10,327,800	179,683	18	21	18	99
Turkey	8,730	73,914,260	1,361,944	18	22	20	96
Turkmenistan	3,420	5,043,618	109,802	22	48	43	96
Ukraine	2,800	46,258,200	471,834	11	15	14	90
Uzbekistan	1,100	27,313,700	573,271	22	38	34	98
Vanuatu	2,620	233,866	6,648	30	33	27	76
Vietnam	1,010	86,210,781	1,617,487	17	14	12	93
Yemen, Republic of	1,060	22,917,485	882,049	37	69	53	69
LMICs	Sum	3,767,315,190	78,975,864				
	Weighted Average <sup>b</sup>	1,655		20	51	37	82
LMICs (except China and India)	Sum	1,302,695,258	35,166,776				
	Weighted Average <sup>b</sup>	1,902		26	65	44	81
LMICs in study, except China (in-depth and remote studies)	Sum	552,312,873	11,423,009				
	Weighted Average <sup>b</sup>	2,448		20	31	25	87
UMICs in study (4 in-depth and remote studies)	Sum	129,143,374	2,566,603				
	Weighted Average <sup>b</sup>	7,445		20	39	30	85

<sup>a</sup> Albania transitioned from LMIC status to UMIC status during the study.

<sup>b</sup> Averages weighted by 2008 population

Sources:

World Bank. World Development Indicators [Internet]. Washington (DC): WBG; c2010 [updated 2009 Oct 8; cited 2010 Sep 2]. Available from:  
<http://www.data.worldbank.org>.

World Health Organization. Global Health Observatory [Internet]. Geneva (Switzerland): WHO; c2009 [cited Sep 2 2010]. Available from  
<http://apps.who.int/ghodata/>

Table C–2. Health Financing, 2000—2008

Country	Total Expenditure on Health as % of Gross Domestic Product			General Government Expenditure on Health as % of Total Expenditure on Health			General government Expenditure on Health as % of Total Government Expenditure			Total Government Expenditure on Vaccines as % of Government Health Expenditure	Per Capita Government Health Expenditure (PPP int. \$)		
	2000	2004	2008	2000	2004	2008	2000	2004	2008	2008 <sup>a</sup>	2000	2004	2008
Albania <sup>b</sup>	6.4	6.8	6.8	36.3	40.5	42.4	7.1	9.3	8.8	0.00	97	153	227
Angola	2.4	2.1	2.7	79.2	76.0	81.7	3.2	4.1	6.2	–	43	47	131
Armenia	6.4	5.8	3.8	17.7	31.6	43.7	4.6	9.0	7.6	–	23	65	100
Azerbaijan	4.8	4.1	3.6	18.1	24.8	24.0	4.2	4.0	2.6	0.83	19	36	76
Belize	3.7	4.0	4.0	58.3	47.6	66.3	6.7	6.1	8.8	0.48	107	118	191
Bhutan	5.2	3.8	3.9	73.6	68.3	80.3	8.6	7.9	8.7	–	95	84	155
Bolivia	6.1	5.7	5.2	60.1	67.1	63.5	9.8	11.6	9.9	0.16	110	129	142
Cameroon	4.5	4.8	5.5	21.5	24.9	28.4	6.4	7.5	7.9	0.00	16	23	34
Cape Verde	4.6	5.1	4.3	73.5	77.9	72.5	9.6	12.7	9.8	0.00	74	99	109
China	4.6	4.5	4.3	38.7	39.7	46.7	11.1	10.1	9.9	0.05	42	65	121
Congo, Republic of	2.1	2.7	1.8	57.7	53.8	65.4	4.8	5.3	5.1	0.00	34	47	46
Djibouti	5.8	5.4	8.5	67.8	64.0	76.1	12.0	9.3	14.1	–	61	62	139
Ecuador	4.2	5.1	5.9	31.2	41.3	39.5	6.4	7.8	7.4	1.85	63	132	187
Egypt, Arab Republic	5.5	6.0	6.4	39.6	37.4	38.3	7.3	7.1	7.1	0.18	78	92	127
El Salvador	8.0	7.2	6.0	45.2	48.8	58.0	14.3	14.6	13.3	0.64	166	187	238
Georgia	7.4	8.5	8.7	16.7	15.4	20.7	6.4	5.3	4.9	0.16	25	40	89
Guatemala	6.2	5.9	7.3	39.8	37.2	28.0	16.7	15.6	14.1	0.10	77	86	97
Guyana	5.5	6.4	8.0	84.5	86.4	87.3	10.0	12.5	14.8	–	95	132	179
Honduras	5.3	5.7	5.7	56.3	59.0	61.4	15.1	16.6	15.1	0.10	77	102	139



Country	Total Expenditure on Health as % of Gross Domestic Product			General Government Expenditure on Health as % of Total Expenditure on Health			General government Expenditure on Health as % of Total Government Expenditure			Total Government Expenditure on Vaccines as % of Government Health Expenditure	Per Capita Government Health Expenditure (PPP int. \$)		
	2000	2004	2008	2000	2004	2008	2000	2004	2008	2008 <sup>a</sup>	2000	2004	2008
India	4.4	4.2	4.0	24.5	22.5	28.0	3.8	3.5	4.1	0.01	16	19	33
Indonesia	2.0	2.3	2.0	36.6	36.8	55.3	4.5	4.5	5.7	0.00	17	25	45
Iraq	1.4	5.2	2.7	28.7	80.7	81.2	1.3	3.4	3.1	0.01	11	109	76
Jordan	9.8	9.8	8.5	48.9	54.1	62.2	11.3	11.0	11.3	1.33	153	209	268
Kiribati	10.8	12.9	15.0	98.8	98.9	82.7	8.7	5.5	8.2	0.19	137	216	241
Kosovo	–	–	–	–	–	–	–	–	–	–	–	–	–
Lesotho	6.7	6.6	6.4	51.0	57.3	56.4	6.5	8.3	7.9	–	35	46	57
Maldives	9.6	8.8	11.2	51.6	56.3	69.6	13.5	13.8	12.8	–	140	207	436
Marshall Islands	20.3	14.3	13.4	98.0	97.4	97.2	21.1	16.7	14.6	–	370	310	329
Mauritania	2.8	2.5	2.6	71.2	63.9	67.3	6.5	4.2	5.3	–	25	23	36
Micronesia, Federated States of	8.4	11.1	13.1	93.9	95.3	95.8	10.5	16.1	18.8	–	204	293	347
Moldova	5.9	7.8	10.7	50.3	54.3	50.5	8.7	12.0	13.0	–	43	90	161
Mongolia	4.9	4.7	3.8	80.1	77.4	78.7	10.7	10.3	9.1	0.00	71	86	107
Morocco	4.2	5.2	5.3	29.4	27.4	35.0	4.0	5.1	6.2	0.09	32	48	80
Nicaragua	6.6	7.4	8.5	53.5	55.3	54.8	13.1	16.6	16.3	0.12	70	96	133
Nigeria	4.6	6.8	6.8	33.5	30.7	24.7	4.2	7.1	6.5	0.01	20	34	33
Pakistan	3.0	2.9	2.9	21.3	24.4	29.7	2.4	2.9	3.3	0.03	10	13	21
Panama	7.8	8.1	7.2	68.1	70.3	69.3	21.3	11.5	13.5	2.24	381	481	628
Papua New Guinea	4.0	4.2	3.2	81.7	84.7	80.1	9.9	10.0	7.3	0.28	57	68	56
Paraguay	9.2	7.7	6.3	40.2	33.7	37.7	17.5	15.3	11.9	0.00	124	97	112
Philippines	3.4	3.6	3.8	47.6	38.5	32.9	7.0	6.3	6.5	0.01	37	38	44
Samoa	5.6	4.8	5.1	70.9	82.3	84.8	10.8	13.1	12.6	0.04	109	148	198

Country	Total Expenditure on Health as % of Gross Domestic Product			General Government Expenditure on Health as % of Total Expenditure on Health			General government Expenditure on Health as % of Total Government Expenditure			Total Government Expenditure on Vaccines as % of Government Health Expenditure	Per Capita Government Health Expenditure (PPP int. \$)		
	2000	2004	2008	2000	2004	2008	2000	2004	2008	2008 <sup>a</sup>	2000	2004	2008
São Tomé and Príncipe	10.2	14.6	9.5	35.7	35.6	41.3	9.0	10.0	13.2	0.00		69	69
Senegal	4.4	5.7	5.7	37.5	37.5	55.8	8.8	9.4	12.1	0.00	21	32	57
South Africa	8.5	9.2	8.3	40.5	37.0	40.3	10.9	10.6	10.2	–	223	264	333
Sri Lanka	3.7	4.1	4.0	47.9	45.7	42.9	6.8	8.2	7.6	0.00	49	62	79
Sudan	3.1	3.9	3.6	29.2	33.9	36.6	8.3	7.2	6.3	–	11	20	28
Swaziland	5.7	6.8	5.9	58.6	67.3	64.8	11.6	12.2	9.2	0.08	119	190	189
Syrian Arab Republic	4.8	4.5	3.2	40.4	48.0	45.1	6.5	6.1	6.0	0.20	64	82	65
Thailand	3.4	3.5	4.0	56.1	64.9	75.1	10.0	11.3	14.1	–	89	137	242
Timor–Leste	8.8	11.1	10.5	70.9	75.3	80.2	12.7	13.8	10.9	–	49	59	73
Tonga	5.6	5.0	4.0	71.9	76.4	68.7	15.2	13.9	8.5	0.30	118	133	105
Tunisia	6.0	6.2	6.0	54.9	51.8	49.6	8.1	8.7	8.9	0.14	159	199	235
Turkey	4.9	5.9	5.0	62.9	72.3	69.0	9.8	12.1	10.3	0.00	272	416	479
Turkmenistan	3.9	3.6	1.8	81.7	66.6	54.5	13.7	12.5	8.7	–	110	96	66
Ukraine	5.9	6.6	6.8	48.9	58.4	56.1	8.4	9.3	8.6	0.12	95	203	279
Uzbekistan	5.7	4.9	5.0	44.1	46.3	50.5	6.0	7.5	8.7	–	36	41	67
Vanuatu	3.7	3.5	4.1	74.4	72.9	79.2	9.8	12.2	11.4	0.00	85	77	123
Vietnam	5.4	5.7	7.3	30.1	26.8	38.5	6.6	5.1	8.7	0.00	23	29	77
Yemen, Republic of	4.5	5.0	3.7	53.8	40.0	40.7	8.3	6.2	4.5	0.00	47	43	42
LMICs Weighted Average <sup>c</sup>	4.3	4.4	4.3	34.2	34.4	40.2	7.1	6.9	7.1	0.04	32.7	47.5	79.7
LMICs (except China and India) Weighted Average <sup>c</sup>	3.9	4.5	4.5	38.0	39.4	44.1	6.0	6.5	7.0	0.08	38	55	79
LMICs in case studies (except China)	3.4	3.7	3.7	41.2	41.0	49.5	6.3	6.4	7.3	0.10	46	62	94

Country	Total Expenditure on Health as % of Gross Domestic Product			General Government Expenditure on Health as % of Total Expenditure on Health			General government Expenditure on Health as % of Total Government Expenditure			Total Government Expenditure on Vaccines as % of Government Health Expenditure	Per Capita Government Health Expenditure (PPP int. \$)		
	2000	2004	2008	2000	2004	2008	2000	2004	2008	2008 <sup>a</sup>	2000	2004	2008
Weighted Average <sup>c</sup>													
UMICs in study													
Weighted Average <sup>c</sup>	6.4	7.3	6.3	53.9	58.1	57.6	10.4	11.4	10.3	0.10	252	354	422

<sup>a</sup> Data not available for 2000 or 2004

<sup>b</sup> Albania transitioned from LMIC status to UMIC status during the study.

<sup>c</sup> Averages weighted by 2008 population

Source:

World Health Organization. National Health Accounts [Internet]. Geneva (Switzerland): WHO; c2010 [updated 2010 Mar; cited 2010 Sep 2].

Available from <http://www.who.int/nha/country/en/>

**Table C–3. Target Vaccine Introduction Years and Burden of Disease Data**

.. Vaccine not yet introduced

Country	Year of Vaccine Introduction				Burden of Disease for Target Vaccines			
	Hep B	Hib	Pneumo	Rota	<u>Hep B</u> 2004 Hep B deaths/100,000 population/year	<u>Hib</u> 2000 Hib incidence in children < 5	<u>Pneumo</u> 2000 <i>S.</i> <i>pneumoniae</i> incidence in children < 5	<u>Rota</u> 2004 Rota deaths/1,000 children < 5/year
Albania <sup>a</sup>	1994	2009	..	..	0.08	3.5	5.9	0.19
Angola	2006	2006	..	..	3.38	21.9	39.5	3.66
Armenia	1999	2009	..	..	0.32	3.7	6.2	0.23
Azerbaijan	2001	2009	..	..	0.56	3.7	0.5	1.14
Belize	1999	2001	..	..	0.34	10.4	1,145.6	0
Bhutan	1997	2009	..	..	3.33	15.3	129.2	3.87
Bolivia	2000	2000	..	..	1.64	4.5	1.1	0.66
Cameroon	2005	2009	2010	..	0.78	18.3	1.9	1.55
Cape Verde	2002	..	..	..	0.23	7.4	613.2	0.33
China	2002	..	..	..	1.58	11.5	0.5	0.31
Congo, Republic of	2007	2009	2010	..	0.16	20.1	0.1	1.17
Djibouti	2007	2007	2010	..	2.99	10.4	0.8	1.63
Ecuador	1999	2003	..	2006	0.16	6.0	59.8	0.19
Egypt, Arab Republic	1992	..	..	..	5.83	6.4	1.6	0.29
El Salvador	1999	2002	..	..	0.08	9.6	3.0	0.37
Georgia	2001	2010	..	..	0.10	3.7	39.6	0.45
Guatemala	2005	2005	..	..	0.05	11.7	26.8	0.38
Guyana	2000	2000	2008	2008	0.75	15.7	500.9	1.17
Honduras	2000	1999	2009	..	0.25	7.9	3.9	0.45
India	2002	2009	..	..	2.37	18.9	3.8	0.96
Indonesia	2003	..	..	..	1.61	13.9	2.2	0.61

Country	Year of Vaccine Introduction				Burden of Disease for Target Vaccines			
	Hep B	Hib	Pneumo	Rota	<u>Hep B</u> 2004 Hep B deaths/100,000 population/year	<u>Hib</u> 2000 Hib incidence in children < 5	<u>Pneumo</u> 2000 S. <i>pneumoniae</i> incidence in children < 5	<u>Rota</u> 2004 Rota deaths/1,000 children < 5/year
Iraq	1985	2009	..	..	7.08	10.2	0.2	1.10
Jordan	1985	2001	..	..	2.45	6.7	12.4	0.26
Kiribati	1995	2008	..	..	1.24	6.8	309.0	–
Kosovo	–	–	–	–	–	–	–	–
Lesotho	2003	2008	..	2010	0.11	21.5	60.8	0.21
Maldives	1995	..	..	..	1.15	20.1	2,285.8	0.91
Marshall Islands	1988	1998	..	..	0.69	8.5	1,846.7	0
Mauritania	2005	2009	..	..	0.53	17.8	3.5	1.74
Micronesia, Federated States of	1989	1996	2008	..	0.30	7.2	87.6	0
Moldova	1995	2008	..	..	0.10	4.6	27.4	0.05
Mongolia	1991	2008	..	..	2.87	8.8	1.1	0.83
Morocco	1999	2007	..	..	0.96	6.8	40.0	0.38
Nicaragua	1999	1999	2008	..	0.65	7.2	131.1	0.33
Nigeria	2004	2009	..	..	1.79	17.7	0.0	2.11
Pakistan	2002	2008	..	2006	2.10	20.4	0.0	0.87
Panama	1999	2000	2009	..	0.40	9.6	67.0	0.21
Papua New Guinea	1989	2008	..	2007	3.28	15.6	17.0	1.15
Paraguay	2001	2002	..	..	0.13	12.5	28.7	0.25
Philippines	1992	..	..	..	0.78	13.9	1.2	0.33
Samoa	1990	2007	..	..	0.53	10.8	0.1	0
São Tomé and Príncipe	2003	2009	..	..	4.43	15.4	1,476.9	1.25
Senegal	2004	2005	..	..	0.65	14.9	2.1	1.51
South Africa	1995	1999	..	..	0.51	8.1	1.0	0.05
Sri Lanka	2005	2008	..	..	0.67	8.5	138.3	0.15
Sudan	2004	..	..	..	1.89	24.1	0.2	0.72
Swaziland	1996	2008	..	..	0.59	16.1	7.7	0.94

		Year of Vaccine Introduction				Burden of Disease for Target Vaccines			
		Hep B	Hib	Pneumo	Rota	<u>Hep B</u> 2004 Hep B deaths/100,000 population/year	<u>Hib</u> 2000 Hib incidence in children < 5	<u>Pneumo</u> 2000 S. <i>pneumoniae</i> incidence in children < 5	<u>Rota</u> 2004 Rota deaths/1,000 children < 5/year
Country									
Syrian Arab Republic		1993	2001	..	..	0.49	2.7	2.5	0.13
Thailand		1992	..	..	..	1.33	17.4	0.2	0.30
Timor-Leste		2007	..	..	..	2.84	14.1	5.6	1.11
Tonga		1988	2005	..	..	0.27	9.4	149.4	0
Tunisia		1995	..	..	..	10.88	3.8	54.2	0.16
Turkey		1998	2006	..	..	1.43	3.8	0.4	0.38
Turkmenistan		2002	2010	..	..	2.56	3.7	0.1	1.40
Ukraine		2003	2006	..	..	1.12	4.5	1.5	0.02
Uzbekistan		2001	2009	..	2006	3.37	3.7	0.2	0.95
Vanuatu		1995	2009	..	..	0.42	13.2	1,293.5	0.38
Vietnam		2003	2009	..	..	2.58	17.3	13.0	0.22
Yemen, Republic of		1999	2005	..	..	0.63	19.1	28.9	1.11
LMICs	# that have adopted (/54) <sup>c</sup>	55	45	7	6				
	Weighted Average <sup>b</sup>					2.0	14.7	5.1	0.68
LMICs (except India and China)	# that have adopted (/52) <sup>c</sup>	53	44	7	6				
	Weighted Average <sup>b</sup>					2.0	14.1	10.8	0.80
LMICs in case studies (except China)	# that have adopted (/11)	11	5	0	1				
	Weighted Average <sup>b</sup>					1.4	11.9	6.8	0.43

		Year of Vaccine Introduction				Burden of Disease for Target Vaccines			
		Hep B	Hib	Pneumo	Rota	<u>Hep B</u> 2004 Hep B deaths/100,000 population/year	<u>Hib</u> 2000 Hib incidence in children < 5	<u>Pneumo</u> 2000 <i>S.</i> <i>pneumoniae</i> incidence in children < 5	<u>Rota</u> 2004 Rota deaths/1,000 children < 5/year
UMICs in case studies	# that have adopted (/4)	4	4	1	0				
	Weighted Average <sup>b</sup>					1.0	5.5	2.5	0.25

<sup>a</sup> Albania transitioned from LMIC status to UMIC status during the study.

<sup>b</sup> Averages weighted by 2008 population

<sup>c</sup> Kosovo is not included in this denominator because data are not available.

#### Sources:

United Nations Population Division. World Population Prospects: the 2008 Revision. "Quinquennial Population by Five..Year Age Groups .. Both Sexes." [updated 2008; cited 19 Aug 2010]. Available from:

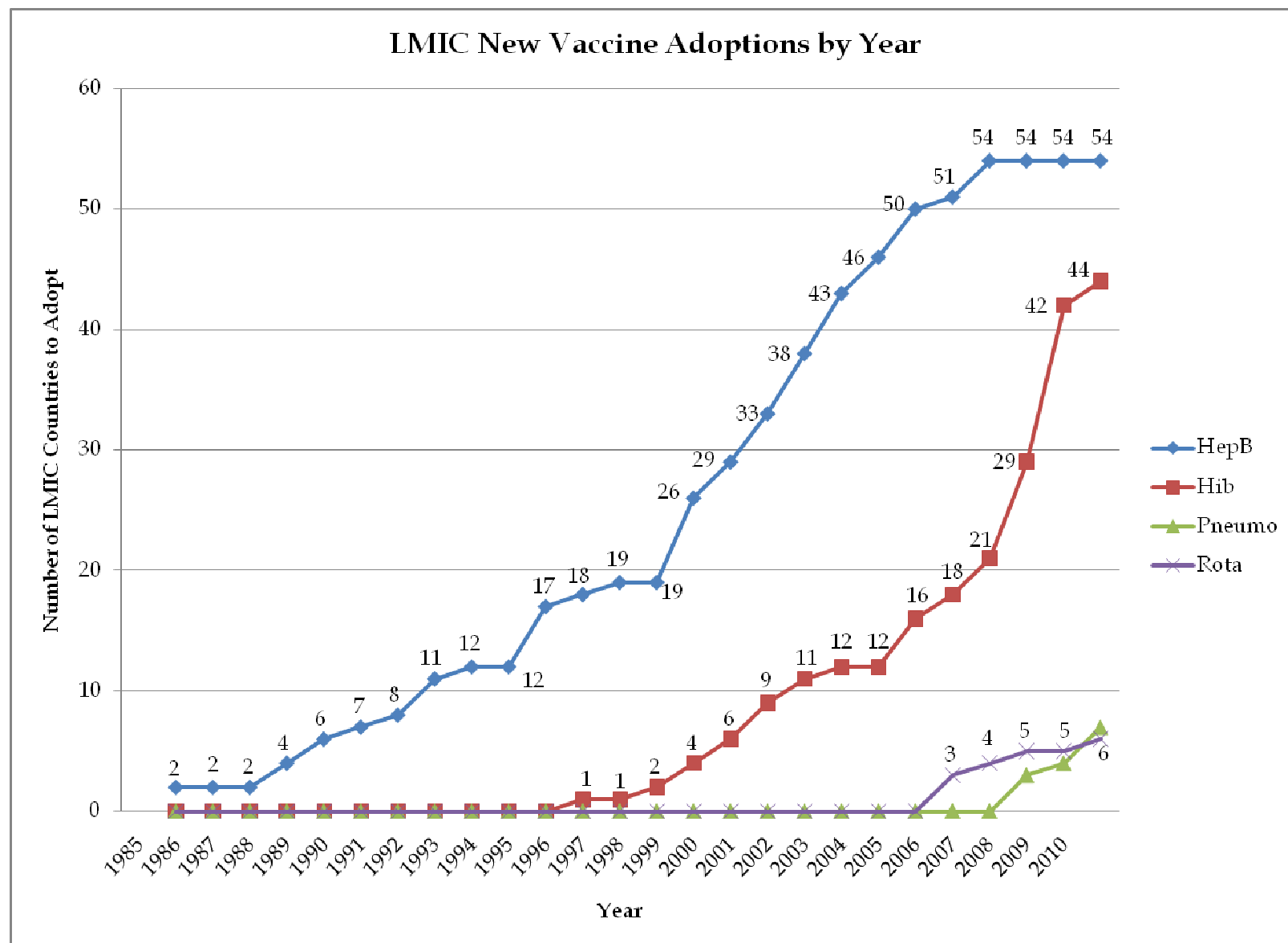
[http://esa.un.org/unpd/wpp2008/peps\\_population..by..age..and..sex\\_5x5.htm](http://esa.un.org/unpd/wpp2008/peps_population..by..age..and..sex_5x5.htm).

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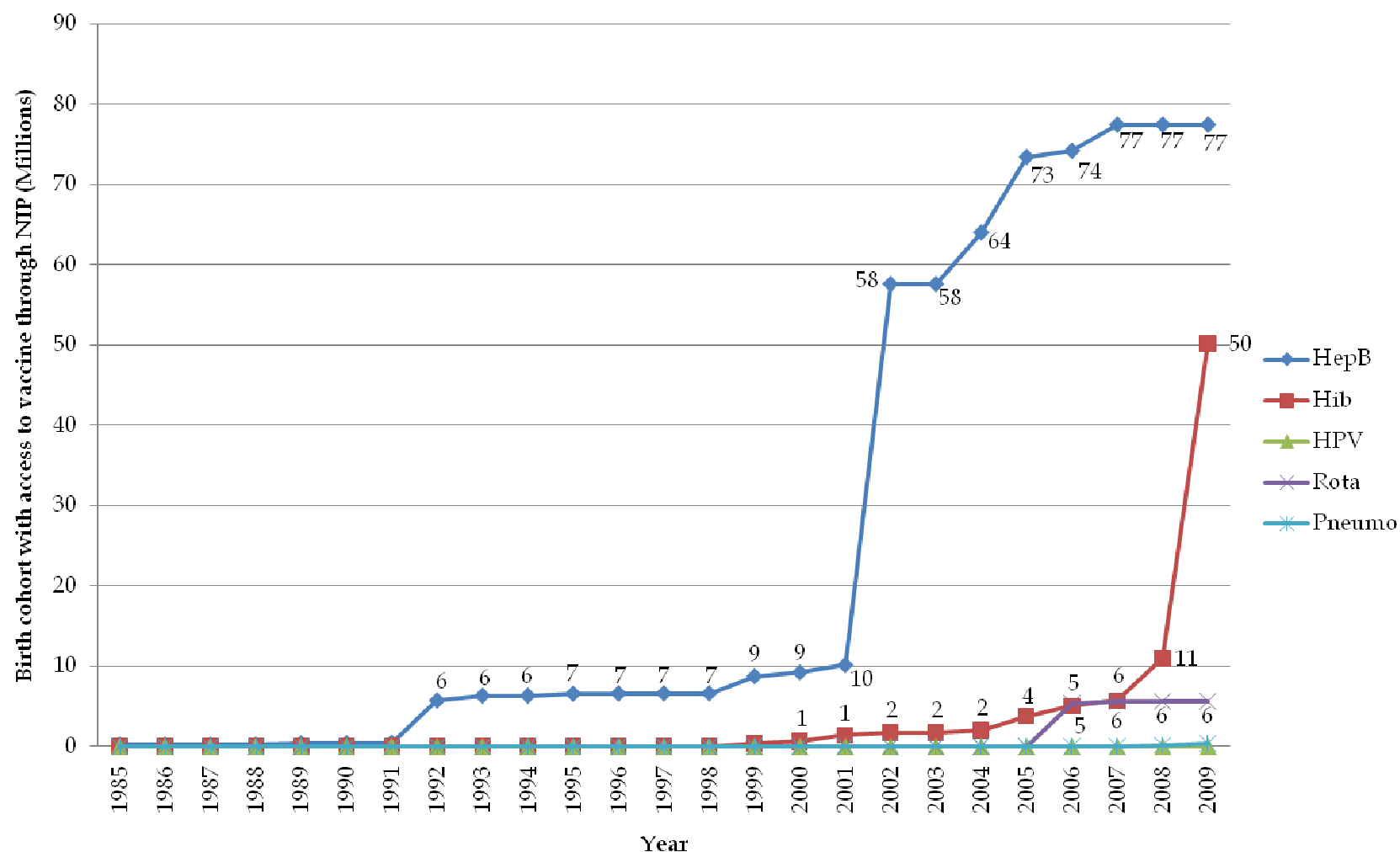
[http://www.who.int/immunization\\_monitoring/burden/Pneumo\\_hib\\_estimates/en/index2.html](http://www.who.int/immunization_monitoring/burden/Pneumo_hib_estimates/en/index2.html).

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# LMIC Birth Cohort Population with Public Access to New Vaccines, 1985-2009



**Table C-4. Progress on Millennium Development Goal (MDG) 4**

Country	Infant Mortality Rate			Under-5 Mortality Rate			MCV Coverage (%)		
	1990	2008	% Change	1990	2008	% Change	1990	2008	% Change
Albania <sup>a</sup>	37	13	65	46	14	70	88	98	10
Angola	154	130	16	260	220	15	38	79	41
Armenia	48	21	56	56	23	59	-	94	-
Azerbaijan	78	32	59	98	36	63	-	66	-
Belize	35	17	51	43	19	56	86	96	10
Bhutan	91	54	41	148	81	45	93	99	6
Bolivia	88	46	48	122	54	56	53	86	33
Cameroon	92	82	11	149	131	12	56	80	24
Cape Verde	49	24	51	63	29	54	79	96	17
China	37	18	51	46	21	54	98	94	-4
Congo, Republic of	-	-	-	-	-	-	38	67	29
Djibouti	95	76	20	123	95	23	85	73	-12
Ecuador	41	21	49	53	25	53	60	66	6
Egypt, Arab Republic	66	20	70	89	23	74	86	92	6
El Salvador	48	16	67	62	18	71	98	95	-3
Georgia	41	26	37	47	30	36	-	96	-
Guatemala	58	29	50	77	34	56	68	96	28
Guyana	64	46	28	87	61	30	73	95	22
Honduras	43	26	40	55	31	44	90	95	5
India	83	52	37	116	69	41	56	70	14
Indonesia	56	31	45	86	41	52	58	83	25
Iraq	42	36	14	53	45	15	75	69	-6
Jordan	31	17	45	38	20	47	87	95	8
Kiribati	65	38	42	89	48	46	75	72	-3
Kosovo	-	-	-	-	-	-	-	-	-
Lesotho	80	63	21	101	79	22	80	85	5
Maldives	79	24	70	111	28	75	96	97	1
Marshall Islands	39	30	23	48	36	25	52	94	42
Mauritania	81	75	7	129	118	9	38	65	27
Micronesia, Federated States of	45	32	29	58	39	33	81	92	11
Moldova	30	15	50	37	17	54	-	94	-
Mongolia	71	33	54	98	41	58	92	97	5
Morocco	68	32	53	88	36	59	79	96	17
Nicaragua	51	23	55	67	27	60	82	99	17
Nigeria	120	96	20	230	186	19	54	62	8
Pakistan	101	72	29	130	89	32	50	85	35

Country	Infant Mortality Rate			Under-5 Mortality Rate			MCV Coverage (%)		
	1990	2008	% Change	1990	2008	% Change	1990	2008	% Change
Panama	24	19	21	30	23	23	73	85	12
Papua New Guinea	67	53	21	91	69	24	67	54	-13
Paraguay	34	24	29	42	28	33	69	77	8
Philippines	42	26	38	61	32	48	85	92	7
Samoa	40	22	45	50	26	48	89	45	-44
São Tomé and Príncipe	65	64	2	101	97	4	71	93	22
Senegal	72	57	21	149	108	28	51	77	26
South Africa	44	48	-9	56	67	-20	79	62	-17
Sri Lanka	23	13	43	29	17	41	80	98	18
Sudan	78	70	10	124	109	12	57	79	22
Swaziland	62	59	5	84	83	1	85	95	10
Syrian Arab Republic	30	14	53	37	16	57	87	81	-6
Thailand	26	13	50	32	14	56	80	98	18
Timor-Leste	138	75	46	184	93	49		73	-
Tonga	19	17	11	22	19	14	86	99	13
Tunisia	40	18	55	50	21	58	93	98	5
Turkey	69	20	71	84	22	74	78	97	19
Turkmenistan	81	43	47	99	48	52	-	99	-
Ukraine	18	14	22	21	15	29	-	94	-
Uzbekistan	61	34	44	74	38	49	-	98	-
Vanuatu	23	27	-17	27	33	-22	66	65	-1
Vietnam	39	12	69	56	14	75	88	92	4
Yemen, Republic of	90	53	41	127	69	46	69	62	-7
Zambia	105	92	12	172	148	14	90	85	-5
LMICs Weighted Average <sup>b</sup>	61	37	43	87	51	46	73	83	8
LMICs (except China and India) Weighted Average <sup>b</sup>	68	44	39	102	65	43	62	84	15
LMICs in case studies (except China) Weighted Average <sup>b</sup>	50	25	49	72	31	56	72	88	15
UMICs in case studies Weighted Average <sup>b</sup>	58	30	39	71	39	37	78	84	5

<sup>a</sup> Albania transitioned from LMIC status to UMIC status during the study.

<sup>b</sup> Averages weighted by 2008 population

Source:

World Health Organization. Global Health Observatory [Internet]. Geneva (Switzerland): WHO; c2009 [cited Sep 2 2010]. Available from <http://apps.who.int/ghodata/>

## Annex D. Quantitative Analysis

One component of data collection for the study is the quantitative analysis of several factors hypothesized to have an impact on the rate of new vaccine adoption among lower-middle-income countries (LMICs).

The Hib Initiative published a similar study in 2010<sup>1</sup> on factors affecting the rate of *Haemophilus influenzae* type B (Hib) adoption among countries. The main results reported statistical significance in their model for the following factors, all of which were positively associated with faster adoption rates among countries: (1) GAVI eligibility, (2) Having one or more neighbor countries that have adopted, and (3) lower vaccine price. Additionally, the Democracy score (from Polity IV Project), which was positively associated, and GAVI Co-financing Uncertainty (2004–06), which was negatively associated, were also statistically significant. Comparing other regions to Organization for Economic Cooperation and Development (OECD) countries (high income), both the Other European & Central Asian region and the East Asia & Pacific region, were statistically significantly associated with slower adoption.

### Methods

We used data for 142 countries classified by the World Bank as low income, lower middle income, or upper middle income<sup>2</sup> to examine how many years it took from 1990 (the year the first middle-income countries adopted Hepatitis B vaccine policies) until the countries made a policy decision to adopt (1) a Hepatitis B (Hep B) vaccine and (2) an Hib vaccine. The object was to determine the main factors associated with the speed of these two adoptions, as these may also play a role in further adoption of newer vaccines.

### Model

In order to analyze a time-dependent outcome, we use survival analysis to compare the rates of adoption and to understand which factors are important in determining whether countries are likely to adopt. First we graphed the Kaplan-Meier (K-M) curves, or survival functions, which are step-wise graphs that show the percentage of countries that had not adopted the policy as of the beginning of each year. To compute the survival analysis model, we divided the time period for each country into calendar-year intervals. During each calendar year, we looked at the countries that had not adopted the vaccine as of January 1 of that year. During the year, some countries adopted, and others did not. The survival model estimates the probability of adoption during each year given the country's situation as described by the variables in the model. This provides results similar to multivariate regression by testing which variables are significantly associated with adoption when other variables are taken into consideration. We used Cox regression to estimate the adoption probabilities.

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<sup>1</sup> Shearer JC, Stack ML, Richmond MR, Bear AP, Hajjeh RA, Bishai DM. Accelerating policy decisions to adopt *Haemophilus Influenzae* type B vaccine: a global, multivariable analysis. *PLoS Medicine*. 2010;7(3).

<sup>2</sup> World Bank Country Classification. <http://data.worldbank.org/about/country-classifications>. Kosovo was excluded as there were no available data.

In our first model, the dependent variable is the number of years from 1990<sup>3</sup> until the year of adoption of Hep B vaccine by each of the 142 countries, up to and including 2008. In the tables, the model coefficients are expressed as hazard ratios. A second model measures the time to adoption of Hib during the same time interval. For each model, we conducted the analysis first for all countries—upper-middle-income countries (UMICs), lower-middle-income countries (LMICs), and low-income countries (LICs)—and then conducted it with only the UMICs and LMICs (excluding LICs), for a total of 4 analyses.

In our models, we calculated a hazard ratio, which is the ratio of the number of countries that adopt during an interval (year) to the number of countries that have not yet adopted that entered that same time interval. Once a country adopts, it is censored and not considered in subsequent time periods.

The analyses then fit the models and determined the effect (coefficient) of each independent variable. The hazard ratio in our regression analysis is similar to an odds ratio: It describes the odds that a country will adopt in each subsequent time interval, given the particular values it has for each of the independent variables. From the models, we got hazard ratio estimates for each particular independent variable (controlling for the others), which is the increased ( $> 1.0$ ) or reduced ( $< 1.0$ ) odds of adopting the vaccine per unit change of the independent variable (e.g., for coverage, it is per 1 percentage point increase) in any time interval.

We conducted log-rank tests of significance to determine statistical differences<sup>4</sup> in the survival functions (K-M curves). We also conducted Wald tests of significance for our estimates, along with confidence intervals. As we hypothesized that particular factors will either help or hinder countries in deciding to adopt a vaccine, we conducted one-tailed level .05 tests.<sup>5</sup> We used Stata to conduct the regression, statistical tests, and got outputs for the K-M curves.

## Independent Variables

We considered 12 independent variables (items for which data were easily available and that we hypothesized might affect decision making on Hep B and Hib adoption). We explain the independent variables below and show them in Table D-1.

### *Economic Factors*

#### **1. GNI per Capita (in US\$1,000)**

We hypothesize that countries in higher income (GNI) per capita have more resources that permit them to adopt new vaccines sooner. GNI per capita is a continuous variable that changes from year to year. Data are provided from the World Bank for nearly every observation in the study. If data for a given year were missing, we interpolated a value based on the previous and following years.

#### **2. Income Group**

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<sup>3</sup> The first recombinant vaccines were licensed a few years earlier, but none of the countries in our study had adopted Hep B or Hib before 1990.

<sup>4</sup> When an estimate is found to be significant, this indicates that the variation in the dependent variable (time from availability to adoption) is related to the independent variable in a way that differs statistically from a random relationship

<sup>5</sup> We only test whether variables are significantly associated in the direction of our hypotheses (faster adoption), not if they are associated with slower adoption.

Another formulation of the hypothesized relationship between income and new vaccine is the World Bank groupings according to per capita GNI. This is a categorical variable—binary in the analyses that exclude LICs—using the following 3 World Bank (WB) categories, which are defined by levels of GNI per capita (US\$, Atlas method) for fiscal year (FY) 2008 data:

- a) LICs                               <= \$975
- b) LMICs                         \$976–\$3,855
- c) UMICs                         \$3,856–\$11,905

We used this variable because the overall study focuses on groups of countries defined by one of these broad income categories. In keeping with this focus on groups, we did not allow this variable to change over time: all countries were assigned to a group, according to their 2008 status, and remained there for the entire study period. (The previous variable looks at the effect of income changes over time.) We used LICs as the comparison group for the analyses that include all 3 categories.

### 3. Government Health Spending per Capita (US\$)

We hypothesize that countries that have higher spending on health will also be likely to introduce new vaccines sooner. This is a continuous time-varying variable, and the data come from WHO and are available for 1995–2006 for all countries, with the following exceptions: (1) No data were provided for American Samoa, Mayotte, and West Bank/Gaza, so they were entirely excluded from this analysis. If data for a given year were missing, we interpolated a value based on the previous and following years.

### 4. Government Immunization Spending per Capita (US\$)

We hypothesize that countries with higher government spending for immunization services will be adopting new vaccines sooner. What *immunization spending* means may vary for each country, as immunization service budgets are decentralized in many places. The data come from WHO and are available for 2006–2007, though 2006 data are missing for 53 countries and 2007 data are missing for 33 countries. Although actual spending varied from year to year, we had essentially no information about its changes. Therefore, we assigned each country a constant level of spending, based on the average of the one or two observed values. Countries were excluded from the analysis if no data were available for either year.

### 5. Budget Line Item for Immunization

We hypothesize that countries with a dedicated line item in their budgets for immunization have a higher commitment and will be more likely to adopt new vaccines. This is a binary variable (yes/no), comes from WHO, and is available for the years 1998–2007 for all countries.<sup>6</sup> If data for a given year were missing, we extended the earliest known value backward and the latest known value forward to complete the data.

## Programmatic/Evidence-Based Factors

### 1. DTP3 Coverage Rate

We hypothesize that countries with stronger immunization programs add new vaccines sooner. The percent of children receiving 3 doses of DTP vaccine (DTP3) is often used as a

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<sup>6</sup> No data were provided for American Samoa, Mayotte, and West Bank/Gaza, so they were entirely excluded from this analysis.

proxy or indicator for program strength. This is a continuous time-varying variable with coverage rates provided for every year of the study, except 2008, for all countries.<sup>7</sup> If data for a given year were missing, we interpolated a value based on the logit of previous and following years' values.

## **2. Quality of Disease Burden Evidence**

We hypothesize that countries that have studies or that have a good knowledge of their disease burden will be more likely to adopt the new vaccines.

We classify as having Good Evidence those countries that WHO considers being at the highest levels, where:

“death registration data, complete or incomplete, containing usable information on causes of death is available for the country, and used to adjust regional YLD distributions for causes with significant case fatality. Partial country-specific information on incidence or prevalence of nonfatal causes available.”

We classify as having Some Evidence those countries that do not meet this WHO standard but that may still have estimates based on:

“other forms of information on child and adult mortality or causes of death (e.g., verbal autopsy) available. Country-specific information on mortality for specific causes available. Partial country-specific information on incidence or prevalence of nonfatal causes available.”

All other countries—those with no evidence of disease burden—are combined in a reference category None. This is a categorical variable with three levels that do not change from year to year in our data. The data come from WHO.

## **3. Burden of Disease Hepatitis B Disability-Adjusted Life Years (DALYs) per 1,000 Total Disease DALYs**

We hypothesize that countries with a higher burden of disease of Hep B, in relation to the country's overall disease burden, to be more likely to introduce vaccination against Hep B. This is a continuous variable and is considered to be the same for all years of the study. The data come from a WHO estimate prepared in 2009 and based on 2004 data.

## **4. Burden of Disease: Meningitis DALYs per 1,000 Total Disease DALYs**

We hypothesize that countries with a higher burden of disease of Hib, in relation to the country's overall disease burden, to be more likely to introduce vaccination against Hep B. Few, if any, of the countries in our study have the data to attribute a burden of disease to Hib. We selected meningitis as the most salient of Hib-related diseases and used the meningitis burden of disease in our analysis of Hib. This is a continuous variable and is considered to be the same for all years of the study. The data come from the same 2009 WHO estimate, based on 2004 data.

### *Social/Contextual Factors*

We hypothesize that countries are influenced by their neighbors or by regional policies of WHO and UNICEF. For this section, regions are defined by the WHO regions in the world: Sub-Saharan Africa (AFRO), Eastern Mediterranean (EMRO), Europe (EURO), Americas (PAHO), Southeast Asia (SEARO), and Western Pacific (WPRO).

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<sup>7</sup> No data were provided for American Samoa, Mayotte, and West Bank/Gaza, so they were entirely excluded from this analysis.

### 1. Region

This is a categorical variable that remains constant for each country for all years. We selected Sub-Saharan Africa as the reference category, as it has the highest proportion of LICs, and we hypothesize that other regions would adopt more quickly. Coefficients in the model tables provide direct comparisons of each other region with Africa. In addition, we tested other pairwise comparisons of other regions and found no significant differences.

### 2. One Neighboring Country Adopts

This is a binary variable that remains constant for each country until a neighboring country adopts the vaccine. It then changes and remains constant for the remaining years.<sup>8</sup>

### 3. Two or More Neighboring Countries Adopt

This variable is the same.

**Table D-1. Variables for Cox Regression**

Variable	LICs	LMICs	UMICs
GNI per Capita (in US\$1,000)	0.27	0.96	3.22
Income Group	42 (29.6%)	54 (38.0%)	46 (32.4%)
DTP3 Coverage Rate	64%	85%	92%
Region			
Sub-Saharan Africa (N=45, 31.7%)	28 (62.2%)	9 (20.0%)	8 (17.8%)
Americas (N=29, 20.4%)	1 (3.4%)	9 (31.0%)	19 (65.5%)
Eastern Mediterranean (N=16, 11.3%)	3 (18.8%)	11 (68.8%)	2 (12.5%)
Europe (N=23, 16.2%)	3 (8.7%)	8 (34.8%)	13 (56.5%)
Southeast Asia (N=11, 7.7%)	4 (36.4%)	7 (63.6%)	0
Western Pacific (N=18, 12.7%)	3 (16.7%)	11 (61.1%)	4 (22.2%)
Government Health Spending per Capita (US\$)	4	25.5	107.5
Government Immunization Spending per Capita (US\$)	0.05	0.18	0.28
Budget Line Item for Immunization	74%	92%	100%
Quality of Disease Burden Data			
Any Evidence	9%	47%	78%
Good Evidence	7%	29%	67%
None			
Hep B DALYs per 1,000 Total Disease DALYs	1.25	0.84	0.39
Meningitis DALYs per 1,000 Total Disease DALYs	9.67	5.54	3.17
One Neighboring Country Adopts (Hep B)	26%	20%	15%
Two or More Neighboring Countries Adopt (Hep B)	12%	49%	72%

<sup>8</sup> Neighboring countries based on

[http://en.wikipedia.org/wiki/List\\_of\\_countries\\_and\\_territories\\_by\\_land\\_and\\_maritime\\_borders](http://en.wikipedia.org/wiki/List_of_countries_and_territories_by_land_and_maritime_borders)



One Neighboring Country Adopts (Hib)	5%	13%	17%
Two or More Neighboring Countries Adopt (Hib)	2%	16%	33%

## Results

LMICs adopted Hep B at a similar rate to UMICs, with 94% and 91%, respectively of each adopting by 2008. However, both adopted about twice as rapidly as LICs, where only 80% had adopted by 2008. (See Figure D-1.) The difference was statistically significant.<sup>9</sup> We see that the difference in adoption rates was primarily due to the difference before 2000–2001, when GAVI started helping LICs.

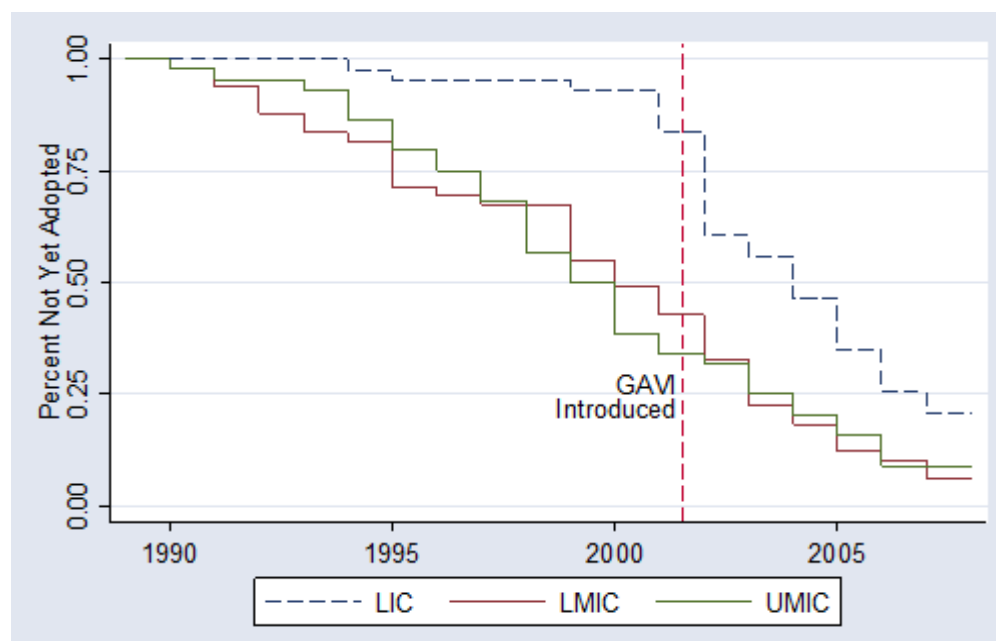
For Hib, we see that UMICs adopted at a faster rate (80% by 2008) than both LMICs (50%) and LICs (60%), which were comparable<sup>10</sup> (Figure D-2).

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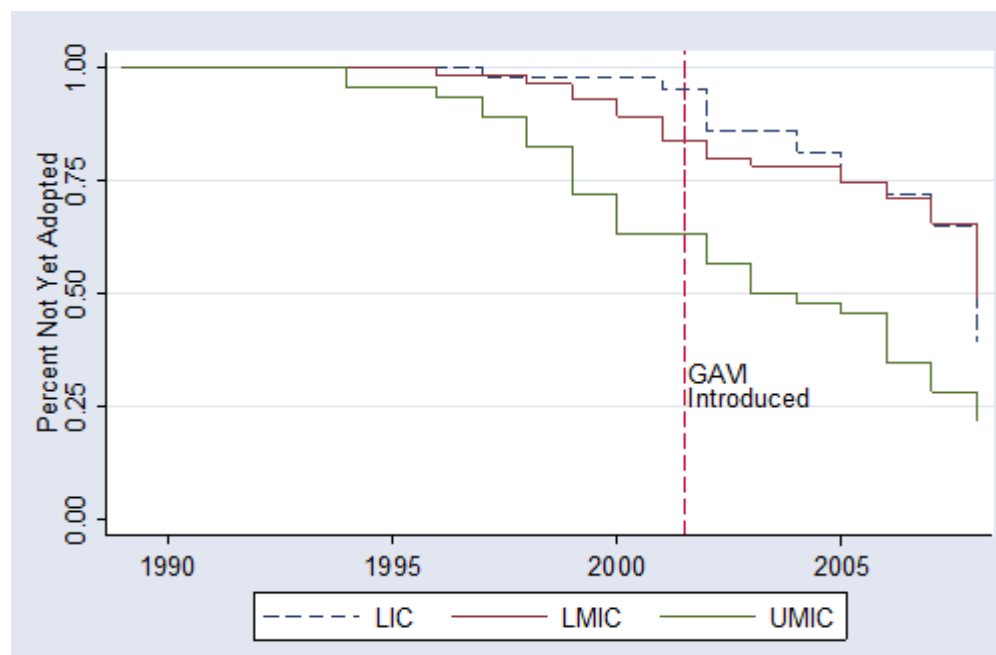
<sup>9</sup> Log-rank test for equality of survivor functions, chi square = 15.50 with 2 degrees of freedom, p = .0004

<sup>10</sup> Log-rank test for equality of survivor functions, chi square = 17.37 with 2 degrees of freedom, p = .0002

**Figure D-1. Kaplan-Meier Curves for Hepatitis B Vaccine Adoption by Income Group**



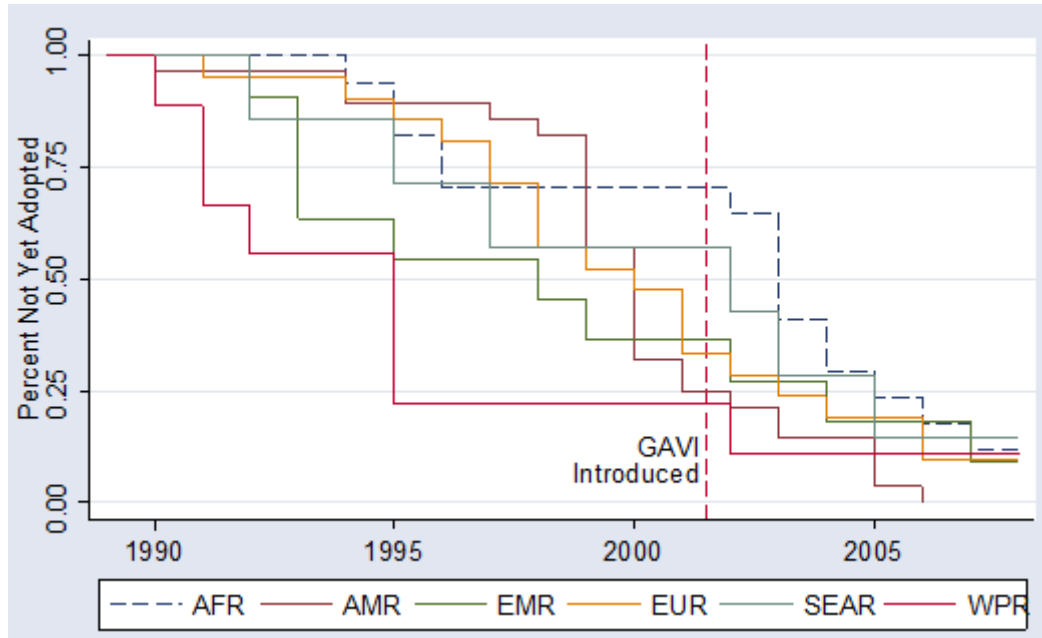
**Figure D-2. Kaplan-Meier Curves for Hib Adoption by Income Group**



Looking at regions, we see faster adoption for Hep B in the Americas (100%, by 2006), Europe (57%), and the Western Pacific (73%) than in other regions (Figure D-3). There is a statistically significant difference

within this category when considering the differences in adoption among all regions;<sup>11</sup> however, as previously mentioned, there were no significant differences in pairwise comparisons between any 2 regions.

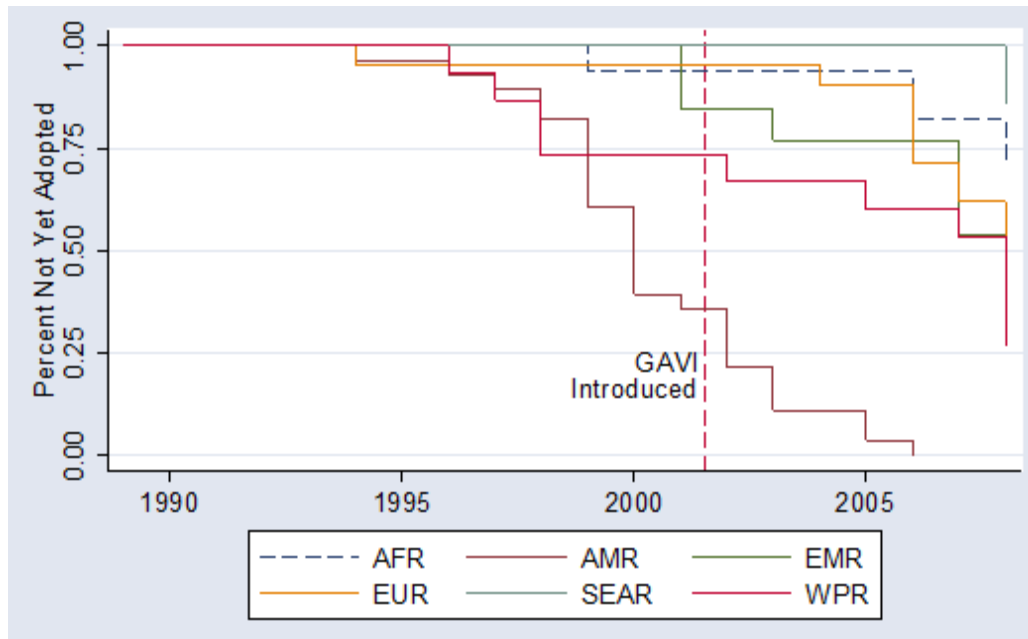
**Figure D-3. Kaplan-Meier Curves for Hepatitis B Vaccine Adoption by Region**



<sup>11</sup> Log-rank test for equality of survivor functions, chi square = 14.27 with 5 degrees of freedom,  $p = .014$

For Hib adoption, the Americas (100%, by 2006) were much faster than the other regions, with Southeast Asia (14%) being the slowest (Figure D-4). Again, a statistically significant difference exists within this category when considering the differences in adoption among all regions; however, there were no significant differences in pairwise comparisons between any 2 regions.<sup>12</sup>

**Figure D-4. Kaplan-Meier Curves for Hib Adoption by Region**



Results of the two regression analyses for the Hep B model are found in Tables D-2 and D-3. Tables D-4 and D-5 show the results for the 2 regression analyses for the Hib model. There was no consistent finding across all 4 analyses to explain the correlations with faster adoption among countries.

The following are the 3 consistent results across multiple analyses:

- 1) Having *neighboring countries adopt* Hep B was a significant predictor for faster Hep B adoption
  - a) In the LICs/LMICs/UMICs analysis, having 1 Neighbor adopt increased the odds of a decision in that year by a factor of 1.87, or 87% ( $p < 0.04$ , 95% CI 1.03–3.37), and having 2 or More Neighbors adopt increased the odds by a factor of 2.62 ( $p < 0.00$ , 95% CI 1.54–4.46).
  - b) In the LMICs/UMICs analysis, having 2 or More Neighbors adopt increased the odds by a factor of 1.91 ( $p < 0.04$ , 95% CI 1.04–3.50).
- 2) Having higher *DTP3 coverage* (proxy for program strength) was a predictor of faster adoption for Hep B and Hib in the LICs/LMICs/UMICs analysis (but not in the LMICs/UMICs analysis).
  - a) Hep B: Each percentage point increase in DTP3 increased the odds of adoption for that year by a factor of 1.03 ( $p < 0.00$ , 95% CI 1.01–1.04); so, for a 10 percentage point increase, the factor would be  $(1.03)^{10} = 1.34$ .

<sup>12</sup> Log-rank test for equality of survivor functions, chi square = 82.76 with 1 degree of freedom,  $p < .0001$

- b) Hib: Each percentage point increase in DTP3 increased the odds of adoption for that year by a factor of 1.02 ( $p < 0.04$ , 95% CI 1.00–1.04).
- 3) Being in *PAHO*, compared with *AFRO*, was a reflection of faster adoption for Hib.
  - a) In the LICs/LMICs/UMICs analysis, being in *PAHO* increased the odds of adoption by a factor of 4.84 ( $p < 0.00$ , 95% CI 2.42–9.68).
  - b) In the LMICs/UMICs analysis, being in *PAHO* increased the odds of adoption by a factor of 19.46 ( $p < 0.00$ , 95% CI 6.56–57.77).

Other statistically significant results associated with more rapid adoption found in only 1 of the 4 analyses are as follows:

- 1) In the Hep B analysis for LICs/LMICs/UMICs, for every increase in *US\$1,000 GNI per capita*, there was an increase in the odds of adoption by a factor of 1.51 ( $p < 0.04$ , 95% CI 1.08–2.10).
- 2) In the Hep B analysis for LMICs/UMICs:
  - a) *Having a Line Item for Immunization* increased the odds of adoption by a factor of 2.15 ( $p < 0.09$ , 95% CI 1.03–4.47).
  - b) Compared with *AFRO*, being in *WPRO* increased the odds of adoption by a factor of 4.95 ( $p < 0.02$ , 95% CI 1.66–14.76).
- 3) In the Hib analysis for LMICs/UMICs:
  - c) Compared with *AFRO*, being in *EMRO* increased the odds of adoption by a factor of 4.32 ( $p < 0.02$ , 95% CI 1.50–12.44).
  - d) Compared with *AFRO*, being in *WPRO* increased the odds of adoption by a factor of 6.11 ( $p < 0.00$ , 95% CI 2.29–16.31).

## Discussion

Consistent with our hypotheses, adoption time of Hep B and Hib was associated with certain programmatic and social/contextual factors. Specifically, having neighbors who had already adopted Hep B was associated with an increased rate of Hep B adoption, a stronger immunization program (represented by an increase in DTP3) was associated with an increased rate of adoption for both Hep B and Hib in our analyses of all countries, and being in *PAHO* was associated with a faster rate of adopting Hib.

Unfortunately, none of these results were found in all 4 analyses. Having neighbors who had adopted Hib was not associated with more rapid adoption by countries as it was with Hep B. When we excluded LICs and only looked at the middle-income countries (LMICs and UMICs), there was no association between a stronger immunization program and faster adoption rates, indicating that other variables explained more of the difference between these countries. And although being in *PAHO* was associated with much quicker adoption rates for Hib, there was no such association for Hep B.

A few of the factors explaining this might include changing policies of *PAHO* from when Hep B was being introduced compared with later, when countries adopted Hib vaccine; differing perceptions of the 2

vaccines based on different needs and epidemiology of the targeted diseases within countries and regions; or greater global and regional assistance being available since Hib became widely available in comparison to when Hep B became widely available earlier.

It is important to remember that these results are explanatory, not predictive. They measure the odds that faster adoption of Hep B or Hib was associated with certain factors. They will not necessarily be prescriptive for factors that will be associated with newer vaccine adoption.

Limitations of the study include limited power in detecting associations due to the relatively small data, especially when LICs are excluded, as compared with the number of variables in our models. Additionally, there may be some interaction or collinearity between variables that might change the hazard ratios or affect the outcomes. Including interaction terms would reduce the power of the model further, and the usefulness, or even applicability, of testing for collinearity in survival analysis is debated. Finally, there are missing data for a number of variables, and for some variables we chose only 1 year of data to represent all 18 years of the study, so the model does not fully represent the situation.

**Table D-2. Cox Regression Results of Hepatitis B Vaccine Adoption in LICs, LMICs, and UMICs**

Variable	Haz.	Std. Err.	z	P>z	90% Conf. Interval	
GNI per Capita (in US\$1,000)	1.51	0.30	2.04	0.02	1.08	2.10
Income Group (compared to LICs)						
LMICs	1.28	0.41	0.76	0.23	0.75	2.16
UMICs	0.50	0.24	-1.47	0.07	0.23	1.09
DTP3 Coverage Rate	1.03	0.01	3.29	0.00	1.01	1.04
Region (compared to Sub-Saharan Africa)						
Americas	0.34	0.17	-2.12	0.02	0.15	0.79
Eastern Mediterranean	1.37	0.68	0.64	0.26	0.61	3.10
Europe	0.45	0.26	-1.40	0.08	0.17	1.15
Southeast Asia	0.44	0.23	-1.59	0.06	0.19	1.03
Western Pacific	1.20	0.53	0.41	0.35	0.58	2.48
Government Health Spending per Capita	1.00	0.00	-0.73	0.23	0.99	1.00
Government Immunization Spending per Capita	1.09	0.18	0.51	0.31	0.83	1.42
Budget Line Item for Immunization	1.68	0.53	1.64	0.05	1.00	2.82
Quality of Disease Burden (compared to None)						
Good Evidence	1.26	0.59	0.49	0.31	0.58	2.73
Some Evidence	1.95	0.89	1.45	0.08	0.91	4.15
Hep B DALYs per 1,000 Total Disease	1.07	0.09	0.81	0.21	0.93	1.24
1 Neighboring Country Adopts	1.87	0.67	1.74	0.04	1.03	3.37
2 or More Neighboring Countries Adopt	2.62	0.85	2.97	0.00	1.54	4.46

**Table D-3. Cox Regression Results of Hepatitis B Vaccine Adoption in LMICs and UMICs**

Variable	Haz.	Std. Err.	z	P > z	90% Conf. Interval	
GNI per Capita (in US\$1,000)	1.29	0.24	1.33	0.09	0.94	1.76
DTP3 Coverage Rate	1.02	0.01	1.57	0.06	1.00	1.03
Region (compared to Sub-Saharan Africa)						
Americas	0.66	0.40	-0.68	0.25	0.24	1.79
Eastern Mediterranean	1.74	0.98	0.99	0.16	0.69	4.38
Europe	0.79	0.52	-0.36	0.36	0.26	2.36
Southeast Asia	0.87	0.55	-0.21	0.42	0.31	2.45
Western Pacific	4.95	3.29	2.41	0.01	1.66	14.76
Government Health Spending per Capita	1.00	0.00	-0.94	0.18	0.99	1.00
Government Immunization Spending per Capita	1.02	0.16	0.11	0.46	0.79	1.31
Budget Line Item for Immunization	2.15	0.96	1.72	0.04	1.03	4.47
Quality of Disease Burden (compared to None)						
Good Evidence	1.52	0.71	0.90	0.19	0.71	3.27
Some Evidence	1.04	0.57	0.07	0.48	0.42	2.56
Hep B DALYs per 1,000 Total Disease	1.13	0.10	1.34	0.09	0.97	1.32

1 Neighboring Country Adopts	1.43	0.57	0.90	0.19	0.74	2.74
2 or More Neighboring Countries Adopt	1.91	0.70	1.76	0.04	1.04	3.50

**Table D-4. Cox Regression Results of Hib Adoption in LICs, LMICs, and UMICs**

Variable	Haz.	Std. Err.	z	P > z	90% Conf. Interval	
GNI per Capita (in US\$1,000)	0.91	0.15	-0.57	0.29	0.70	1.19
Income group (compared to LICs)						
LMICs	0.45	0.17	-2.08	0.02	0.24	0.85
UMICs	0.51	0.28	-1.24	0.11	0.21	1.24
DTP3 Coverage Rate	1.02	0.01	1.85	0.04	1.00	1.04
Region (compared to Sub-Saharan Africa)						
Americas	4.84	2.04	3.74	0.00	2.42	9.68
Eastern Mediterranean	1.60	0.76	0.98	0.17	0.73	3.50
Europe	0.60	0.30	-1.02	0.16	0.27	1.36
Southeast Asia	0.13	0.14	-1.92	0.03	0.02	0.75
Western Pacific	1.24	0.50	0.54	0.30	0.64	2.40
Government Health Spending per Capita	1.01	0.00	1.55	0.06	1.00	1.01
Government Immunization Spending per	1.04	0.16	0.28	0.39	0.81	1.35
Budget Line Item for Immunization	1.40	0.56	0.84	0.20	0.72	2.72
Quality of Disease Burden (compared to						
Good Evidence	0.72	0.27	-0.88	0.19	0.38	1.34
Some Evidence	1.14	0.49	0.32	0.38	0.57	2.31
Meningitis DALYs per 1,000 Total Disease	0.95	0.04	-1.26	0.11	0.89	1.02
1 Neighboring Country Adopts	1.58	0.50	1.45	0.08	0.94	2.66
2 or More Neighboring Countries Adopt	1.44	0.47	1.11	0.14	0.84	2.47

**Table D-5. Cox Regression Results of Hib Adoption in LMICs and UMICs**

Variable	Haz.	Std. Err.	z	P > z	90% Conf.	
GNI per Capita (in US\$1,000)	1.01	0.16	0.06	0.48	0.78	1.32
DTP3 Coverage Rate	1.01	0.01	0.41	0.35	0.98	1.03
Region (compared to Sub-Saharan Africa)						
Americas	19.46	12.87	4.49	0.00	6.56	57.77
Eastern Mediterranean	4.32	2.78	2.27	0.01	1.50	12.44
Europe	2.04	1.36	1.07	0.15	0.68	6.13
Southeast Asia	0.54	0.61	-0.55	0.29	0.08	3.43
Western Pacific	6.11	3.65	3.03	0.00	2.29	16.31
Government Health Spending per Capita	1.01	0.00	1.56	0.06	1.00	1.01
Government Immunization Spending per	0.97	0.15	-0.18	0.43	0.75	1.26
Budget Line Item for Immunization	1.06	0.54	0.12	0.45	0.46	2.46
Quality of Disease Burden (compared to						
Good Evidence	0.70	0.27	-0.93	0.18	0.37	1.31
Some Evidence	0.81	0.39	-0.44	0.33	0.37	1.77
Meningitis DALYs per 1,000 Total Disease	0.92	0.06	-1.29	0.10	0.82	1.02



1 Neighboring Country Adopts	1.52	0.57	1.12	0.13	0.82	2.82
2 or More Neighboring Countries Adopt	1.36	0.52	0.81	0.21	0.73	2.56

## Annex E. Manufacturer Interview Questions

### DCVMN Members

1. Let me begin by asking you to tell me about your company's vaccine business overall and your company's approach to lower-middle-income countries within your overall vaccine business.
2. Now, let me turn to more specific questions. How important are these markets to you currently? How many countries do you sell to? If your company sells primarily to one country, how much [in doses or dollars] of [specify vaccine(s)] does your company sell to that country, and how much does your company sell to other LMICs?
3. If your company sells primarily to one country, please describe your company's strategy for that country. Otherwise, please describe your company's strategy for China, India, and Brazil. What about middle-income markets more broadly?
4. What does your company see as the major lessons from the entry of GAVI into the global vaccine market? How do these lessons apply to the LMICs?
5. Your company sells [specify vaccine(s)]. Is it sold only in private channels, or do you have public business?
6. Do you offer your product in multidose vials for use in public-sector immunization programs? If not, what are some factors that would influence your company's decision to change vaccine presentation or packaging for use in public-sector programs?
7. One issue GAVI encountered was the difficulty of meeting rapidly increased demand for vaccines in LICs. For the vaccines we are interested in (Pneumo, Rota, and HPV), do you think this would be a problem for industry or for your company specifically? By how much would demand need to grow before new capacity was necessary? Would your company be able to scale up production to meet a vastly increased demand for your product if it were to become part of routine public programs in nearly all of the LMICs with a birth cohort of more than 50 million? How fast? Would your company be able to scale up capacity to meet LMIC public-sector demand by 2015? What would need to be in place to justify adding capacity to meet this demand? Would you require outside technical assistance?
8. a) Has your company sought, or would your company be interested in seeking, partnerships with IFPMA members? How interested is your company in pursuing collaboration with IFPMA manufacturers? What kind of collaborations would/do you consider and why? If your company has had collaborations before, what have been the main obstacles encountered? What could IFPMA members do to facilitate such collaborations in the future?  
  
b) In what ways does your company collaborate with other DCVMN members?
9. Pricing is an important question. Has GAVI created an attractive price-volume relationship for industry? Has your company seen a negative impact on private markets? What do you think an appropriate approach to pricing for LMICs might be in the context of significant uptake increases? Do you think that GAVI-like pricing (e.g., an average of less than \$3 per dose for

pentavalent) would work for LMICs from industry's perspective? What is current pricing into the public sector in LMICs like? Can you comment (need not be your company) on pricing of newer vaccine introductions into LMICs?

10. In many instances, vaccines can be sold in private markets in LMICs at prices much higher than public markets, but these private markets are limited to a small share of the population. Can these high-profit private markets be preserved when public programs adopt the vaccine and offer it to all at low or no price? Do you have any examples of this? Do you have suggestions as to how such cannibalization might be avoided?
11. Do you think that IFPMA products are perceived differently than DCVMN products by consumers, purchasers, or providers? Do you notice this in certain markets more than others? Do you have suggestions for what can be done to address this misperception?
12. What is your company's marketing strategy? How much of an emphasis is on marketing within your company? Who does your marketing target? How much contact does your company have with (a) pediatricians and (b) decision makers within the government? In what ways do you work to encourage brand loyalty?
13. What is your company's position concerning pooled procurement arrangements, such as the use of the UNICEF Supply Division, the PAHO Revolving Fund, or other pooling arrangements that might develop? Can you cite specific experiences you have had?
14. Can you give an example of (a) a successful introduction of a newer vaccine in an MIC and (b) an example of an unsuccessful or failed attempt? Can you suggest reasons for the outcome in each case?
15. Is there local or regional marketing staff in your company who we might talk to about specific countries and challenges?
16. How would you complete this sentence: The most successful outcome in 10 years for my company in LMICs would be . . .
17. Would you describe your company's strategy for LMICs as (a) aggressive, (b) interested, (c) see what happens, or (d) something else (specify)?

## **IFPMA Members**

1. Let me begin by asking you to tell me about your company's vaccine business overall and your company's approach to lower-middle-income countries within your overall vaccine business.
2. Now, let me turn to more specific questions. Does your company think about the LMICs as a market, or does it have another way of looking at them? How are you organized to address these markets? Do you have direct representation, or do you have partnerships or use distributors?
3. Please describe your company's strategies for China, India, and Brazil? What about middle-income markets more broadly?

4. What does your company see as the major lessons from the entry of GAVI into the global vaccine market? How do these lessons apply to the LMICs?
5. Your company sells [specify vaccine(s)]. Do you actively market this vaccine in some or all LMICs? Is it sold only in private channels, or do you have public business? How important are these markets to you currently? How much [in doses or dollars] of [specify vaccine(s)] does your company sell to LMICs?
6. Do you offer your product in multidose vials for use in public-sector immunization programs? If not, what are some factors that would influence your company's decision to change vaccine presentation or packaging for use in public-sector programs?
7. One issue GAVI encountered was the difficulty of meeting rapidly increased demand for vaccines in LICs. For the vaccines we are interested in, do you think this would be a problem for industry or for your company specifically? By how much would demand need to grow before new capacity was necessary? Would your company be able to scale up production to meet a vastly increased demand for your product if it were to become part of routine public programs in nearly all of the LMICs with a birth cohort of more than 50 million? How fast? Would your company be able to scale up capacity to meet LMIC public-sector demand by 2015? What would need to be in place to justify adding capacity to meet this demand?
8. Has your company sought, or would your company be interested in seeking, partnerships with manufacturers in LMICs (e.g., India, Brazil) to meet much greater demand? Do you think local partnerships aid the introduction of new vaccines? Do you think local independent producers help create an environment where new vaccines are introduced more easily? How interested is your company in pursuing collaboration with developing country vaccine manufacturers?
9. Pricing is an important question. Has GAVI created an attractive price-volume relationship for industry? Has your company seen a negative impact of GAVI on private markets? What do you think an appropriate approach to pricing for LMICs might be in the context of significant uptake increases? Do you think that GAVI-like pricing (e.g., an average of less than \$3 per dose for pentavalent) would work for LMICs from industry's perspective? What is current pricing into the public sector in LMICs like? Can you comment (need not be your company) on pricing of newer vaccine introductions into LMICs?
10. In many instances, vaccines can be sold in private markets in LMICs at prices that approach those charged in Europe or North America, but these private markets are limited to a small share of the population. Can these profitable private markets be preserved when public programs adopt the vaccine and offer it to all at low or no price? Do you have any examples of this? Do you have suggestions as to how such cannibalization might be avoided?
11. What is your company's position concerning pooled procurement arrangements, such as the use of the UNICEF Supply Division, the PAHO Revolving Fund, or other pooling arrangements that might develop? Can you cite specific experiences you have had?

12. Can you give an example of (a) a successful introduction of a newer vaccine in an MIC and (b) an example of an unsuccessful or failed attempt? Can you suggest reasons for the outcome in each case?
13. Is there local or regional marketing staff in your company who we might talk to about specific countries and challenges?
14. How would you complete this sentence: The most successful outcome in 10 years for my company in LMICs would be . . .
15. Would you describe your company's strategy for LMICs as (a) aggressive, (b) interested, (c) see what happens, or (d) something else (specify)?

## Appendix 1. Types of Economic Evaluation for Vaccine Introduction

There are generally 3 types of cost studies conducted to evaluate whether a vaccine is a good public health deal, or “cost effective.”

Study Type	Outcome Measure	Requirement
Cost-Effectiveness (CEA)	Cost-effectiveness ratio: Cost per death/Case	Define outcome of interest
Cost-Benefit (CBA)	Cost-benefit ratio: Net present value of costs/Net present value of benefits	Assign cost value to outcome(s) of interest; choose discount rate to use to convert future costs and benefits to present terms
Cost-Utility (CUA)	Cost-utility ratio: Cost per DALY/QALY	Assign QALY/DALY to outcome(s) of interest; choose discount rate

Cost-effectiveness studies are the least data intensive. They require only cost data on the intervention (immunization), basic incidence, or mortality impact data. CEA results show the cost per case or death averted by the intervention and can be compared to costs of alternative ways of preventing cases or deaths to assist in decision making.

Cost-benefit studies assign a value (benefit) to mortality and morbidity cases averted. This usually is the cost of treatment of the illness that is avoided by its prevention. The results tell Ministries of Health how the costs of the intervention compare to the costs saved by it. When the intervention and its benefits (treatment of cases averted) occur at very different times (e.g., for Hep B and HPV vaccines, where the cancers averted are far into the future), the costs and benefits must be “discounted” to present-value terms. Some CBA includes both indirect and direct costs. Cost-utility studies allow the comparison of all health interventions in common terms by comparing their costs to averted disability-affected life years (DALYs) or quality-adjusted life years (QALYs) that put morbidity and mortality gains into a common measure. When the intervention’s health impact is in the distant future, discounting must be done to put the impacts into present terms in CEA.

### Costs

- Direct Costs:
  - Medical—Costs for medical treatment (hospitalization, outpatient visit, medication) and vaccines and additional program costs
  - Nonmedical—Other costs incurred from the disease, such as transportation to clinic
- Indirect Costs: Productivity lost because of time away from work or other activities

At a minimum, studies must use direct medical costs and must usually try to estimate all direct costs. Studies that also include indirect costs are said to be conducted from a social perspective.

### Other Considerations

- Time Frame: How many years into the future (analytic horizon) will benefits and costs be calculated?
- Discount Rate: A figure used to adjust benefits occurring in the distant future to equivalent values in the present
- Sensitivity Analysis: Regardless of how many variables in economic analyses are estimated, it is important to see how reasonable variations in them can affect the outcome.