SECOND GAVI EVALUATION
GAVI ALLIANCE

13 September 2010
SG2 EVALUATION REPORT

Prepared by:

Applied Strategies
In association with:

CEPA LLP
## Acronyms and Abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>Auto Disable</td>
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<tr>
<td>ADIP</td>
<td>Accelerated Development and Introduction Plan</td>
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<tr>
<td>AFRO</td>
<td>Regional Office for Africa</td>
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<td>AMC</td>
<td>Advance Market Commitments</td>
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<td>AMRO</td>
<td>Regional Office for the Americas</td>
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<td>APR</td>
<td>Annual Progress Report</td>
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<td>AVI</td>
<td>Accelerated Vaccine Introduction</td>
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<td>CAGR</td>
<td>Compound Annual Growth Rate</td>
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<td>CDC</td>
<td>Center for Disease Control and Prevention</td>
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<td>CEPA</td>
<td>Cambridge Economic Policy Associates</td>
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<td>CFPR</td>
<td>Co-Financing Policy Revision</td>
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<td>CGD</td>
<td>Center for Global Development</td>
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<td>cMYP</td>
<td>Comprehensive Multi-Year Plan</td>
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<td>CAR</td>
<td>Central African Republic</td>
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<td>CRS</td>
<td>Creditor Reporting System</td>
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<td>CSO</td>
<td>Civil Society Organisation</td>
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<td>CTT</td>
<td>Co-financing Task Team</td>
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<td>DAC</td>
<td>Development Assistance Committee</td>
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<td>DAH</td>
<td>Development Assistance for Health</td>
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<tr>
<td>DTaP</td>
<td>Diphtheria Tetanus and acellular Pertussis</td>
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<td>DTP</td>
<td>Diphtheria Tetanus Pertussis</td>
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<tr>
<td>DTwP</td>
<td>Diphtheria Tetanus and whole-cell Pertussis</td>
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<tr>
<td>DFID</td>
<td>UK Department For International Development</td>
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<tr>
<td>EC</td>
<td>European Commission</td>
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<td>EMRO</td>
<td>Regional Office for the Eastern Mediterranean</td>
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<td>EPI</td>
<td>Expanded Program on Immunisation</td>
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<td>EURO</td>
<td>Regional Office for Europe</td>
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<tr>
<td>FSP</td>
<td>Financial Sustainability Plan</td>
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<td>FTF</td>
<td>Financing Task Force</td>
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<td>GAVI</td>
<td>Global Alliance for Vaccines and Immunisation</td>
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<td>GDP</td>
<td>Gross Domestic Product</td>
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<td>GFA</td>
<td>GAVI Fund Affiliate</td>
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<td>GFATM</td>
<td>Global Fund to Fight AIDS, Tuberculosis and Malaria</td>
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<td>GHP</td>
<td>Global Health Partnership</td>
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<td>GNI</td>
<td>Gross National Income</td>
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<td>GPEI</td>
<td>Global Polio Eradication Initiative</td>
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<td>HSS</td>
<td>Health System Strengthening</td>
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<td>IDA</td>
<td>International Development Association</td>
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<td>IF</td>
<td>Immunisation Funding (database)</td>
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<td>IF&amp;S</td>
<td>Immunisation Financing and Sustainability</td>
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<td>IFF</td>
<td>International Finance Facility</td>
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<td>IFFIm</td>
<td>International Finance Facility for Immunisation</td>
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<td>IHME</td>
<td>Institute of Health Metrics and Evaluation</td>
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SUMMARY AND CONCLUSIONS

1. Evaluation questions for SG2

The GAVI Alliance’s second strategic goal is to ‘Accelerate the uptake and use of underused and new vaccines and associated technologies and improve vaccine supply stability.’ The evaluation questions are:

- SG2.1: To what extent has GAVI accelerated the uptake of underused and new vaccines by partner countries?
- SG2.2: To what extent have countries introducing underused and new vaccines been able to take them to scale quickly, i.e. achieve full-scale coverage?
- SG2.3: To what extent has GAVI improved the stability of global and country level vaccine supply?
- SG2.4: To what extent has GAVI made vaccines and related technologies more affordable?
- SG2.5: To what extent has GAVI contributed to the advancement of the evidence base required for countries to address the policy decision related to the introduction of new vaccines?
- SG2.6: To what extent has GAVI developed and used vaccine demand forecasts that are accurate and timely?

2. Vaccine uptake (SG2.1)

GAVI has added value by accelerating the introduction of underused vaccines and the rate of country introduction has increased post-GAVI. GAVI’s impact on accelerating vaccine uptake for YF and HepB- and Hib-containing vaccines was also supported by the counterfactual analysis that showed earlier country adoption occurred sooner than would have been expected based on pre-GAVI introduction rates.

For pneumococcal vaccines, it is too soon to tell whether GAVI has accelerated introduction, however, the evidence strongly suggests GAVI has accelerated the demand based on 21 GAVI application approvals with 2 country introductions and 19 countries awaiting introduction. It is unclear whether actual introduction will be as fast as projected given the challenges associated with GAVI’s current funding gap and the potential impact of country graduation on pneumococcal introduction.

It is also too soon to tell if GAVI has accelerated rotavirus vaccine introduction. To date, there have been four country introductions, but only six additional countries have approved applications. Current GAVI introduction projections, based on application status, indicate rotavirus could introduce more slowly than pneumococcal, HepB-, and Hib-containing vaccines.
3. **Scaling up vaccine coverage (SG2.2)**

GAVI’s reliance on countries to quickly take vaccine programs to scale has been effective. The analyses showed most GAVI-eligible countries have effective immunisation systems in place. For both HepB- and Hib-containing vaccines, the results of this analysis indicate that ≥ 80 percent of GAVI-eligible countries reached peak coverage within two years of vaccine introduction.

The analysis also showed that median time to peak coverage rate was longer for vaccine additions (2 years for HepB and Hib monovalent vaccines and 3 years for YF vaccines) compared to vaccine switches (1 year).

Because GAVI’s current model is to provide countries with the financial and technical support to prepare for and introduce a vaccine and then rely on countries to take the vaccine programmes to scale, GAVI was not expected to accelerate time to peak coverage. Therefore, GAVI's current model of providing countries with the financial and technical support to prepare for and introduce a vaccine appears to be effective.

4. **Vaccine supply stability (SG2.3)**

For this evaluation, supply stability was defined as having sufficient supply to meet demand, over time, with more than one supplier.

GAVI has added value by improving supply stability for underused vaccines by creating a more stable market that attracted additional prequalified suppliers. This has improved supply stability for YF and pentavalent vaccines and has resulted in supply stability for HepB mono- and tetravalent vaccines.

Although YF supply stability was improved from 2004-08, there was limited supply in 2009 and UNICEF projects continued supply instability for 2010-12.

GAVI achieved supply stability for HepB mono- and tetravalent vaccines, however, demand for these vaccines is minimal due to the shift to pentavalent vaccines.

For pentavalent vaccines, GAVI has improved supply stability by attracting more prequalified suppliers, but supply has remained ‘limited’ through 2009. UNICEF predicts excess supply from 2010-2012.

For pneumococcal vaccines, GAVI has added value by securing two 10-year commitments for 30m doses per year from both GSK and Pfizer beginning in 2012 and 2013, respectively. In addition, GAVI has secured approximately 50m doses total from these suppliers for use in the 2010-12 timeframe, which is predicted to be sufficient to meet 2010-11 demand. Supply beyond these initial commitments is still uncertain given AMC supply tenders are issued on an annual basis.

GAVI has not yet secured any supply commitments for rotavirus vaccine.
5. Vaccine affordability (SG2.4)

GAVI defines affordability as a vaccine “price that countries can eventually finance in a sustainable manner.”\(^1\)

GAVI has not improved the affordability of YF vaccines. GAVI did attract three additional YF vaccine suppliers to the market by 2009, but YF vaccine prices increased 12-19% over the 2004–10 timeframe and by greater than 40-50% over 2002 non-GAVI UNICEF prices.

GAVI has probably improved the affordability of Hep B-containing vaccines. GAVI also attracted four additional HepB monovalent and four additional HepB tetravalent vaccine suppliers to the market by 2009. HepB monovalent vaccine prices for all presentations and HepB tetravalent vaccine prices for the 10 dose presentation declined by 32-56% and by 37% respectively between 2001–09 (2004–09 for the 10 dose HepB monovalent vaccine). Ordinarily it might be reasonable to conclude that the additional suppliers attracted by GAVI would have contributed to the observed price reductions. However, the entry of the new suppliers also coincided with a significant decline in demand for these vaccines as GAVI-eligible countries adopted or transitioned to the pentavalent vaccine. Therefore, it is difficult to attribute these price declines to GAVI actions.

GAVI has not improved the affordability of pentavalent vaccines through 2009, although prices have started to decline in 2010. GAVI attracted three additional pentavalent vaccine suppliers to the market between 2004–09. The price of the liquid/lyophilized formulation did not decline through 2009, however, a 16% decrease did occur in 2010. This decline was likely driven by the need to protect supplier share due to the increased demand for the liquid formulation. Additional price reductions are expected now that the second liquid/lyophilized product has been prequalified (May2010).

The liquid pentavalent vaccine formulation, introduced in 2007, declined in price by 9% between 2007–09 and by 20% through 2010. The presence of three liquid pentavalent vaccine suppliers by 2008 drove the price declines.

Although GAVI can be credited with attracting additional suppliers to the pentavalent vaccine market, the price declines to date have been driven by competitive market forces. While any declines in price do make the vaccine more affordable to GAVI-eligible countries, the declines to date are not sufficient to make the vaccine affordable in a sustained way once GAVI financing support is no longer available.

For pneumococcal and rotavirus vaccines, the GAVI price is either far lower or expected to be far lower than middle income public market prices. While much effort has gone into appropriately pricing these vaccines for low income markets, these vaccine prices are unlikely to be sustainable for most countries without continued GAVI funding.

Overall, our judgement is that vaccine pricing has been an area of weak performance by GAVI. The primary failure in our view is that GAVI has not been sufficiently proactive in understanding the nature of price drivers for its key vaccines or in working with suppliers to maximise price reductions through explicit strategies.

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\(^1\) DOC # AF-9 Vaccine market development, GAVI Board meeting 6-7 December 2005.
Although GAVI has not yet achieved its goal of creating affordable vaccines for GAVI countries, country visits made it clear that without GAVI financing, countries would not have been able to vaccinate their children. The continued efforts of GAVI to fund new vaccines with ‘affordable’ country co-payments will remain a critical and important activity for GAVI.

6. **Advancing the evidence base (SG2.5)**

GAVI has added value by advancing the evidence base required for vaccine introduction decision-making. The evaluation confirmed the significant value GAVI has added by advancing the evidence base required for country policy decisions related to the introduction of YF, Hib-containing, pneumococcal, and rotavirus vaccines. Significant contributions were made to the evidence base for disease burden, vaccine safety and effectiveness, cost-effectiveness, and programmatic feasibility through the GAVI-funded Yellow Fever Initiative, Hib Initiative, PneumoADIP, and RVP. WHO was also highlighted as a major provider of evidence to inform country decision-making.

7. **Accurate and timely vaccine demand forecasts (SG2.6)**

GAVI has added value by developing timely forecasts for use by its partners and suppliers (WHO forecasts produced for UNICEF, UNICEF forecasts produced for suppliers, and GAVI-funded ADIP and AVI forecasts produced for GAVI and UNICEF). The process for creating and updating demand forecasts is well established for the underused vaccines, and recently established for the new vaccines.

Determining the accuracy of the forecasts was more challenging. For underused vaccines, the evidence showed the variance between WHO forecasted demand and GAVI approved doses (used as a proxy for demand) has not improved consistently over the three procurement rounds. The UNICEF Long Term Arrangements (LTA) and annual updated forecasts exhibited less variance than the WHO forecasts for HepB tetravalent and pentavalent vaccines and their variance has improved over the three procurement rounds for YF vaccines.

It is too soon to make conclusions about the accuracy of the new vaccine demand forecasts.

8. **Overall assessment of GAVI’s performance on SG2**

GAVI’s greatest SG2 value-add has been the acceleration of underused vaccine introduction in GAVI-eligible countries. This acceleration is due to affordable country financing (via country co-pay), improved supply stability, and the availability of the appropriate evidence to support country and supplier decision-making. GAVI still has significant work to do to ensure supply at prices countries can afford post-GAVI support.

Although GAVI still has the potential to accelerate the introduction of pneumococcal and rotavirus vaccines, acceleration is at risk unless GAVI can resolve its current financing gap and secure vaccine prices that are affordable to countries post-GAVI support.
Based on this evaluation, GAVI has only partially achieved its SG2 goals.

- GAVI has accelerated the uptake of underused vaccines. It is too soon to tell whether it has accelerated the uptake of new vaccines.
- GAVI countries are capable of quickly taking GAVI vaccine programmes to scale.
- GAVI has improved or achieved supply stability for the underused vaccines, although YF supply stability declined after 2008 and is projected by UNICEF to be ‘still fragile’ through 2012. For new vaccines, GAVI has secured AMC supplier commitments in sufficient quantities to meet projected pneumococcal vaccine demand for the short-term (2010-11), and has secured long-term commitments for a large proportion (60m doses) of future demand. GAVI has not yet secured any supply commitments for rotavirus vaccine.
- The GAVI Alliance and the GAVI-funded ADIPs and Initiatives, have contributed significantly to advancing the evidence base required for country policy decisions related to vaccine introduction.
- GAVI has not made YF vaccines more affordable to countries over the evaluation period. Other HepB- and Hib-containing vaccines did become more affordable over time, but demand for these vaccines is minimal given the transition to pentavalent vaccines. Pentavalent vaccine prices have declined recently, but it is unlikely these vaccines will be affordable to countries in the absence of GAVI.
- The GAVI Alliance and the GAVI-funded ADIPs and Initiatives, have contributed significantly to advancing the evidence base required for country policy decisions related to vaccine introduction.
- WHO and UNICEF have delivered timely vaccine demand forecasts to suppliers in support of the vaccine procurement process, however, the accuracy of the underused vaccine forecasts has varied widely from one procurement round to another. The ADIPs (and more recently AVI), have delivered timely demand forecasts in support of supplier and donor decision-making processes. It is too soon to evaluate the accuracy of these forecasts.
1. **INTRODUCTION AND BACKGROUND**

The GAVI Alliance’s second strategic goal is to ‘Accelerate the uptake and use of underused and new vaccines and associated technologies and improve vaccine supply stability.’ This goal covers GAVI’s flagship program – New and Underused Vaccine Support (NVS). As part of its NVS program, GAVI provides support for the following six vaccines: hepatitis B (HepB), *Haemophilus influenzae* type B (Hib), yellow fever (YF), pneumococcal, rotavirus, and measles second dose. This evaluation covers five of these six vaccines. The measles second dose program is not included in this evaluation because only two countries have adopted the measles second dose with GAVI support (Vietnam and Korea DPR), and the program only represents 0.12% of GAVI approvals from 2001-15.

Yellow Fever, HepB, and Hib-containing vaccines were approved for support in 2000 and are referred to as ‘underused’ vaccines in the evaluation. Pneumococcal and rotavirus vaccines, approved for support in 2006, are referred to as ‘new’ vaccines.

Although the GAVI Board approved the meningitis A (MenA) conjugate vaccine strategy as outlined in the investment case and funded a MenA emergency response capability ($55.2m) during its June 2008 meeting, the Board has not yet approved funding of MenA preventive campaign activities. Therefore, MenA vaccine was not included in this evaluation.

Two other vaccines, polio and tetanus, have been funded by GAVI under Strategic Goal 2. In July 2005, the Executive Committee of the GAVI Board reviewed IFIIm-dependent investment cases for one-time support of a polio stockpile and maternal and neonatal tetanus (MNT) elimination. Funding for these programs was approved in the November 2005 GAVI Board Executive Committee electronic meeting ($191m for polio and $62m for MNT).

The polio vaccine stockpile investment was intended to establish an emergency stockpile of appropriate polio vaccines for use by countries once they stop routine OPV use after polio eradication. This upfront financing was needed to provide an incentive for suppliers to produce the necessary vaccines. In May 2007, the GAVI Board reprogrammed ~$105m of the polio stockpile funds for a one-time financing of intensified polio eradication activities. The 2007–10 GAVI Work Plan indicates a report on program achievements and lessons learned would be produced by 2008, however, this report was not available. Work plan updates to the Board post-2007 do not include updates on the polio program. Alternative information (e.g., actual stockpile delivery data) to support an

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3 GAVI Phase I & Phase II consolidated disbursements.xls, provided by the GAVI Secretariat, 10 March 2010.


6 Final Summary Report, GAVI Alliance & Fund Board Meeting, 25-26 June 2008

7 Final Summary Report, GAVI Alliance & Fund Board Meeting, 29-30 October 2008

8 Final Summary Report, GAVI Alliance & Fund Board Meeting, June and September 2006.


10 Investment Case for the Polio Stockpile, Submitted to the GAVI Review Committee, 20 June 2005

11 Final Summary Report, GAVI Alliance & Fund Board Meeting, 11-12 May 2007


14 [http://www.gavialliance.org/resources/03b_GAVI_2010_administrative_and_work_plan_budget.pdf](http://www.gavialliance.org/resources/03b_GAVI_2010_administrative_and_work_plan_budget.pdf) (accessed July 2010)

evaluation was not available for this program, therefore, the polio stockpile and eradication activity program was not included in this evaluation.

The maternal and neonatal tetanus elimination investment was intended to rapidly achieve and sustain MNT elimination in 36 GAVI-eligible countries by supporting supplementary immunisation activities in high risk districts.\textsuperscript{16} The initial funding request was to support vaccine purchases and operational costs in Phase I ($82m in 2006) and operational costs in Phase II ($373m for 2007-10). Documentation supporting the GAVI Board decision to fund only $62m of this request was not available, but it was assumed this funding was for Phase I support. The 2007–10 GAVI Work Plan indicates a report on program achievements and lessons learned would be produced by 2008, however, this report was not available.\textsuperscript{17} Work plan updates to the Board post-2007 do not include updates on the MNT program.\textsuperscript{18,19,20} Alternative information (e.g., vaccine purchases, increased MNT immunisation coverage in high risk districts) to support an evaluation was not available for this program, therefore, the MNT program was not included in this evaluation.

1.1. **Evaluation approach**

1.1.1. **Scope of evaluation**

The evaluation questions under SG2 are as follows:

SG2.1: To what extent has GAVI accelerated the uptake of underused and new vaccines by partner countries?

SG2.2: To what extent have countries introducing underused and new vaccines been able to take them to scale quickly, i.e. achieve full-scale coverage?

SG2.3: To what extent has GAVI improved the stability of global and country level vaccine supply?

SG2.4: To what extent has GAVI made vaccines and related technologies more affordable?

SG2.5: To what extent has GAVI contributed to the advancement of the evidence base required for countries to address the policy decision related to the introduction of new vaccines?

SG2.6: To what extent has GAVI developed and used vaccine demand forecasts that are accurate and timely?

Each question is addressed for each vaccine, as appropriate.

1.1.2. **Methodological considerations and limitations**

The six questions were evaluated using available quantitative and qualitative data. The methodology section for each question contains a description of the evaluation methodology, data sources, and analysis limitations. The limitations indicate that if GAVI

\textsuperscript{16} Investment Case for Maternal and Neonatal Tetanus Elimination, Submitted to the GAVI Review Committee, 20 June 2005

\textsuperscript{17} http://www.gavi.org/resources/AF_5_GAVI_2007_Work_Plan_update.pdf (accessed July 2010)

\textsuperscript{18} http://www.gavi.org/resources/9_Workplan_and_admin_budget.pdf (accessed July 2010)

\textsuperscript{19} http://www.gavi.org/resources/03b_GAVI_2010_administrative_and_work_plan_budget.pdf (accessed July 2010)

\textsuperscript{20} http://www.gavi.org/resources/04___2009_Work_Plan_Information_and_Update.pdf (accessed July 2010)
invested in harmonising data from multiple sources, restructuring it to a unified format, and storing it in a single searchable repository, the data’s overall utility would be greatly enhanced and it would considerably reduce the time needed for data access in the future. In turn, these enhancements would facilitate ongoing monitoring and evaluation of GAVI programs.

For this evaluation, the methodological considerations and limitations that apply to all the SG2 sub-questions include:

- During GAVI’s Phase I (2000–06), 75 countries were eligible for GAVI support. In 2006, the list of eligible countries was updated to reflect new GNI per capita data. Four countries (Albania, China, Bosnia and Herzegovina, and Turkmenistan) were no longer eligible, and one country (Kiribati) became eligible.\(^{21}\) Thus, only 72 countries were eligible as GAVI entered its Phase II period (2006–09).
  - For underused vaccines, the evaluation time frame covered both Phase I and II, and thus all countries eligible for GAVI funding in any phase (n=76) were included in the evaluation.
  - For new vaccines, the current 72 GAVI-eligible countries were included in the evaluation.
- GAVI has always supported the use of combination vaccines, thus the evaluation was conducted by antigen and / or by vaccine as appropriate to each question.\(^{22}\)
- Data that would have enriched various analyses were often not available. The specific data that were not available is noted in each sub-question.
- There were often many sources for the same data (e.g. vaccine introduction dates), and the data from multiple sources often did not match. To avoid confusion, data were cited to indicate which sources were used and discrepancies were identified, as appropriate.
- Data for use in the evaluation were typically provided in raw form, which required significant work to enable analysis (e.g. consolidation and triangulation of data from many sources, conversion from PDF tables to Excel, additional research to enable interpretation of the data).
- Some data used in this analysis were updated after evaluation analyses were completed, therefore, late-breaking data may not have been included. In all cases, the date that data were accessed is noted.

The limitations of the evaluation regarding the electronic survey, the EPI manager survey, and the structured interviews also held for SG2. Additional limitations specific to each question are provided in the individual sections.

The sources attributed to figures and tables are provided in the Methodology section, unless otherwise noted.

1.1.3. Analysis of robustness

To assess the strength of a conclusion, a ‘robustness score’ was assessed for each main finding. The definitions of the four scores (A-D) are summarised in Table 1.2.

Table 1.1: Robustness ranking for evaluation findings

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<th>Ranking</th>
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<tr>
<td>A</td>
<td>The finding is consistently supported by the full range of evidence sources, including quantitative analysis and qualitative evidence (i.e. there is very good triangulation); and/or the evidence source(s) is/are of relatively high quality and reliable to draw a conclusion (e.g. solid sample sizes are available and there are no major data quality or reliability issues).</td>
</tr>
<tr>
<td>B</td>
<td>There is a good degree of triangulation across evidence, but there is less or ‘less good’ quality evidence available. Alternatively, there is limited triangulation and not very good quality evidence, but at least two different sources of evidence.</td>
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<tr>
<td>C</td>
<td>Limited triangulation, and/or only one evidence source that is not regarded as being of a good quality.</td>
</tr>
<tr>
<td>D</td>
<td>There is no triangulation and/or evidence is limited to a single source and is relatively weak; or the quality of supporting data/information for that evidence source is incomplete or unreliable.</td>
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In general, the score provides an assessment of the extent to which:

- A range of evidence types and sources point to the same conclusion (i.e. successful triangulation of data).
- The data types and evidence sources supporting a conclusion were credible and of high quality (e.g. sufficient sample size, complete data set).

1.1.4. Prior Evaluator Relationships with GAVI Alliance Partners

Applied Strategies has worked with the GAVI Alliance on numerous projects in the past, including the: (i) new vaccine introduction readiness assessment project (co-sponsored by the Gates Foundation, GAVI, and the World Bank); (ii) pneumo vaccine pilot AMC supplier consultations and economic expert group support projects; (iii) GAVI 2009-2013 vaccine investment strategy project; and (iv) GAVI existing and pending vaccine portfolio metrics analysis and prioritization project. Applied Strategies has also supported the PneumoADIP in its efforts to: (i) develop appropriate strategic demand forecasting methods and models; (ii) plan and facilitate two industry and key global health stakeholder roundtables to discuss demand forecasting issues and challenges and review and refine the strategic demand forecasting methods and models, respectively; (iii) support the demand forecasting analysis component of its GAVI investment case; and (iv) conduct demand forecasting and financial implications analyses for the pilot AMC candidate paper submitted to the AMC pilot recommendation committee. Applied Strategies also provided strategic demand forecasting model delivery and training support to RVP for use in its GAVI investment case. In addition, Applied Strategies provided supply & demand
forecasting analysis support to the Hib Initiative for GAVI-eligible countries in general and India states more specifically.

1.2. Background

1.2.1. GAVI NVS Program

GAVI’s NVS program was designed to accelerate the introduction of new and underused vaccines in developing countries, and has been GAVI’s largest program to date, representing 74% of approved funding ($3 billion) from 2001 to 2015. Between 2001 and 2010, a total of approximately $1.5 billion was disbursed.25

Figure 1.1 provides total approvals versus disbursements over time.

Figure 1.1: Total approvals and disbursements

GAVI’s NVS program was initially designed to support the introduction of underused vaccines, including YF, HepB, and Hib-containing vaccines. In Phase II, GAVI expanded its NVS support to include new vaccines, including pneumococcal and rotavirus. GAVI also approved support for a second dose of measles vaccine.

Throughout its existence, GAVI has maintained a policy whereby eligible countries must meet certain criteria to qualify for support for a given vaccine.27 To receive support for HepB-containing, Hib-containing, pneumococcal, and rotavirus vaccines, a country must have a DTP3 coverage rate of at least 50% (under GAVI’s new eligibility policy, the required DTP3 coverage rates will increase to 70%) and the government must not already be funding the vaccine.28 In addition, the country must meet WHO criteria for recommendation of immunisation based on disease burden. To receive support for yellow fever vaccination, a country does not need to meet the DTP3 coverage rate requirements. Instead, it must have YF vaccine coverage that is lower than that for measles, and it must

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23 GAVI Phase I & Phase II consolidated disbursements.xls, provided by the GAVI Secretariat, 10 March 2010.
25 GAVI Phase I & Phase II consolidated disbursements.xls, provided by the GAVI Secretariat, 10 March 2010.
26 GAVI Phase I & Phase II consolidated disbursements.xls, provided by the GAVI Secretariat, 10 March 2010.
28 GAVI Alliance Board meeting 17-18 November 2009
meet WHO criteria for recommendation of immunisation based on disease burden. Countries can apply for support to introduce a second dose of measles vaccine if they meet WHO criteria.

In Phase I, GAVI’s NVS program provided five-year support grants for YF, HepB-, and Hib-containing vaccines with the expectation that countries would cover the entire vaccination cost after the GAVI support window ended. This initial strategy was based on the idea that through pooled procurement, GAVI could drive down the price of the vaccines within five years to a point where countries could cover the cost of the vaccines themselves once GAVI support concluded.

Several factors and lessons learned in Phase I prompted GAVI to revise its policies in Phase II:

- Vaccine prices were not decreasing to the extent GAVI predicted.
- It became clear that countries would not be able to sustain immunisation themselves.
- The number of available vaccines was increasing.

In light of these developments, GAVI revised its policies. First, GAVI extended support for some countries that had already introduced in Phase I to ease the transition to the new Phase II policies. Countries approved for support in 2005 would remain eligible for five years of free support, countries receiving support for monovalent HepB immunisation would receive an additional two years of free vaccine, and all countries receiving support for yellow fever routine immunisation would receive an additional five years of subsidised support.

Second, GAVI also revised its support timelines to be based on country planning cycles, with total support not to exceed 10 years or 2015. Finally, GAVI implemented a system whereby countries would co-finance certain vaccines beginning in 2007. The objective of the co-financing program was to enhance evidence-based decision making by countries regarding new vaccine introduction and to help countries achieve financial sustainability.

It should be noted that the GAVI Board endorsed an operational definition of financial sustainability wherein “self-sufficiency is the ultimate goal”, but “in the nearer term sustainable financing is the ability of a country to mobilise and efficiently use domestic and supplementary resources on a reliable basis to achieve current and future target levels of immunisation performance.” The co-financing policy did not apply to measles second dose vaccination.

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30 1st GAVI Board meeting minutes, October, 1999.
32 Doc A/B. Revision and alignment of country support policies in Phase II. GAVI Alliance Delhi Board Meeting, 6–7 December 2005.
33 Ibid.
34 Ibid.
In the new system, countries were classified into one of four groups according to their per capita GNI and United Nations development status, including “Least Poor”, “Intermediate”, “Poorest”, and “Fragile States”. Minimum country contributions ranged from $0.10 per dose for the “Fragile States” to $0.30+15% annually for “Least Poor” for the first vaccine and $0.15 per dose to $0.15+15% annually per dose for the second and third vaccines. GAVI encouraged countries to contribute more whenever possible to progress more rapidly toward financial sustainability.

In Phase II, GAVI also agreed to provide support for pneumococcal and rotavirus vaccines.

1.2.2. GAVI Alliance support by vaccine

In GAVI Phase I, the majority of GAVI approvals were for HepB monovalent, DTwP-HepB tetravalent, and DTwP-HepB-Hib pentavalent vaccines. YF and measles second dose represented a much smaller portion of approvals.

However, beginning in Phase II, the proportion of approvals for pentavalent grew steadily and is now expected to account for all GAVI spending on HepB- and Hib-containing vaccines from 2010 onward. This reflects GAVI’s policy of encouraging adoption of pentavalent vaccines as a more efficient method to vaccinate against multiple diseases.

Spending on new vaccines will increase in the future as additional approvals are expected. Figure 1.2 provides perspective on the relative funding approved for each vaccine.

Figure 1.2: Approvals by vaccine

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39 Ibid.
40 Ibid.
42 GAVI Phase I & Phase II consolidated disbursements.xls, provided by the GAVI Secretariat, 10 March 2010.
In its first three years, GAVI approved a steady number of introductions (~15 to 20 per year) under NVS. This number dropped between 2004 and 2007 and then increased dramatically in 2008 as a result of applications for pentavalent vaccine.

Figure 1.3 shows the number of applications approved annually for each vaccine.

Figure 1.3: Number of applications approved by year by first vaccine support

Similarly, shipment data show that over time, GAVI shipped an increasing number of vaccines to eligible countries overall, and an increasing fraction of these vaccines has been pentavalent (Figure 1.4). The relatively large constant volume of monovalent HepB shipments comes from GAVI funding India’s pilot program. Not included are countries that have received vaccines through supplier donations. These countries include Gambia and Rwanda (pneumococcal vaccine) and Nicaragua (rotavirus vaccine).44,45

In 2008, GAVI developed a five year investment strategy (2009–13) which considered 10 additional diseases in which vaccines were expected to be prequalified by 2012.46 Based on GAVI’s Vaccine Investment Strategy work, the Board prioritised vaccines to prevent Human papillomavirus (HPV), Japanese encephalitis (JE), rubella, and typhoid. However, GAVI is only investing in preparatory activities for these vaccines while they await the conclusion of the ongoing 2011–15 strategy development process, the completion of the pilot vaccine application prioritisation system, and the appropriate funding available to support these additional vaccines.47

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43 Timeframe of GAVI support to countries as of 30 Nov 09, spreadsheet provided by the GAVI Secretariat, January 2010.
45 Ibid.
47 Doc 09 – Prioritisation Mechanism, GAVI Alliance Board Meeting, 16-17 June, 2010.
The evaluation results are summarised by evaluation question. 

- Sections 2 to 7 (covering SG2.1 to 2.6) deal with each of the evaluation questions under SG2.
- Section 8 provides conclusions related to the evaluation at the SG2 level.

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2. SG2.1: VACCINE UPTAKE

2.1. Introduction

The first Strategic Goal 2 evaluation question is, “To what extent has GAVI accelerated the uptake of underused and new vaccines by partner countries?”

The time from first vaccine licensure to wide-scale introduction into developing countries has been well documented to be 20 to 30 years. Since disease burden is generally the highest in developing countries, this delay has resulted in countless preventable deaths.

GAVI was formed in 2000 to address this delay and make immunisation a key weapon against childhood mortality and morbidity in the world’s poorest countries. GAVI committed 74% of its budget between 2000 and 2015 to the support of new and underused vaccines and an additional 11% to strengthening health and immunisation systems within these countries. With many new vaccines entering the global market since 2000, GAVI continues to focus on accelerating vaccine introduction and thus preventing major infectious diseases in the countries with the greatest need.

2.2. Scope of the evaluation question

This section analyses the impact GAVI had on accelerating introduction of underused vaccines in GAVI-eligible countries from 2000–09 and on the projected introduction of new vaccines based on GAVI application data. The evaluation:

- Compared the number and rate of vaccine introduction in GAVI-eligible countries prior to and after GAVI formation as a measure of acceleration.
- Identified key events and GAVI Alliance actions that may have contributed to changes in rate of country vaccine introduction.
- Conducted two comparative analyses to provide additional insight on accelerated vaccine introduction:
  - Vaccine introduction rates for underused vaccines versus projected introduction rates for new vaccines as an indicator of improvements in introduction rates over time.
  - ‘Income-matched’ introduction rate comparisons between GAVI-eligible and non-GAVI-eligible lower middle income countries as an indicator of how well GAVI countries perform relative to lower middle income non-GAVI countries.
- Conducted a counterfactual analysis assuming pre-GAVI introduction rates would have continued at pre-GAVI rates if GAVI had not been formed.

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52 GAVI Phase I & Phase II consolidated disbursements.xls (emailed by GAVI Secretariat 10 March 2010).
• Summarised others’ perceptions on the extent of GAVI’s impact on accelerating vaccine uptake (e.g. electronic survey, structured interviews)

2.3. Methodology

2.3.1. Overview

Both quantitative and qualitative analyses were conducted to evaluate GAVI’s role in accelerating the uptake of new and underused vaccines.

The quantitative analyses included the number and rate of vaccine introductions prior to and after GAVI formation for YF and HepB- and Hib-containing vaccines. The vaccine introduction dates were assessed as the earliest year of introduction based on the WHO Immunisation surveillance, assessment, and monitoring database. The only exception was the YF vaccine introduction date for Kenya, which was not reported in the WHO database but was assumed in this evaluation to be 1992 based on the first reported vaccination coverage rates from the Global Health Atlas.

Historical events related to vaccine licensure, vaccine prequalification, and policy recommendations for YF and HepB- and Hib-containing vaccines were documented to provide insight on the drivers of introduction rate changes over time. These events were primarily drawn from publically available data, including WHO position papers and recommendations. Because WHO’s Scientific Advisory Group of Experts (SAGE) has been charged with making recommendations intended to guide WHO position papers since SAGE’s formation in 1999, it was assumed WHO position papers/recommendations included SAGE reviews and recommendations.

To generate insight on the potential introduction rates for pneumococcal and rotavirus vaccines, a combination of actual and projected introduction dates based on country application data were used. Actual vaccine introduction dates through 2009 were based on publically available information and the latest projected introduction dates for 2010 and beyond were based on not yet released application data obtained from GAVI (differed from latest publically available application data). Country applications requiring a resubmission were excluded.

Qualitative information on GAVI’s role in accelerating underused and new vaccine introduction was obtained from three sources:

• Responses from the electronic survey to two statements:
  o “GAVI has accelerated the uptake of Hep B, Hib, and YF vaccines by partner countries”

57 Personal communication, AVI, 25 February 2010.
“GAVI has accelerated the uptake of rotavirus, pneumococcal, and meningitis A vaccines by partner countries”.

Responses (n=282) were analysed for both ‘as received’ (referred to as “raw” data) and ‘adjusted’ data (adjusted by removing non-respondents form each statement).

- Responses (n=22) from consultations with current and past GAVI Board members where they were asked to comment on the “extent GAVI accelerated the uptake of new and underused vaccines by partner countries.”
- Relevant comments and insights generated from five country consultations.

The current evaluation is intended to include data from 2001–09, however, where appropriate, 2010 data was included.

The evidence sources used to evaluate this question are summarised in Table 2.1.

**Table 2.1: Evaluation sources and descriptions for the accelerated uptake of underused and new vaccines**

<table>
<thead>
<tr>
<th>Evidence Source</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of documentation</td>
<td>• Vaccine introduction in developing countries</td>
</tr>
<tr>
<td></td>
<td>• Pneumococcal and rotavirus forecasts</td>
</tr>
<tr>
<td></td>
<td>• GAVI investment cases</td>
</tr>
<tr>
<td></td>
<td>• GAVI Board meeting minutes</td>
</tr>
<tr>
<td></td>
<td>• PAHO Executive Committee meeting minutes</td>
</tr>
<tr>
<td>E-survey</td>
<td>The electronic survey sought input on the questions:</td>
</tr>
<tr>
<td></td>
<td>• “GAVI has accelerated the uptake of HepB, Hib, and YF vaccines by partner countries”</td>
</tr>
<tr>
<td></td>
<td>• “GAVI has accelerated the uptake of rotavirus, pneumococcal, and meningitis A vaccines by partner countries”</td>
</tr>
<tr>
<td>Structured interview</td>
<td>Structured interviews included comments from current and ex-GAVI Board members on one question designed to solicit feedback on the evaluation statement “GAVI has made vaccines and related technologies more affordable to countries”</td>
</tr>
<tr>
<td></td>
<td>• Comments from the GAVI Secretariat were not included due to the perceived conflict of interest</td>
</tr>
<tr>
<td></td>
<td>• Comments from other structured interviews were not included due to the limited number of relevant comments</td>
</tr>
<tr>
<td>EPI manager survey</td>
<td>The EPI manager electronic survey did not seek input on this question.</td>
</tr>
<tr>
<td>Country visits</td>
<td>Country consultations resulted in ad hoc comments related to this question.</td>
</tr>
<tr>
<td>Information/data gathering meetings</td>
<td>Meetings were requested with representatives from the GAVI Secretariat to seek input on GAVI application status and forecasted introduction timing for pneumococcal and rotavirus vaccines</td>
</tr>
</tbody>
</table>
2.3.2. Comparative analyses

To further assess the potential impact and the added value of GAVI on accelerating underused and new vaccine introduction, two comparative analyses were conducted:

- The first analysis determined the time between when a vaccine was first introduced in any country (i.e., at time of first vaccine licensure) and when it was first introduced in a GAVI-eligible country. To generate insight on how GAVI may have accelerated vaccine introduction in these markets, a comparison of GAVI vaccine introduction delay to non-GAVI vaccine introduction delay in low income markets would be required. Given there are no current examples of non-GAVI vaccine introduction in low income markets, this analysis compares the delay in introduction for GAVI’s initial vaccines (i.e., underused vaccines) with the delay in introduction for GAVI’s most recent vaccines (i.e., pneumococcal and rotavirus vaccines) to determine if the delay has been shortened with time.

- The second analysis compared the introduction of HepB- and Hib-containing vaccines between GAVI-funded and non-GAVI funded lower middle income countries. YF vaccines were not included in the LMIC analysis because the two GAVI-eligible lower middle income countries did not use GAVI funding for YF introduction (Côte d’Ivoire and Bolivia). Country income level at time of vaccine introduction was based on World Bank analytical classifications based on country Gross National Income per capita.\(^{58}\)

2.3.3. Counterfactual analyses

The counterfactual analysis forecasted vaccine introduction in the absence of GAVI using a linear extrapolation across two different time frames (1992–00 and 1997–00) for YF, HepB-, and Hib-containing vaccines. The number of GAVI-eligible countries projected to have introduced a vaccine without GAVI was compared to the actual number of countries that introduced a vaccine with GAVI funding.

Determining the number of deaths averted from the counterfactual analysis is not possible because this requires an assumption on which specific countries may have introduced which specific vaccine from 2000–09 in the absence of GAVI. This calculation would also require country-specific infant population data, vaccination coverage rate data, and a credible estimate of deaths averted per 1000 vaccinated for each vaccine.

2.3.4. Limitations

These analyses have limitations due to:

- Inconsistencies in introduction dates across WHO databases, e.g.
  - WHO vaccine introduction dates versus WHO vaccination coverage rates

• Lack of prequalification dates for prequalified vaccines\textsuperscript{59} 
  o Unable to document early prequalification dates of products no longer provided to UNICEF markets 
  o Conflicting prequalification dates from different sources (e.g. for Institut Pasteur YF vaccine, one WHO document lists PQ as 1999 and the WHO prequalification website lists it as 2001\textsuperscript{60,61})

• Use of projected introduction dates for pneumococcal and rotavirus vaccine introductions

• Limited number of lower middle income countries for comparative analyses (17 to 40 countries per analysis)

• Inclusion of a counterfactual that cannot be verified (using past rates of introduction to infer future rates of introduction in the absence of GAVI)

• Limited qualitative data 
  o Of 22 GAVI Board member interviewees, 19 commented on underused vaccine introduction but only 9 commented on new vaccine introduction
  o Limited country-level stakeholder representation from five country consultations (7% of total stakeholder countries in four out of six WHO regions).

2.4. Evaluation analysis

2.4.1. Yellow fever vaccine introduction analysis

YF has a long history of vaccine development, and this evaluation begins with the first 17D vaccine licensed in 1948. The key vaccine-related events relevant to YF are shown in Table 2.2.

Table 2.2: Key YF vaccine-related events

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year Licensed</th>
<th>Year Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} YF vaccine</td>
<td>1948</td>
<td>1987</td>
</tr>
<tr>
<td>2\textsuperscript{nd} YF vaccine</td>
<td>1960s</td>
<td>2001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Global Policy</th>
<th>Year of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial WHO recommendation</td>
<td>1988</td>
</tr>
<tr>
<td>Updated WHO recommendation</td>
<td>2003</td>
</tr>
</tbody>
</table>

In 1988, the EPI Global Advisory Group recommended routine vaccination in countries with high risk of YF, and this recommendation was endorsed by WHO’s and UNICEF’s

\textsuperscript{59} WHO recently updated its website to include vaccine prequalification dates on current products although prequalification information on older vaccines is still not available (accessed 15 June 2010).


Technical Group on Immunisation in Africa.\textsuperscript{62} WHO published updated recommendations in 2003 that included routine vaccination of infants and implementation of mass preventive vaccination campaigns to protect susceptible older age groups in countries at high risk for YF.\textsuperscript{63}

To assess whether GAVI Alliance support accelerated the introduction of YF vaccines into GAVI-eligible countries, the number of countries introducing YF vaccines in a given year and the cumulative percent of GAVI-eligible countries adopting YF vaccines over time was determined. GAVI provides YF vaccine support to 28 countries thought to be endemic for YF.\textsuperscript{64} Figure 2.1 summarises the annual number of GAVI-eligible country introductions pre- and post-GAVI.

\textit{Figure 2.1: YF vaccine introduction in GAVI-eligible countries over time}

<table>
<thead>
<tr>
<th>Year of Introduction</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1948</td>
<td>1st YF vaccine licensed 1948</td>
</tr>
<tr>
<td>1987</td>
<td>WHO recommends vaccination 1988</td>
</tr>
<tr>
<td>1998</td>
<td>WHO updates recommendations 2003</td>
</tr>
<tr>
<td>2000</td>
<td>GAVI-funded YF Initiative launched 2000</td>
</tr>
<tr>
<td>2003</td>
<td>GAVI stockpile funded (6m/yr) 2003</td>
</tr>
<tr>
<td>2006</td>
<td>GAVI stockpile expanded (~12m/yr) 2006</td>
</tr>
<tr>
<td>2007</td>
<td>2nd YF vaccine WHO PQ 2001</td>
</tr>
<tr>
<td>2008</td>
<td>GAVI funding 2008</td>
</tr>
<tr>
<td>2010</td>
<td>Non pre-funded stockpile</td>
</tr>
<tr>
<td>2013</td>
<td>(2m/yr) 2010</td>
</tr>
<tr>
<td>2000</td>
<td>1st YF vaccine WHO PQ 1998</td>
</tr>
<tr>
<td>1992</td>
<td>1st YF vaccine licensed 1948</td>
</tr>
<tr>
<td>1997</td>
<td>GAVI stockpile funded (6m/yr) 2003</td>
</tr>
<tr>
<td>1998</td>
<td>GAVI stockpile expanded (~12m/yr) 2006</td>
</tr>
<tr>
<td>1999</td>
<td>2nd YF vaccine WHO PQ 2001</td>
</tr>
<tr>
<td>2000</td>
<td>GAVI funding 2008</td>
</tr>
<tr>
<td>2001</td>
<td>Non pre-funded stockpile</td>
</tr>
<tr>
<td>2002</td>
<td>(2m/yr) 2010</td>
</tr>
<tr>
<td>2003</td>
<td>1st YF vaccine WHO PQ 1998</td>
</tr>
<tr>
<td>2004</td>
<td>GAVI stockpile funded (6m/yr) 2003</td>
</tr>
<tr>
<td>2005</td>
<td>GAVI stockpile expanded (~12m/yr) 2006</td>
</tr>
<tr>
<td>2006</td>
<td>2nd YF vaccine WHO PQ 2001</td>
</tr>
<tr>
<td>2007</td>
<td>GAVI funding 2008</td>
</tr>
<tr>
<td>2008</td>
<td>Non pre-funded stockpile</td>
</tr>
<tr>
<td>2009</td>
<td>(2m/yr) 2010</td>
</tr>
</tbody>
</table>

Thirteen countries introduced a YF vaccine prior to GAVI funding, but no more than two GAVI-eligible countries had ever introduced a YF vaccine in a single year prior to 2000.\textsuperscript{65} After GAVI was formed, 11 countries introduced a YF vaccine and 3 to 4 countries adopted a YF vaccine each year between 2002 and 2004 (including Bolivia in 2003 without GAVI funding). The cumulative number of countries introducing YF vaccines increased from 46\% in 2000 to 86\% in 2009, a nearly two-fold improvement.

In the nine years prior to GAVI funding (1992–2000), an average rate of 0.8 countries per year introduced a YF vaccine compared to an average 1.1 per year (38\% increase) in the nine years with GAVI funding (2001–09). By the end of 2009, four GAVI-eligible countries had not yet started YF immunisation, although two of these countries (Ethiopia and Mauritania) have not reported YF outbreaks for over 20 years.\textsuperscript{66} Sudan and Uganda,

\textsuperscript{62} Yellow Fever. WHO, 1998; WHO/EPI/GEN/98.11.
\textsuperscript{63} Weekly Epidemiological Record (2003) 78(40):349-360.
\textsuperscript{64} GAVI, email communication verifying qualifying countries, 24 February 2010.
\textsuperscript{65} http://www.who.int/immunisation_monitoring/data/year_vaccine_introduction.xls (accessed 19 February 2010).
\textsuperscript{66} http://apps.who.int/globalatlas/dataQuery/default.asp (accessed 8 February 2010).
however, have reported YF cases over the past nine years and have yet to introduce a YF vaccine.\textsuperscript{67}

While GAVI has had an impact on accelerating introduction, it has also created additional value through the development and funding of two YF investment cases in 2005 and 2008.\textsuperscript{68,69} These investments expanded a vaccine stockpile, expanded disease surveillance, developed risk assessment tools, and implemented high-quality campaigns. The impact of this work has been the improvement of:

- YF supply security
- Infant immunisation sustainability
- Infant vaccination coverage rates
- Vaccine availability for outbreaks and preventative campaigns.

The importance of creating a stockpile and more secure supplies is illustrated by historic YF immunisation challenges. These challenges included unsustainable immunisation programs and low immunisation rates. As an example, Figure 2.2 provides the country-reported vaccination coverage rates for Central African Republic (CAR), Niger, and Senegal.

\textit{Figure 2.2: Three examples of unsustained YF vaccination pre- and post-GAVI’s YF stockpile}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.2.png}
\caption{Country Reported Vaccination Coverage Rates for Central African Republic, Niger, and Senegal.}
\end{figure}

Vaccination coverage rates for these countries were reported sporadically between 1985 and 2000, and except for one year, vaccination coverage rates were $\leq 60\%$. Supply shortages played a primary role in hindering program sustainability (one YF supplier through 2001). During outbreaks, countries would leverage their infant vaccine stock for emergency campaigns, which would disrupt routine infant immunisation.


\textsuperscript{68} Yellow Fever Stockpile Investment Case, submitted by the Yellow Fever Task Force to the GAVI, December 2005.

\textsuperscript{69} Yellow Fever Investment Case. Continuation Proposal. Submitted by the Yellow Fever Initiative to GAVI, May 2008.
For each of these countries, vaccination was sustained from 2001 onward and vaccination coverage rates improved from 10%–35% in 2000 to 71%–93% in 2009. Despite the improvements, CAR and Niger still reported some erratic coverage rates. The GAVI-funded Yellow Fever Initiative noted that routine infant coverage rates increased from 16% in 2000 to 43% in 2008 in Africa and from 64% to 91% over the same time period in Latin America.\(^70\) These improvements in sustained immunisation and vaccine coverage rates are due to GAVI’s investment in routine immunisation and YF stockpile for outbreak control and preventative campaigns.

2.4.2. HepB-containing vaccine introduction analysis

Historically, plasma-derived vaccines were first developed in 1981 and replaced over time by recombinant protein vaccines. The key vaccine-related events for HepB-containing vaccines are shown in Table 2.3.

Table 2.3: Key HepB vaccine-related events

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year Licensed</th>
<th>Year Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st HepB monovalent vaccine</td>
<td>1981</td>
<td>1987</td>
</tr>
<tr>
<td>1st HepB tetravalent vaccine</td>
<td>1995</td>
<td>1998</td>
</tr>
<tr>
<td>1st pentavalent vaccine (liquid/lyo)</td>
<td>1996</td>
<td>1998</td>
</tr>
<tr>
<td>2nd pentavalent vaccine (liquid)</td>
<td>2005</td>
<td>2006</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Global Policy</th>
<th>Year of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial WHO recommendation</td>
<td>1991</td>
</tr>
<tr>
<td>Updated WHO recommendation</td>
<td>2004</td>
</tr>
<tr>
<td>Updated WHO recommendation</td>
<td>2009</td>
</tr>
</tbody>
</table>

The first WHO recommendation for routine immunisation worldwide was in 1991.\(^71\) In 2004, the WHO updated its recommendations for routine immunisation worldwide to incorporate a first dose within 24 hours after birth in countries where a high proportion of infections are acquired perinatally. In addition, it recommended consideration of catch-up campaigns targeted at older age groups at risk.\(^72\) More recently, the WHO issued an updated recommendation for first birth dose for all infants, regardless of endemicity.\(^73\)

To assess whether GAVI support accelerated the introduction of HepB-containing vaccines into GAVI-eligible countries, the number of countries introducing HepB-containing vaccines in a given year and the cumulative percent of GAVI-eligible countries adopting the vaccines over time was evaluated. Seventy-five countries were eligible for GAVI Phase I financing for HepB monovalent and HepB combination vaccines beginning in 2000, and, beginning in 2007, 72 countries were eligible for Phase II financing for HepB combination vaccines. As shown in Figure 2.3, 22 countries adopted a HepB-containing vaccine between 1987–00 and 52 countries introduced a HepB-containing vaccine from 2001–09 (including Nigeria in 2004 and Timor-Leste in 2007 without GAVI funding).

In the nine years prior to GAVI funding (1992–2000), an average rate of 1.8 countries per year introduced a HepB-containing vaccine compared to an average of 5.8 countries per year (3.2-fold increase) in the nine years with GAVI funding (2001–09). Eight to 12 countries per year introduced a HepB-containing vaccine immediately after GAVI funding began (2001–03). By 2009, all but two GAVI-eligible countries had introduced a HepB-containing vaccine (Haiti and Somalia). The cumulative number of countries introducing a HepB-containing vaccine increased from 29% in 2000 to 97% in 2009, a greater than 3-fold improvement.

The reduction in the number of countries introducing a HepB-containing vaccine from 2004–06 was due to the uncertainty of continued GAVI funding after Phase I and the country preference for a DTwP-HepB-Hib pentavalent vaccine which had a shortage of supplies (see SG2.4). This was evidenced by the majority of the countries introducing a HepB monovalent vaccine with GAVI funding in 2004–05 (4 out of 5) while the majority of countries introduced a pentavalent vaccine from 2007–09 (12 out of 15).

Given that the HepB program was not supported by a specific GAVI-funded initiative like YF or Hib, the increased rate of HepB-containing vaccine introduction is attributed primarily to GAVI financing. In addition, GAVI advocated for the introduction of HepB combination vaccines by making it financially beneficial to do so and by emphasising the additional safety benefits inherent in reducing the number of injections needed to deliver essential vaccines. GAVI provided five years of financing through Phase I and then an affordable country co-pay policy in Phase II. Phase II policies emphasised GAVI’s preference for combination vaccines by dropping financial support for HepB and Hib monovalent vaccines and by creating a financing policy that encouraged countries to introduce pentavalent vaccines (i.e. same co-pay for all vaccines).

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74 Investment Case for Bridge Financing Update for GAVI Board; 2005.
75 15th GAVI Board Meeting document, April 2005.
2.4.3. Hib-containing vaccine introduction analysis

Historically, the first Hib vaccine licensed in 1985 was a polysaccharide vaccine for use in ≥18 months old. The first infant conjugate vaccine was licensed in 1988 and is the vaccine type used in this evaluation. The key vaccine-related events for conjugate Hib-containing vaccines are shown in Table 2.4.

Table 2.4: Key Hib vaccine-related events

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year Licensed</th>
<th>Year Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Hib monovalent vaccine</td>
<td>1988</td>
<td>1997</td>
</tr>
<tr>
<td>1st Hib tetravalent vaccine</td>
<td>1993</td>
<td>2002</td>
</tr>
<tr>
<td>1st pentavalent vaccine (liquid/lyo)</td>
<td>1996</td>
<td>1998</td>
</tr>
<tr>
<td>2nd pentavalent vaccine (liquid)</td>
<td>2005</td>
<td>2006</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Global Policy</th>
<th>Year of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial WHO recommendation</td>
<td>1998</td>
</tr>
<tr>
<td>Updated WHO recommendation</td>
<td>2006</td>
</tr>
</tbody>
</table>

WHO recommended routine Hib vaccination in 1998 where disease burden was evident. In 2006, it updated its recommendations to state that the lack of disease surveillance data should not delay vaccine introduction, recognising the difficulty in confirming Hib cases and that laboratory-confirmed Hib case numbers grossly underestimated the burden of Hib disease.

To assess whether GAVI support accelerated the introduction of Hib-containing vaccines into GAVI-eligible countries, the number of countries introducing Hib-containing vaccines in a given year and the cumulative percent of GAVI-eligible countries adopting a Hib-containing vaccine over time was evaluated. Seventy-five countries were eligible for GAVI Phase I financing for Hib monovalent and Hib combination vaccines beginning in 2000, and 72 countries were eligible for Phase II financing for Hib combination vaccines only beginning in 2007. As shown in Figure 2.4, only five countries had introduced Hib-containing vaccines prior to GAVI funding, and 58 countries introduced a Hib-containing vaccine from 2001–09 (including Ukraine in 2006 without GAVI funding and Azerbaijan in 2009 with a GAVI application pending).

In the nine years prior to GAVI funding (1992–00), an average rate of 0.6 countries per year (nearly 11-fold improvement) introduced a Hib-containing vaccine compared to an average of 6.4 countries per year in the nine years with GAVI funding (2001–09). The cumulative number of countries introducing a Hib-containing vaccine increased from 7% in 2000 to 83% in 2009, an approximately 12-fold improvement.

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The most significant increases in vaccine introduction occurred in 2008 and 2009 when 18 and 20 countries introduced a Hib-containing vaccine, respectively. This recent acceleration was due to at least four events occurring between 2005 and 2007:

- The formation and activities of the GAVI-funded Hib Initiative, a collaboration between Johns Hopkins University, US Center for Disease Control, London School of Hygiene and Tropical Medicine, and WHO, which provided:
  - Communication
  - Advocacy
  - Evidence to country decision-makers
  - GAVI application support to countries
- WHO activities:
  - Updated recommendations
  - Prioritised prequalification review for pentavalent vaccines
- An increase in pentavalent vaccine supply with the prequalification of a second supplier with a first fully liquid pentavalent vaccine
- The continued focus of GAVI on combination vaccines, especially pentavalent vaccines.

The lag between the more recent GAVI efforts from 2005–07 and the significant increase in the number of country introductions in 2008 and 2009 was due to the time it takes to communicate the evidence at the country level, prepare a GAVI NVS application, undergo IRC review, obtain approval, and begin vaccinating.
As corroborating evidence, a publication from members of the Hib Initiative also confirmed the value of GAVI in accelerating Hib vaccine introduction decisions.\textsuperscript{78} In this study, data from 1990–07 for 147 countries were mined for insights on policy decisions regarding Hib vaccines. In multivariate models that controlled for gross national income, region, and disease burden, a number of additional variables were assessed to account for timing of country Hib vaccine adoption decisions. These included variables describing the underlying country context (e.g., population, region, DTP3 coverage rate, and democracy score), costs and benefits of Hib vaccination (e.g., vaccine price, GNI, cost per bed-day, Hib incidence, and availability of Hib in combination with DTwP and/or HepB vaccine), and other modifying factors (e.g., local incidence/disease burden studies, neighbouring countries adopting Hib-containing vaccines, WHO position papers, GAVI eligibility, and co-financing uncertainty). This study identified a number of variables associated with longer times to an adoption decision, including region (non-OECD European and Central Asian countries), vaccine price, and GAVI co-financing uncertainty from 2004 to 2006, and several variables associated with shorter times to an adoption decision, including democracy score, neighbouring countries adopting, and GAVI eligibility. While the authors point out limitations of their study, their findings suggest that GAVI and partner efforts accelerated country decision maker’s awareness of Hib vaccination through advocacy, interpersonal contact with country decision makers, and technical support.

### 2.4.4. Pneumococcal vaccine introduction analysis

The first pneumococcal vaccine (PCV7) was licensed in 2000; however, this vaccine lacks two serogroups shown to be responsible for a significant portion of invasive pneumococcal disease in developing countries. PCV10 and PCV13 vaccines have now been developed and licensed. The key vaccine-related events for pneumococcal vaccines are shown in Table 2.5.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year Licensed</th>
<th>Year Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st pneumococcal vaccine (PCV7)</td>
<td>2000</td>
<td>2009</td>
</tr>
<tr>
<td>2nd pneumococcal vaccine (PCV10)</td>
<td>2009</td>
<td>2009</td>
</tr>
<tr>
<td><strong>Global Policy</strong></td>
<td></td>
<td><strong>Year of Recommendation</strong></td>
</tr>
<tr>
<td>Initial WHO recommendation</td>
<td></td>
<td>2007</td>
</tr>
</tbody>
</table>

In 2003, WHO considered recommending PCV7 for inclusion into national immunisation programs, but it felt more information was needed to assess the impact of this vaccine in developing countries and considered further development of safe and efficacious vaccines as highest priority.\textsuperscript{79} After further studies, WHO issued a recommendation in 2007 to include PCV7 into national immunisation programs, especially in high disease burden countries.\textsuperscript{80} Two countries, Gambia and Rwanda, began vaccination using PCV7 through supplier donation in 2009. The WHO also recognised that countries introducing this


\textsuperscript{79} Weekly Epidemiological Record (2003) 78(14):97–120.

\textsuperscript{80} Weekly Epidemiological Record (2007) 82(12):93–104.
vaccine would want to consider switching to vaccines providing broader coverage (PCV10 or PCV13) when they become available.

Unlike YF, HepB, and Hib, assessing GAVI’s impact on accelerating pneumococcal vaccine introduction can only be done by forecasting introductions based on recent GAVI applications. Seventy-two countries have been eligible for pneumococcal vaccine support since 2006. Figure 2.5 shows the actual and projected number of countries introducing a pneumococcal vaccine in a given year and the cumulative percent of GAVI-eligible countries projecting to adopt a pneumococcal vaccine.

The projected number of country adoptions are based on approved applications (n=21), of which 19 countries are awaiting introduction.

*Figure 2.5: Projected pneumococcal vaccine introduction in GAVI-eligible countries*

While there was still a nine-year delay from first licensed vaccine to first GAVI-eligible country introduction, as stated previously, data supporting the use of PCV7 in developing countries was not available until 2007 when the WHO updated its recommendation. In addition, PCV7 was submitted for WHO prequalification in late 2006 but was not prequalified until 2009 due to a request for a change in the presentation from single dose pre-filled syringes to single dose vials.

If actual introduction were to match the current forecast, at least 35% of GAVI-eligible countries will have introduced a pneumococcal vaccine by 2011, much faster than any previous vaccine. However, several reasons suggest it is unlikely 19 countries will introduce a pneumococcal vaccine in 2010–11:

- No new introductions have occurred between the initial two in 2009 and July 2010.
- GAVI’s current financing gap may potentially motivate approved countries to reconsider or delay planned adoption.

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Impact of GAVI’s new eligibility policy on graduating country’s likelihood to introduce as planned (unlikely most graduating countries will be able to afford up to $3.50 per dose cost upon graduation).

While it is still too early to tell whether GAVI has accelerated the introduction of pneumococcal vaccines, GAVI’s efforts have truly accelerated the demand for pneumococcal vaccines. GAVI prioritised pneumococcal vaccines when it funded the PneumoADIP in 2003 to establish the value of vaccination, provide the evidence to decision-makers through effective communication, and ensure a predictable supply of quality vaccines at an affordable price. Through the efforts of the PneumoADIP, strategic demand forecasts were created and shared with vaccine suppliers to provide information on the potential supply needs for GAVI-eligible countries (see SG2.6). In addition, WHO prioritised the prequalification of pneumococcal vaccines, and GAVI made a commitment to finance pneumococcal vaccines in 2006 in response to the PneumoADIP investment case. PneumoADIP’s work has now transitioned to GAVI’s Accelerated Vaccine Introduction (AVI) initiative which started in 2009 and continues to advocate for pneumococcal vaccination and accelerated country decision-making.

Now that demand has been accelerated through the efforts of GAVI, the challenge will be to overcome GAVI’s current financing gap and to ensure the new AMC eligibility policy (i.e., graduating countries have access to AMC prices but not GAVI financing beyond the later of graduation year or 2015) does not slow country adoption decisions.

2.4.5. Rotavirus vaccine introduction analysis

The first rotavirus vaccine was licensed in 1998 and withdrawn from the market in 1999 due to increased risk of intussusception. It took an additional five years before the next rotavirus vaccine was licensed. The key vaccine-related events for rotavirus vaccines are shown in Table 2.6.

Table 2.6: Key rotavirus vaccine-related events

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year Licensed</th>
<th>Year Prequalified</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st rotavirus vaccine - withdrawn</td>
<td>1998</td>
<td>-</td>
</tr>
<tr>
<td>2nd rotavirus lyo vaccine (AMRO, EURO only)</td>
<td>2004</td>
<td>2007</td>
</tr>
<tr>
<td>3rd rotavirus liquid vaccine (AMRO, EURO only)</td>
<td>2006</td>
<td>2008</td>
</tr>
<tr>
<td>3rd rotavirus liquid vaccine (global)</td>
<td>2008</td>
<td>2009</td>
</tr>
</tbody>
</table>

Global Policy | Year of Recommendation
---|-------------------------|
Initial WHO recommendation (AMRO, EURO only) | 2007 |
Updated WHO recommendation (global) | 2009 |

In 2007, the WHO recommended use of rotavirus vaccines where the existing data supported its use (AMRO and EURO) and stated that additional data would be needed to recommend global immunisation. In 2009, the WHO updated its recommendation to

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include rotavirus vaccines in all national immunisation programs based on clinical trials conducted in Asia and Africa.\textsuperscript{84}

The Rotavirus Vaccine Program (RVP) was formed in 2003 and funded by GAVI. RVP focused on establishing the value of vaccination and helped accelerate global prequalification by working closely with suppliers to conduct pivotal trials in Africa and Asia needed for prequalification. The GAVI-funded RVP also developed a strategic demand forecast and developed an investment case that was the basis for GAVI funding of rotavirus vaccines in 2006.\textsuperscript{85} Like the PneumoADIP, RVP’s work to accelerate the introduction of rotavirus vaccines was transitioned to GAVI’s AVI in late 2008 where vaccine forecasting has now been consolidated under one group.

As with pneumococcal vaccines, assessing GAVI’s impact on the accelerated introduction of rotavirus vaccines can only be done by forecasting introductions based on recent GAVI applications.\textsuperscript{86} GAVI currently makes rotavirus vaccine support available to 72 GAVI-eligible countries. The actual and projected number of countries introducing a rotavirus vaccine in a given year and the cumulative percent of GAVI-eligible countries projecting to adopt a rotavirus vaccine through 2014 is shown in Figure 2.6.

\textit{Figure 2.6: Projected rotavirus vaccine introduction in GAVI-eligible countries}

The projected number of country adoptions are based on approved applications (n=10; 4 countries already introduced), of which six countries are awaiting introduction.\textsuperscript{87}

Nicaragua was the first GAVI-eligible country to introduce a rotavirus vaccine in 2006 as a result of three years of donated vaccine from the supplier. This was only eight years after the first licensed vaccine (withdrawn), and only two years after the licensure of the second vaccine, faster than any other new vaccine. However, unlike pneumococcal vaccines, where 19 countries are projected to introduce a pneumococcal vaccine in 2010–11, rotavirus

\textsuperscript{85} Accelerating the Introduction of Rotavirus Vaccines into GAVI-Eligible Countries, submitted by the Rotavirus Vaccine Program to GAVI on October, 2006
\textsuperscript{86} Personal communications, AVI, Feb–Jun 2010.
\textsuperscript{87} Ibid.
vaccine introduction is projected to be slower over the next several years. This current projection shows that only 6% of GAVI-eligible countries will have introduced a rotavirus vaccine five years after GAVI funding began compared to 35% of projected pneumococcal vaccine introductions, and 80%, 49%, and 13% of remaining countries introductions for YF, HepB-, and Hib-containing vaccines over the same five year funding timeframe (see Figures 2.2, 2.3, and 2.4). This is not a completely fair comparison given the global WHO recommendation was not in place for the first three years of GAVI funding. However, based on current approved applications, only 14% of GAVI-eligible countries are expected to introduce a rotavirus vaccine within five years of the global recommendation.

Future rotavirus vaccine introduction is expected to be highly uncertain for several reasons:

- GAVI’s current financing gap may delay approval of pending applications.
- Latin America and Europe have been slow to adopt rotavirus vaccines even though the vaccine became accessible to them after the regional WHO recommendation in 2007. Only 4 of the 14 countries initially eligible to adopt have done so in the 2007-2010 timeframe and the ten remaining countries have yet to submit a GAVI application for rotavirus vaccine funding.\(^{88,89}\)
- GAVI’s new eligibility policy may impact graduating country’s likelihood to submit applications or introduce as planned.

In conclusion, as with pneumococcal vaccines, GAVI has added value in creating demand for rotavirus vaccines primarily through the work of the GAVI-funded RVP and AVI. However, the current demand for rotavirus vaccine is believed to be much less than the current demand for pneumococcal vaccines. GAVI will need to quickly increase its focus on rotavirus vaccine introduction if it is to accelerate its introduction.

2.5. Comparative analysis

2.5.1. Underused vs. new vaccines comparison

To determine the potential impact and added value GAVI had on accelerating introduction of the new vaccines, the historic delay from first licensed vaccine to the introduction of YF, HepB-, and Hib-containing vaccines was compared to the forecasted delay in introduction for new vaccines in GAVI-eligible countries (Figure 2.7).

Historically, the delayed introduction of underused vaccines has been linked to a number of factors such as vaccine affordability, disease burden awareness, the lack of country health and immunisation infrastructure, the availability of prequalified vaccines, and clear policy guidance.\(^{90,91,92}\)

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89 Revision of GAVI’s Vaccine Supply Strategy: Proposed Project Plan, Doc. 04, Programme and Policy Committee Meeting, 17–18 February 2010.
91 Brookes A, Cutts FT, Justice J, Walt G. Policy Study of Factors Influencing the Adoption of New and Underutilised Vaccines in Developing Countries, 1999. Children’s Vaccine Initiative and USAID.
As summarised previously, GAVI partners and the GAVI-funded Yellow Fever and Hib Initiatives have added value by accelerating the introduction of YF and HepB- and Hib-containing vaccines since GAVI’s inception in 2000.

The lag between the first licensed pneumococcal vaccine and the first country introduction is not notably different from the HepB-containing vaccines (six years) and Hib-containing vaccines (11 years) when considering PCV7 licensure and introduction (nine years). However, the number of countries projected to adopt post the initial introduction, indicate pneumococcal vaccine introduction could be faster than any other GAVI vaccine introduction to date.

The lag between the first licensed rotavirus vaccine and the first country introduction is also not notably different (eight years) than pneumococcal or the HepB- and Hib-containing vaccines. However, current introduction projections based on approved applications indicate rotavirus introduction may be the slowest GAVI introduction to date. GAVI will need to increase its focus on rotavirus vaccine introduction in order to achieve introduction rates similar or better than pneumococcal and HepB- and Hib-containing vaccines.

2.5.2. Pre- and post-GAVI underused vaccine introduction comparison

While the cumulative rates of vaccine introduction provide an important perspective on GAVI’s impact on vaccine introduction, providing a more quantitative assessment is difficult because of the diversity among the GAVI-eligible countries and the economic differences across decades.

Recognising these limitations, Table 2.7 compares the number of introductions and the introduction rates of YF, HepB-, and Hib-containing vaccines into GAVI-eligible countries in the nine years before and after the formation of GAVI.
Table 2.7: Number of GAVI-eligible country introductions with and without GAVI funding

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Number of GAVI partner country introductions (Average # country introductions/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-GAVI funded from 1992–00</td>
</tr>
<tr>
<td>YF (n=28)</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>HepB (n=76)</td>
<td>16 (1.8)</td>
</tr>
<tr>
<td>Hib (n=76)</td>
<td>5 (0.6)</td>
</tr>
</tbody>
</table>

*YF excludes Bolivia, HepB excludes Nigeria and Timor-Leste, and Hib excludes Ukraine because these countries introduced without GAVI funding post-2001.

Overall, since GAVI was established, there was a 3-fold and a greater than 10-fold increase in country vaccine introductions for HepB- and Hib-containing vaccines, respectively. The increase in post-GAVI introduction of YF vaccine is more modest, but still represents a 38% increase in the rate of introduction.

The comparative data are consistent with the previous evidence and supports GAVI’s value in accelerating the introduction of underused vaccines. While the acceleration of YF is not as pronounced as that of the HepB- and Hib-containing vaccines, GAVI has added additional value by improving YF vaccine supply security and immunisation rates and sustainability.

2.5.3. Lower middle income country introduction comparison

While there is much diversity across the 72 GAVI-eligible countries, a direct comparison can be done with lower middle income countries that have similar GNI per capita levels. The following analysis examines introduction rates of income-matched non-GAVI-eligible to GAVI-eligible lower middle income countries for HepB- and Hib-containing vaccines. Even though this comparison has been conducted on income-matched lower middle income countries, by definition, GAVI’s lower middle income countries had 2003 GNI per capita of $766–$1000 while the non-GAVI countries had 2003 GNI per capita of $1000–$3035. While the number of comparable countries is limited, this is the most robust comparison that can be made because it controls for income level as a potential influencer of adoption timing.

HepB-containing vaccine introduction

The cumulative rate of HepB-containing vaccine introduction in GAVI- and non-GAVI-eligible lower middle income countries from the first licensed vaccine is shown in Figure 2.8.

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For non-GAVI-eligible countries, it took 14 years for 40 percent of the countries to introduce a HepB-containing vaccine versus 16 years for GAVI-eligible countries. From 1993 to 2000, GAVI-eligible lower middle income countries lagged in HepB-containing vaccine introduction compared to income-matched non-GAVI-eligible countries. The rate of introduction in GAVI-eligible countries was also less than in non-GAVI-eligible countries, as indicated by the shallower slope of the introduction curve.

Following the availability of GAVI funding in 2000, the rate of introduction increased in GAVI-eligible countries as shown by the roughly equivalent slopes of the country introduction curves. However, a two-year gap remained between non-GAVI-eligible countries and GAVI-eligible countries reaching an equivalent percentage of countries that had introduced HepB-containing vaccines. This gap was only closed in 2007, when 100% of GAVI-eligible and 97% of non-GAVI-eligible lower middle income countries had introduced a HepB-containing vaccine.

**Hib-containing vaccine introduction**

The cumulative rate of Hib-containing vaccine introduction in GAVI- and non-GAVI-eligible lower middle income countries from first licensed vaccine is shown in Figure 2.9.

For non-GAVI-eligible countries, it took 15 years for 40 percent of the countries to introduce a Hib-containing vaccine versus 20 years for GAVI-eligible countries. GAVI-eligible middle income countries lagged in Hib-containing vaccine introduction compared to income-matched non-GAVI-eligible countries, in spite of GAVI financing.
For Hib-containing vaccines, the lag of GAVI-eligible lower middle income countries is evident from the beginning and lags up to six years behind non GAVI-eligible countries. This is counter to expectations which would suggest that free vaccine (GAVI Phase I financing) or an affordable country co-pay (GAVI Phase II financing) would have motivated GAVI-eligible countries to introduce these vaccines much more quickly, especially because of the relatively high price of Hib-containing vaccines (see SG2.4). By 2007, this pattern was changing, as shown by the significant steepening of the GAVI-eligible country introduction curve. By 2009, both GAVI-eligible and non GAVI-eligible lower middle income countries had introduced a Hib-containing vaccine into ~70% of each respective country category. As with the HepB-containing vaccines, the reasons for this difference are not known, but metrics evaluating these differences should be considered.

2.6. Counterfactual analysis

2.6.1. New and underused vaccine introduction analysis

A counterfactual analysis of vaccines introduced without GAVI was not possible. Vaccine introductions not financed by GAVI either occurred under very different market conditions and times (e.g. BCG), or have not yet been introduced in GAVI-eligible countries (e.g. HPV).

However, a counterfactual analysis could be conducted on the assumed rate of country introduction without GAVI. Projected vaccine introduction rates prior to GAVI funding were compared to actual vaccine introduction rates following GAVI funding. Although there was no way to validate this assessment, the analysis assumed that GAVI-eligible countries would have continued to introduce YF, HepB-, and Hib-containing vaccines at the same linear rate post 2000 in the absence of GAVI. To account for the uncertainty in the assumptions used, two different timeframes were included in this analysis: the nine years prior to GAVI (1992–2000), and the four years prior to GAVI (1997–2000).
Yellow Fever vaccine introduction counterfactual

Figure 2.10 shows the two projected rates of YF vaccine introduction compared to the actual cumulative country introduction.

Figure 2.10: YF vaccine introduction scenarios using pre-GAVI rates compared to actual introduction with GAVI funding

When the 1992–2000 introduction rate was used, 18 GAVI-eligible countries were projected to have introduced a YF vaccine by 2009 compared to 24 countries with GAVI funding. When the 1997–2000 introduction rate was used, then 22 GAVI-eligible countries were projected to have introduced a YF vaccine, two countries less than actual country introduction with GAVI funding. However, with GAVI funding, country introduction was accelerated from 2000–04 compared to either linear projection.

Based on this counterfactual analysis, GAVI has added value by increasing the number and accelerating the timing of YF vaccine introduction.

HepB-containing vaccine introduction counterfactual

Figure 2.11 shows two projected rates of HepB-containing vaccine introduction compared to the actual cumulative country introduction.

When the 1992–2000 introduction rate was used, only 38 GAVI-eligible countries were projected to have introduced a HepB-containing vaccine by 2009, compared to 72 countries that introduced with GAVI funding. When the 1997–2000 introduction rate was used, then 49 GAVI-eligible countries were projected to have introduced a HepB-containing vaccine. The actual rate of HepB-containing vaccine introduction in the presence of GAVI was greater than expected based on the linear projections.

Based on this counterfactual analysis, GAVI has added value by significantly increasing the number and accelerating the timing of HepB-containing vaccine introduction.
Hib-containing vaccine introduction counterfactual

Figure 2.12 shows the two projected rates of Hib-containing vaccine introduction compared to the actual cumulative country introduction.

When the 1992–2000 introduction rate was used, only 10 GAVI-eligible countries were projected to have introduced a Hib-containing vaccine by 2009, compared to 62 countries that introduced with GAVI funding. When the 1997–2000 introduction rate was used, only 14 GAVI-eligible countries were projected to have introduced a Hib-containing vaccine. The actual rate of Hib-containing vaccine introduction in the presence of GAVI was much greater than expected based on the linear projections.
When assuming linear pre-GAVI introduction rates continued beyond 2000, the counterfactual analysis strongly suggested a significant impact of GAVI on accelerating the introduction of HepB- and Hib-containing vaccines. As with other evidence provided, the counterfactual analysis suggested a more modest impact of GAVI on YF vaccine introduction.

Based on this counterfactual analysis, GAVI has added value by significantly increasing the number and accelerating the timing of Hib-containing vaccine introduction.

2.7. Qualitative Analyses

2.7.1. Electronic survey feedback

To assess the perception of key global stakeholders on GAVI’s impact on accelerating new and underused vaccine introduction, responses to the following statements were evaluated:

- GAVI has accelerated the uptake of HepB, Hib, and YF by partner countries
- GAVI has accelerated the uptake of rotavirus, pneumococcal, and meningitis A vaccines by partner countries.

As shown in Figure 2.13, over 80% of survey respondents ‘strongly agreed’ or ‘agreed’ that GAVI had accelerated the uptake of underused vaccines, while only 2% ‘strongly disagreed’ or ‘disagreed’. Fifty of the 80 respondents (62%) who provided a qualitative response specifically mentioned that acceleration was due to GAVI.

Figure 2.13: E-survey responses to question 11 – ‘GAVI has accelerated the uptake of Hep B, Hib, and YF vaccines by partner countries (282 responses of which 259 were non-blank)

For new vaccines, 57% of respondents ‘strongly agreed’ or ‘agreed’ that GAVI had accelerated the uptake of new vaccines, while more than 10% ‘strongly disagreed’ or ‘disagreed’ (Figure 2.14).
Of the 108 respondents who provided a qualitative response to this question, 15 (14%) felt that it was too early to comment. Another 13 respondents (12%) commented that introduction had been stalled, delayed, or slow.

Results from the electronic survey strongly support GAVI’s role in accelerating underused vaccines; however, responses were mixed on GAVI’s impact on accelerating the introduction of new vaccines.

### 2.7.2. Structured interview results

Of the 22 current and past GAVI Board members who participated in the structured interviews, 19 (86%) commented on the extent GAVI had accelerated the uptake of new and underused vaccines by partner countries. Of these 19, 16 respondents (84%) felt GAVI had done a ‘good’ or ‘excellent’ job accelerating uptake in general, or specifically the uptake of underused vaccines. Only nine interviewees commented on GAVI’s role in accelerating new vaccines. These comments varied from acknowledging GAVI’s role in accelerating demand to recognising the financial crisis and its potential adverse impact on introduction.

While these data are limited given the small number included in the structured interviews, the majority of those who commented believed GAVI had accelerated the uptake of underused vaccines.

### 2.7.3. Country visit results

Five country visits were conducted as a part of GAVI’s Phase II evaluation. While structured questions were not asked regarding GAVI’s role in accelerating vaccine introduction, a variety of country-specific insights were generated from these consultations.
Bangladesh

Bangladesh has received GAVI NVS support since 2003 for HepB monovalent vaccine introduction. In 2008, Bangladesh switched to pentavalent vaccination. From 2003–09, Bangladesh received a total of $73.3m in NVS support ($20.2m for HepB and $51.8m for pentavalent). Bangladeshi officials, and in particular the Ministry of Health officials, attribute introduction of HepB and pentavalent vaccines to GAVI’s financial support.

Mali

Mali has received GAVI NVS support since 2002. From 2002–15, $80.5m of support was approved for YF, HepB, pentavalent, and pneumococcal vaccines. Malian officials also credited GAVI’s financial support with helping diversify the antigens included in its national immunisation program.

Nigeria

Nigeria has received GAVI NVS support for YF vaccines since 2003. From 2003–09, $22.7m was disbursed. Nigerian officials confirmed that prior to receiving GAVI NVS support, Nigeria was routinely vaccinating with YF, but availability of the vaccine was irregular. GAVI’s financial support helped stabilise the YF supply. Nigerian officials said that additional demand creation at the local level is still needed to increase YF uptake.

Nigerian officials also reported concerns about the process of submitting applications for HepB and pentavalent support. Application resubmission was requested by GAVI and there was confusion within the Nigerian government as to why this was required. The resubmission request resulted in Nigeria investing in cold chain capacity that will not be used. This created internal political ramifications, as those who worked to build political support and secure funds to cover the co-financing amounts lost credibility after the resubmission request. The resubmission request also resulted in delayed DTP vaccine procurement, since the country’s DTP order was cancelled in anticipation of pentavalent introduction.

Bolivia

Bolivia has received GAVI NVS support for rotavirus vaccine in 2008 with $14m approved for support between 2008–15. Bolivia purchases all of its vaccines through the PAHO Revolving Fund. Bolivian officials commented the country’s experience with rotavirus introduction was good due to the acceptability of the oral presentation. The single dose presentation was also felt to reduce wastage.

Delays in GAVI disbursements to the Revolving Fund meant Bolivia had to use its own funds to secure rotavirus vaccine, and these were funds meant for other vaccines. Bolivia was excluded from the Revolving Fund for three months and, combined with the use of other earmarked funds, was unable to secure enough EPI vaccines for the population. This led to a temporal decline in vaccination coverage for other antigens.

Bolivian officials credited rotavirus vaccine introduction with a 40% reduction in hospitalisations for diarrhoea. When asked, the EPI team indicated they thought the
existence of GAVI had brought forward the introduction of rotavirus vaccine by at least five years for their country.

Uzbekistan

Uzbekistan has received NVS support from 2001-08 for HepB ($4.5 million). GAVI support for pentavalent began in 2009. Uzbek stakeholders were unequivocal in their belief that GAVI support was instrumental in facilitating the introduction and uptake of both of the supported vaccines in country, and especially for the pentavalent vaccine. Some stakeholders suggested in the absence of GAVI support, perhaps Uzbekistan may have introduced the HepB vaccine on its own, although with some delay. However, in the case of pentavalent vaccine, given the higher price, it was understood to be highly unlikely the vaccine would have been introduced without GAVI funding. Going forward, Uzbek officials plan to introduce the rotavirus and pneumococcal vaccines, and stakeholders suggested, again given the price, the introduction of these vaccines would be highly unlikely without GAVI funding support. Uncertainty was expressed about potential upcoming co-financing changes.

2.8. Conclusions

GAVI has added value by accelerating the introduction of underused vaccines. The cumulative number of countries introducing these vaccines, as well as the rate of country introduction has increased post-GAVI. GAVI's impact on accelerating vaccine uptake for YF and HepB- and Hib-containing vaccines was also supported by the counterfactual analysis that showed country adoption occurred sooner than would have been expected based on pre-GAVI introduction rates.

For pneumococcal vaccines, it is too soon to tell whether GAVI has accelerated introduction, however, the evidence strongly suggests GAVI has accelerated the demand based on 21 GAVI application approvals with 2 country introductions and 19 countries awaiting introduction. It is unclear whether actual introduction will be as fast as projected, given the challenges associated with GAVI’s current funding gap and the potential impact of country graduation on pneumococcal introduction.

Although early rotavirus vaccine introduction has been seen in several Latin American countries, it is too soon to tell whether rotavirus vaccine introduction will be accelerated. However, current AVI introduction projections indicate rotavirus could introduce more slowly than pneumococcal and HepB- and Hib-containing vaccines. Several challenges will need to be overcome to accelerate introduction, including overcoming GAVI's current funding gap and increasing the level of advocacy for rotavirus introduction, especially with the upcoming changes in GAVI eligibility.

Comparisons between income-matched lower middle income countries with and without GAVI funding showed GAVI-eligible lower middle income countries for HepB- and Hib-containing vaccines.
Results from the electronic surveys and structured interviews indicated that the majority of the survey respondents and interviewees felt GAVI accelerated uptake of underused vaccines. However, fewer respondents felt that GAVI had accelerated the uptake of pneumococcal and rotavirus vaccines.

Results from the country visits credited GAVI with accelerating introduction of vaccines into their countries.

The robustness of the conclusions included in this section are summarised in Table 2.8 based on a relative rating scale described in section 1.1.3 of the Introduction.

Table 2.8: Relative robustness of the SG2.1 findings

<table>
<thead>
<tr>
<th>Evaluation question SG2.1: To what extent has the GAVI Alliance accelerated the uptake of underused and new vaccines by partner countries?</th>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GAVI’s impact on accelerating YF vaccine introduction</strong></td>
<td>GAVI had a positive impact on accelerating YF vaccine introduction into YF endemic countries.</td>
<td>• The cumulative number of countries introducing YF increased from 46% to 86% since GAVI’s inception. • The average number of country introductions per year increased by 38% post GAVI. • The counterfactual analysis indicated earlier adoption than expected for 2–6 more countries. • In addition, GAVI stockpile funding mitigated use of infant vaccines for outbreak control, thereby improving vaccination coverage rates and immunisation program sustainability.</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td><strong>GAVI’s impact on accelerating HepB-containing vaccine introduction</strong></td>
<td>GAVI had a significant impact on accelerating HepB-containing vaccine introduction.</td>
<td>• The cumulative number of countries introducing HepB-containing vaccines has increased from 29% to 97% since GAVI’s inception. • The average number of country introductions per year increased three-fold post GAVI. • The counterfactual analysis indicated earlier adoption than expected for 23–34 more countries.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Data comes from reliable sources (e.g., WHO introduction year database).</td>
<td>All evaluation analyses (e.g. e-survey, interviews) support the conclusion.</td>
</tr>
</tbody>
</table>
**Evaluation question SG2.1:** To what extent has the GAVI Alliance accelerated the uptake of underused and new vaccines by partner countries?

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
</table>
| GAVI's impact on accelerating Hib-containing vaccine introduction       | • GAVI had a significant impact on accelerating Hib-containing vaccine introduction, especially after 2007.  
- The cumulative number of countries introducing Hib-containing vaccines has increased from 7% to 83% since GAVI's inception.  
- Average number of country introductions per year increased greater than 10-fold post GAVI.  
- Counterfactual analysis indicated earlier adoption than expected for 48 – 52 more countries.                                                                                     | A          |
| GAVI's impact on accelerating pneumococcal vaccine introduction         | • GAVI has accelerated demand based on approved GAVI applications (n=21; 2 introduced, 19 awaiting introduction).  
- It is too soon to know GAVI's actual impact on accelerated introduction, but accelerated introduction may be at risk due to the current funding gap and new GAVI eligibility policy. |
| GAVI’s impact on accelerating rotavirus vaccine introduction            | • Current projections based on actual introductions (n=4) and approved applications (n=6) indicate rotavirus introduction could be slower than previous GAVI-funded vaccine introductions.  
- Only 14% of GAVI countries are projected to introduce within 5 years of the global WHO recommendation decision compared to 80%, 49%, and 13% of remaining YF, HepB-, and Hib-containing introductions in the first five years of GAVI funding, respectively, and compared to 30% of projected pneumococcal vaccine introductions over the first five year funding timeframe. | A          |

A • Data comes from reliable sources (e.g., WHO introduction year database).  
• All evaluation analyses support conclusion.

A • Data comes from reliable sources (e.g., GAVI applications submitted, GAVI Board documents), but conclusions are based on a single analysis of application projections.

A • Data comes from reliable sources (e.g., GAVI applications submitted, GAVI Board documents), but conclusions are based on a single analysis of application projections.
3. **SG2.2: SCALING UP VACCINE COVERAGE**

3.1. **Introduction**

The second Strategic Goal 2 evaluation question is, “To what extent have countries introducing underused and new vaccines been able to take them to scale quickly, i.e. achieve full scale coverage?”

To maximise the impact of life-saving vaccines, it is important for countries to achieve peak vaccination coverage rates as quickly as possible. To maximise the impact of its programs, it is important to GAVI that it provide programs with high scalability. Although GAVI does not make explicit investments focused on accelerating time to peak, it has committed 11% of its budget for 2000–15 to strengthen health and immunisation systems within GAVI-eligible countries (see sections SG1.2 and SG1.3 for details on GAVI’s Health Systems Strengthening and Immunisation Systems Strengthening programs, respectively).

3.2. **Scope of the evaluation question**

This section determines the time to peak vaccination coverage for vaccines introduced by GAVI-eligible countries and explores factors that may influence how quickly peak coverage is reached. This time to peak analysis focuses on YF, HepB-, and Hib-containing vaccines. Because pneumococcal and rotavirus vaccines were not introduced in significant numbers during 2000–09, they have been excluded from this analysis. The evaluation is expected to include data through 2009; however, vaccination coverage rate data was available only through 2008.

The evaluation:

- Calculated time to achieve peak coverage for all GAVI-eligible countries that have introduced YF, and HepB-, or Hib-containing vaccines with GAVI NVS support.
- Analysed Annual Progress Reports (APRs) and incorporated relevant qualitative information to identify causes associated with longer times to achieve peak coverage.
- Examined the relationship between time to achieve peak coverage for HepB- and Hib-containing vaccines and each of the following: GAVI ISS support, WHO region, GAVI financing tier, and country size.
- Conducted a comparative analysis on time to peak coverage for Hib-containing vaccines introduced in GAVI-eligible lower middle income countries (LMICs) versus time to peak coverage in non-GAVI LMICs.
- Attempted to conduct a comparative analysis on time to peak coverage for GAVI-eligible countries introducing vaccines with GAVI NVS support versus GAVI-

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94 CEPA – GAVI Phase I & II consolidated approvals & disbursements; provided by the GAVI Secretariat, 10 March 2010.
eligible countries introducing vaccines without GAVI NVS support at time of introduction or before peak.

- Attempted to conduct a counterfactual analysis on time to achieve peak coverage in GAVI-eligible countries introducing vaccines without any GAVI support versus GAVI-eligible countries introducing these vaccines with at least GAVI NVS support.

### 3.3. Methodology

#### 3.3.1. Overview

The time to peak coverage was defined as the time between vaccine introduction and when peak coverage is reached. The introduction date methodology for all three vaccines differs from the introduction date methodology used in other SG2 evaluation sections. In this section, introduction date was defined as the year in which a country first reports coverage rate data to the WHO.\(^95\) Therefore, this date may differ from the introduction date reported in the WHO introduction year database.\(^96\)

The methodology to determine the time to peak coverage differed between YF and HepB- and Hib-containing vaccines due to the different vaccination schedules for the two sets of vaccines.

YF is a single dose vaccine given at approximately nine months of age, similar to the first dose of measles vaccine (MCV).\(^97\) Therefore, MCV vaccination rates were used as a proxy for achieving peak YF coverage because MCV coverage rates represent the highest percentage of infants vaccinated with the same dosing schedule.\(^98\)\(^99\) If the YF coverage rate was within 10 percentage points of the measles coverage rate in a single year, YF vaccination was assumed to have reached peak coverage in that year.\(^100\) Country reported YF coverage rates were used and compared to reported MCV coverage rates because WHO/UNICEF does not estimate coverage rates for YF vaccines.

HepB- and Hib-containing vaccines are three dose vaccines delivered on the same schedule as DTP vaccines. Therefore, HepB3 and Hib3 coverage rates were compared to DTP3 coverage rates to determine peak coverage. DTP3 vaccination rates were used as a proxy for achieving peak coverage because these coverage rates represent the highest percentage of infants vaccinated with the same dosing schedule used for HepB- and Hib-containing vaccines. If the HepB3 or Hib3 coverage rate was within 10 percentage points of the DTP3 coverage rate in a single year, HepB or Hib vaccination was assumed to have reached peak coverage in that year.\(^101\) Annual DTP3, HepB3, and Hib3 WHO/UNICEF estimated coverage rates were used.\(^102\)\(^103\)\(^104\)

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\(^96\) [http://www.who.int/entity/immunisation_monitoring/data/year_vaccine_introduction.xls](http://www.who.int/entity/immunisation_monitoring/data/year_vaccine_introduction.xls) (accessed 23 June 2010).


\(^101\) Ibid.

It is well known that some vaccine product types are easier to introduce than others.\textsuperscript{105} To account for this, the time to peak analysis for HepB- and Hib-containing vaccines was further segmented into the time to peak for:

- Vaccine additions (i.e. HepB mono or Hib mono vaccines)
- Vaccine switches (e.g. DTwP vaccine switched to DTwP-HepB, DTwP-Hib or DTwP-HepB-Hib vaccine).

Two sources of qualitative information were also analysed in this section. First, country APRs were reviewed to better understand the reasons behind longer than average times to peak coverage.\textsuperscript{106} Second, all relevant comments from the five country visits were included as anecdotal evidence of the issues that could impact time to peak coverage.

The evidence sources used to evaluate this question are summarised in Table 3.1.

\emph{Table 3.1: Evidence sources and descriptions for the time to peak coverage rate analysis}

<table>
<thead>
<tr>
<th>Evidence source</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of documentation</td>
<td>Type of HepB-, or Hib-containing vaccine introduced (e.g. GAVI approvals data, Hib Initiative data on non-GAVI LMI vaccine use) Coverage rates for YF, HepB-, and Hib-containing vaccines Country APRs for slower time to peak coverage rationale</td>
</tr>
<tr>
<td>E-survey</td>
<td>The general electronic survey did not seek input on this question.</td>
</tr>
<tr>
<td>Structured Interview</td>
<td>The structured interviews did not seek input on this question.</td>
</tr>
<tr>
<td>EPI manager survey</td>
<td>The EPI manager survey did not seek input on this question.</td>
</tr>
<tr>
<td>Country visits</td>
<td>Three of the five country consultations resulted in ad hoc comments related to this question.</td>
</tr>
<tr>
<td>Information/data gathering meetings</td>
<td>Missing data/information on product adoptions was requested from WHO and UNICEF.</td>
</tr>
</tbody>
</table>

\subsection{3.3.2. \textbf{Comparative analysis}}

To determine how well GAVI-eligible countries perform on the time to peak coverage dimension, a comparative analysis was conducted on LMICs introducing vaccines during 2001–08 (2008 is the last year for published coverage rate data). GAVI-eligible LMICs that introduced Hib-containing vaccines in this timeframe with GAVI support were compared to non-GAVI-eligible LMICs that introduced Hib-containing vaccines in this timeframe.

YF vaccines were not included in this comparative analysis because there were no YF introductions by GAVI-eligible LMICs in this time period. HepB-containing vaccines were

\begin{footnotesize}
\begin{itemize}
\item \textsuperscript{105} http://apps.who.int/immunisation_monitoring/en/globalsummary/timeseries/tswucovhpep3.htm (accessed 15 May 2010).
\item \textsuperscript{104} http://apps.who.int/immunisation_monitoring/en/globalsummary/timeseries/tswucovhepb3.htm (accessed 15 May 2010).
\item \textsuperscript{106} http://www.gavialliance.org/vision/policies/supply/index.php (accessed 26 July 2010)
\item \textsuperscript{107} http://www.gavialliance.org/performance/country_results/index.php (accessed March – June 2010).
\end{itemize}
\end{footnotesize}
not included in this analysis because the type of HepB-containing vaccine (i.e. addition versus switch) introduced by non-GAVI LMICs during this timeframe was unknown.\textsuperscript{107}

Additional comparative analyses were conducted to determine the potential impact of GAVI NVS support on the differences in time to peak coverage. This analysis compared time to peak results for GAVI-eligible countries introducing a vaccine with GAVI NVS support to those introducing or reaching peak without GAVI NVS support from 2001 - 2008.

The YF vaccine comparative analysis results were not included due to the small sample size. Only 6 countries introduced a YF vaccine in the 2001–08 study period with GAVI NVS support and only 3 without GAVI NVS support. (2 of these 3 countries reached peak within 1 year and 1 required 8 years.)

The HepB-containing vaccine comparative analysis could not be conducted because of dissimilar study periods; the 20 HepB vaccine additions with GAVI NVS support occurred in the 2001–08 timeframe and the 10 HepB product additions without GAVI NVS support occurred in the 1990–95 timeframe. (Time to peak coverage ranged from one to eight years.)

The Hib-containing vaccine comparative analysis results were also not included due to small sample size. Although 24 countries introduced a Hib-containing vaccine as a product switch in the 2001–08 timeframe, only 2 of the 7 countries that introduced without GAVI NVS support did so as a product switch in the 2001–08 timeframe. (Both of these countries achieved peak coverage in the first year.)

3.3.3. Counterfactual analysis

The appropriate counterfactual for assessing whether GAVI-eligible countries receiving GAVI NVS support at time of introduction are able to scale more quickly than if they introduced without GAVI support would be to compare the time to peak for GAVI-eligible countries introducing with and without any kind of GAVI support from 2001–08 (i.e. NVS, HSS, ISS, CSO). However, there was insufficient data available to conduct this type of analysis.

YF vaccines could not be included in this counterfactual analysis because:

- Time to peak coverage for 5 of the 8 countries that introduced without GAVI support could not be determined based on the available data.
- Of the 3 remaining countries, 2 introduced and reached peak in the 1980’s and therefore, could not be compared to introductions by countries with GAVI NVS support that took place from 2001 onward.
- The one remaining country introduced in 2000, but had missing and inconsistent coverage rate reporting, making the time to peak outcome less reliable.

\textsuperscript{107} Personal communication, WHO, 22 June 2010.
HepB-containing vaccines could not be included in the counterfactual analysis because:

- Of the 17 HepB-containing vaccines that introduced or reached peak without GAVI support, 16 introduced a HepB-containing vaccine during the 1990–95 timeframe.
- The country that introduced without GAVI support during the 2001–08 timeframe reached peak in year 3, but this result could not be properly interpreted because the product type was unknown.

Hib-containing vaccines were not included in the counterfactual analysis because of small sample size. Only 2 of the 7 countries that introduced without GAVI support did so in the 2001–08 timeframe. Both these countries achieved peak in the first year compared to 17 of 24 GAVI-supported countries reaching peak in the first year. There were no meaningful insights generated from this analysis.

### 3.3.4. Limitations

These analyses have limitations due to:

- Questionable precision in time to peak coverage calculations due to low quality of immunisation coverage rates reported by countries to UNICEF and WHO.  

- Potential error in reported coverage rates (“± 3 percentage points with perhaps a maximum of ± 20 percentage points” is possible); time to peak calculations could vary by one or more years.

- Missing or erratic coverage rate data for YF vaccines; relying on country reported coverage rates rather than WHO/UNICEF estimated coverage rates.

- Inconsistent and erratic measles coverage rates, which make measles a less appropriate comparison for evaluating YF vaccine time to peak coverage.

- Small sample size for analysing YF introductions with GAVI NVS support (n=6).

- Interpretation challenges with HepB- and Hib-containing vaccine introductions involving a vaccine addition versus a vaccine switch or a switch from one type of HepB- or Hib-containing vaccine to another.

- Lack of data on what type of HepB- and Hib-containing vaccine products were introduced by GAVI-eligible countries not receiving GAVI funding and non-GAVI-eligible LMICs.

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112 Personal communication, WHO, 22 June 2010.
• Small sample sizes when comparing time to peak coverage by region, financing tier, and country size.

• Small set of evaluable cases for comparing GAVI LMIC (n=4) and non-GAVI LMIC (n=7) time to peak for Hib-containing vaccines.

• Lack of cases for comparing GAVI-eligible country vaccine introductions with and without GAVI NVS funding.
  o No evaluable introduction cases without GAVI support for YF or HepB-containing vaccines.
  o Only 2 evaluable introduction cases for Hib-containing vaccines.

• Minimal or no documentation providing rationale for longer than average times to peak coverage for any of the three vaccines evaluated\(^\text{113}\)

• Incomplete APRs, limiting data available for determining potential drivers of longer than average times to peak\(^\text{114}\)

• Minimal or no qualitative data available from structured interviews, electronic surveys, country visits, or other information-gathering meetings.

3.4. Evaluation analysis

3.4.1. YF vaccines time to peak coverage analysis

Of the 28 GAVI-eligible countries that qualified for GAVI YF vaccine support, only 9 were considered evaluable and only 6 qualified for the evaluation analysis. The rationale for SG2.2 evaluation inclusion and exclusion is provided in Table 3.2.

Table 3.2: Rationale for country inclusion/exclusion in YF vaccine time to peak evaluation or other analyses

<table>
<thead>
<tr>
<th>Country Classification</th>
<th>#</th>
<th>Analysis Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduced in 2001-08 timeframe with GAVI NVS support at time of introduction</td>
<td>6</td>
<td>Included in Evaluation Analysis</td>
</tr>
<tr>
<td>Introduced in 2001-08 timeframe and did not receive GAVI funding or received funding only after peak was reached</td>
<td>3</td>
<td>Excluded from comparator analysis due to small sample size</td>
</tr>
<tr>
<td>Have not yet introduced</td>
<td>3</td>
<td>Excluded from the Evaluation</td>
</tr>
<tr>
<td>Introduced before 2001</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Did not reach peak by 2008</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Received GAVI support after introduction, but before peak (unable to segment)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Erratic YF and MCV vaccine coverage rates inhibit time to peak determination (likely due to YF supply shortages, financial constraints, inaccurate reporting)</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>


\(^{114}\) Ibid.
The time to peak coverage for the six GAVI-eligible countries that received GAVI NVS funding support at the time of YF vaccine introduction are summarised in Table 3.3. These rates are compared to the measles containing vaccine (MCV) rates to determine time to peak.

Table 3.3: YF versus MCV coverage rates for countries receiving GAVI support at time of introduction

<table>
<thead>
<tr>
<th>Country</th>
<th>YF versus MCV Coverage Rates (Year)</th>
<th>Time to Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congo, Rep.</td>
<td>YF (MCV)</td>
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</tr>
<tr>
<td></td>
<td>1992</td>
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<td>1993</td>
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<td>2007</td>
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<td></td>
<td>2008</td>
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<tr>
<td>DRC</td>
<td>8% (53%)</td>
<td>1</td>
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<tr>
<td></td>
<td>1992</td>
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<td>2007</td>
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<td></td>
<td>2008</td>
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<tr>
<td>Guinea</td>
<td>0% (56%)</td>
<td>3</td>
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<tr>
<td></td>
<td>1992</td>
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<td></td>
<td>2008</td>
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<tr>
<td>Liberia</td>
<td>0% (50%)</td>
<td>5</td>
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<tr>
<td></td>
<td>1992</td>
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<td>2008</td>
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<tr>
<td>Sao Tome and Principe</td>
<td>2% (52%)</td>
<td>2</td>
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<tr>
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<td>1992</td>
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<td></td>
<td>2006</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td></td>
</tr>
<tr>
<td>Togo</td>
<td>37% (64%)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1992</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1993</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1994</td>
<td></td>
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<td>1995</td>
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<td>2004</td>
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<td>2005</td>
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<td>2006</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td></td>
</tr>
</tbody>
</table>

Grey = Year GAVI NVS support received  
RED = Estimated peak coverage year

Three of these six countries first introduced a YF vaccine in the early 1990’s, but were unable to sustain the vaccination program. Given the 8 – 10 year gap between this initial introduction and the seemingly sustainable introduction in the 2000’s, these three countries were included in the evaluation analysis.

The six countries range in time to peak coverage from 1 to 5 years, with a median time to peak of three years. YF vaccine supply shortages in the 1987–2001 timeframe (SG2.3, section 4.4.1) may have hindered countries from achieving scale more quickly. In the case of Liberia, routine vaccination supplies were leveraged for recurrent outbreaks during the 2002–04 timeframe, resulting in lower than expected YF coverage rates and a slower than average time to peak.115

Relationship analyses were not conducted for YF vaccines due to the small number of evaluable countries (n=6).

3.4.2. HepB-containing vaccines time to peak coverage analysis

Of the 76 GAVI-eligible countries that qualified for GAVI HepB-containing vaccine support, 45 qualified for the evaluation analysis. The rationale for SG2.2 evaluation inclusion and exclusion is provided in Table 3.4.

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Table 3.4: Rationale for country inclusion / exclusion in HepB-containing vaccine time to peak evaluation or other analyses

<table>
<thead>
<tr>
<th>Country Classification</th>
<th>#</th>
<th>Analysis Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduced in 2001-08 timeframe with GAVI support at time of introduction</td>
<td>45</td>
<td>Included in Evaluation Analysis</td>
</tr>
<tr>
<td>Introduced in 2001-08 timeframe and did not receive GAVI funding or received funding only after peak was reached</td>
<td>1</td>
<td>Excluded from comparator analysis due to small sample size</td>
</tr>
<tr>
<td>Have not yet introduced</td>
<td>2</td>
<td>Excluded from the Evaluation</td>
</tr>
<tr>
<td>Introduced before 2001</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Did not reach peak by 2008</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Received GAVI support after introduction, but before peak (unable to segment)</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

The percentage of countries that achieve peak coverage within 1, 2, 3, 4, or 5 years from initial introduction of a HepB-containing vaccine in 45 countries receiving GAVI NVS support at time of introduction is shown in Table 3.5.

Table 3.5: Percent of countries achieving peak coverage within 5 years from initial introduction of a HepB-containing vaccine in countries receiving GAVI support at time of introduction (n=45)

<table>
<thead>
<tr>
<th>Percent of countries achieving peak in specified time frame</th>
<th>Median Time to Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr</td>
<td>2 yr</td>
</tr>
<tr>
<td>58% (n=26)</td>
<td>22% (n=10)</td>
</tr>
</tbody>
</table>

For these 45 countries, 80 percent were able to reach peak coverage within two years and nearly 90 percent within three years. The median time to peak was one year.

To better understand the time to peak results, the data was further segmented by the type of vaccine introduction (i.e. product addition or product switch). A product addition is defined as the introduction of a HepB mono vaccine and a product switch is defined as the introduction of a DTwP-HepB tetravalent or a DTwP-HepB-Hib pentavalent vaccine. The vaccine type was determined based on GAVI country approvals data.\(^{116}\)

Table 3.6 summarises percent of countries that achieve peak coverage within 1, 2, 3, 4, or 5 years from initial introduction for each product type of HepB-containing vaccine in countries receiving GAVI NVS support at time of introduction.

This analysis indicates that product additions take up to three years to reach peak in more than 80 percent of introductions occurring with GAVI NVS support. This is in comparison to product switches, which take only one year to achieve peak in 80 percent of the introductions occurring with GAVI NVS support. The median type to peak for product additions was 2 years and for product switches was 1 year.

\(^{116}\) Timeframe of GAVI support to countries as of 30 Nov 2009; provided by the GAVI Secretariat, January 2010.
Table 3.6: Percent of countries achieving peak coverage within 5 years from initial introduction of a HepB-containing vaccine in countries receiving GAVI support at time of introduction

<table>
<thead>
<tr>
<th>Vaccine Introduction Type</th>
<th>Percent of countries achieving peak in specified time frame</th>
<th>Median Time to Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 yr</td>
<td>2 yrs</td>
</tr>
<tr>
<td>Product Addition (n=20)</td>
<td>25%</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>(n=5)</td>
<td>(n=8)</td>
</tr>
<tr>
<td>Product Switch (n=25)</td>
<td>84%</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td>(n=21)</td>
<td>(n=2)</td>
</tr>
</tbody>
</table>

Regardless of vaccine type, five countries required more than three years to achieve peak coverage. Qualitative information was gathered to determine why these countries may have required additional time. Country APRs and relevant ad hoc responses from the in-country consultations were the main sources of information, as summarised in Table 3.7.

Table 3.7: Potential drivers of delay for countries requiring more than three years to achieve peak coverage

<table>
<thead>
<tr>
<th>Year Peak Coverage Rate Achieved</th>
<th>Country</th>
<th>Intro Year</th>
<th>Product Type</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>5th Year</td>
<td>Nepal(^{117})</td>
<td>2003</td>
<td>mono</td>
<td>Due to delayed vaccine shipments</td>
</tr>
<tr>
<td></td>
<td>Bangladesh(^{118})</td>
<td>2003</td>
<td>mono</td>
<td>Planned for a phased introduction Additional delay due to a tetra supply shortage resulting in monovalent vaccine adoption at start</td>
</tr>
<tr>
<td></td>
<td>Cote d'Ivoire(^{119})</td>
<td>2001</td>
<td>tetra</td>
<td>Delays due to political unrest</td>
</tr>
<tr>
<td>4th Year</td>
<td>Myanmar(^{120})</td>
<td>2003</td>
<td>mono</td>
<td>Planned for a phased introduction</td>
</tr>
<tr>
<td></td>
<td>Tajikistan(^{121})</td>
<td>2002</td>
<td>mono</td>
<td>Planned for a phased introduction</td>
</tr>
</tbody>
</table>

The relationships between time to peak coverage for HepB-containing vaccines and GAVI ISS funding, WHO region, GAVI financing tier, and country size were also examined to understand if these factors influence the time countries require to reach scale. The analysis results indicated no relationship between these factors and time to scale. This is likely due to the fact that 80 percent or more of all HepB-containing vaccine introductions reach peak within two years, leaving little room to discern what factors may result in a faster time to peak coverage.

3.4.3. Hib-containing vaccines time to peak coverage analysis

Of the 76 GAVI-eligible countries that qualified for GAVI Hib-containing vaccine support, 24 qualified for the evaluation analysis. The rationale for SG2.2 evaluation inclusion and exclusion is provided in Table 3.8.


Table 3.8: Rationale for country inclusion/exclusion in Hib-containing vaccine time to peak evaluation or other analyses

<table>
<thead>
<tr>
<th>Country Classification</th>
<th>#</th>
<th>Analysis Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduced in 2001-08 timeframe with GAVI support at time of introduction</td>
<td>24</td>
<td>Included in Evaluation Analysis</td>
</tr>
<tr>
<td>Introduced in 2001-08 timeframe and did not receive GAVI funding or received funding only after peak was reached</td>
<td>2</td>
<td>Excluded from comparator analysis due to small sample size</td>
</tr>
<tr>
<td>Have not yet introduced</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Introduced before 2001</td>
<td>5</td>
<td>Excluded from the evaluation</td>
</tr>
<tr>
<td>Did not reach peak by 2008</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Did not report coverage data</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

The percent of countries that achieve peak coverage within 1, 2, 3, 4, or 5 years from initial introduction for Hib-containing vaccine time to peak coverage for the 24 countries receiving GAVI NVS support at time of introduction is shown in Table 3.9.

Table 3.9: Percent of countries achieving peak coverage within 5 years from initial introduction of a Hib-containing vaccine in countries receiving GAVI support at time of introduction (n=24)

<table>
<thead>
<tr>
<th>Percent of countries achieving peak in specified timeframe</th>
<th>Median Time to Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr (n=17)</td>
<td>2 yr (n=4)</td>
</tr>
<tr>
<td>71%</td>
<td>17%</td>
</tr>
</tbody>
</table>

For these 24 countries, nearly 90 percent were able to reach peak coverage within two years and nearly 95 percent within three years. The median time to peak was 1 year.

To better understand the time to peak results, the data was further segmented by the type of vaccine introduction. For these countries, all 24 introductions were vaccine switches, which help explain the relatively rapid time to peak for these countries.

Two countries took more than 3 years to reach peak coverage. Qualitative information was gathered to determine why these countries may have required additional time. Country APRs and relevant ad hoc responses from the in-country consultations were the main sources of information, as summarised in Table 3.10.

The relationships between time to peak coverage for Hib-containing vaccines and GAVI ISS funding, WHO region, GAVI financing tier, and country size were also examined to understand if these factors influence the time countries require to reach scale. The analysis results indicated no relationship between these factors and time to scale. This is likely due to the fact that nearly 90 percent of all Hib-containing vaccine introductions reach peak within two years, leaving little room to discern what factors may result in a faster time to peak coverage.
Table 3.10: Potential drivers of delay for countries requiring more than three years to achieve peak coverage

<table>
<thead>
<tr>
<th>Year Peak Coverage Rate Achieved</th>
<th>Country</th>
<th>Intro Year</th>
<th>Product Type</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>4th Year</td>
<td>Mali(^{122})</td>
<td>2005</td>
<td>penta</td>
<td>Planned for a phased introduction</td>
</tr>
<tr>
<td></td>
<td>Mongolia(^{123})</td>
<td>2005</td>
<td>penta</td>
<td>No problems reported</td>
</tr>
</tbody>
</table>

3.5. Comparative analysis

3.5.1. GAVI and non-GAVI LMIC time to peak analysis

This comparative analysis examined the differences in time to peak coverage for GAVI-eligible LMICs and non-GAVI-eligible LMICs introducing Hib-containing vaccines from 2001–08. Within the time frame assessed, four GAVI LMICs introduced a Hib-containing vaccine with GAVI NVS support. All four of these vaccine introductions were a pentavalent vaccine as a switch. Within the timeframe assessed, seven non-GAVI LMICs introduced a pentavalent vaccine for comparison.

Table 3.11 summarises the percent of countries that achieve peak coverage within 1, 2, 3, 4, or 5 years from initial introduction for the GAVI and non-GAVI LMICs introducing a pentavalent vaccine as a switch in the 2001–08 timeframe.

Table 3.11: Percent of countries achieving peak coverage within 5 years from initial introduction of a Hib-containing vaccine in GAVI LMICs compared to non-GAVI LMICs.

<table>
<thead>
<tr>
<th>LMIC Category</th>
<th>Percent of countries achieving peak in specified time frame</th>
<th>Median Time to Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 yr</td>
<td>2 yrs</td>
</tr>
<tr>
<td>GAVI (n=4)</td>
<td>75%</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>(n=3)</td>
<td>(n=1)</td>
</tr>
<tr>
<td>Non-GAVI (n=7)</td>
<td>71%</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td>(n=5)</td>
<td>(n=2)</td>
</tr>
</tbody>
</table>

Although based on a small sample size, this comparative analysis indicates both GAVI and non-GAVI LMICs are capable of achieving peak coverage within two years when introducing a pentavalent vaccine switch.

3.6. Qualitative analysis

3.6.1. Country visit results

Bangladesh

Bangladesh reported that it required extra time to reach peak coverage with its HepB monovalent vaccine because of a change in political leadership and delays in creating a vaccine launch plan. Additional staff members were also required before the introduction

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could be carried out. As a result, HepB was introduced in phases. This is in contrast to pentavalent introduction which was introduced in a single nationwide roll out. Based on the interviews, additional training and health worker orientation, combined with donor support to increase cold chain capacity and technical assistance from WHO and UNICEF contributed to the faster roll out of pentavalent vaccine.

Bolivia

Bolivian country officials provided no indication of a delay in reaching peak coverage for any vaccines introduced.

Mali

Mali country officials provided no indication of a delay in reaching peak coverage for any vaccines introduced.

Nigeria

At the time of YF introduction with GAVI support in 2003, Nigeria was already vaccinating with YF vaccine. However, vaccination was irregular based on supply constraints, and Nigeria stated GAVI support helped ensure there were no longer interruptions in YF vaccine coverage, though the exact reason is unclear. Nigeria reported the only issue in vaccine coverage for yellow fever came in 2005 when vaccination was suspended because of a reluctance to introduce AD syringes. Nigeria reported this issue was resolved in 2006.

Uzbekistan

Uzbekistan reported no challenges or “undue burden on country health/immunisation systems” associated with its introduction of HepB monovalent and pentavalent vaccines, both of which were introduced with GAVI support. Prior to vaccine introduction, some additional cold storage was required, but overall, all stakeholders consulted communicated that the health and immunisation systems in Uzbekistan were ready to handle the introduction of the new vaccines.

3.7. Conclusions

The analyses showed most GAVI-eligible countries have effective immunisation systems in place and were capable of quickly taking vaccine programs to scale. For both HepB- and Hib-containing vaccines, the results of this analysis indicated ≥ 80 percent of GAVI-eligible countries reached peak coverage within two years of vaccine introduction.

The analysis also showed that median time to peak coverage rate was longer for vaccine additions (2 to 3 years, HepB and Hib monovalent vaccines and YF vaccines, respectively) compared to vaccine switches (1 year).

An analysis of the relationship between time to peak coverage and ISS funding, WHO region, GAVI financing tier, and country size did not generate any additional insight. This was likely due to the fact that approximately 80% of all vaccine introductions achieve scale
in the first two years and 90% or more of product switches also achieve scale within two years, leaving little room to discern what factors may result in a faster time to peak coverage.

Because GAVI’s current model is to provide countries with the financial and technical support to prepare for and introduce a vaccine and then rely on countries to introduce the vaccines to scale, GAVI was not expected to accelerate time to peak coverage. Therefore, GAVI’s current model of providing countries with the financial and technical support to prepare for and introduce a vaccine appears to be effective.

The robustness of the conclusions included in this section are summarised in Table 3.12 based on a relative rating scale described in section 1.1.3 of the Introduction.

**Table 3.12: Relative robustness of the SG2.2 findings**

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
</table>
| Country ability to scale quickly | • GAVI’s reliance on countries to introduce and take vaccine programs to scale is an effective model because countries are able to quickly take vaccine programs to scale.  
  - For YF, >80% of countries reached peak coverage within 3 years.  
  - For HepB-containing vaccines, >80% of countries reached peak coverage within 2 years.  
  - For Hib-containing vaccines, nearly 90% of countries reached peak coverage within 2 years. | B  
  - The small number of evaluable cases for YF and Hib-containing vaccines makes it difficult to extrapolate results across all country introductions.  
  - YF: 6 of 28 evaluable  
  - HepB: 45 of 76 evaluable  
  - Hib: 24 of 76 evaluable  
  - Variations in reported and estimated coverage rate data (as much as +/- 20%) could change time to peak coverage results by at least 1 year. |
| Scalability based on vaccine type | • Time to peak coverage is longer for vaccines considered additions vs. vaccines considered switches.  
  - Median time to peak for HepB monovalent vaccine additions was 2 years and was 3 years for YF vaccines.  
  • Median time to peak for HepB and Hib tetravalent and pentavalent vaccine switches was 1 year. | B  
  - The small number of evaluable cases makes it difficult to extrapolate results across all country introductions.  
  - YF: 6 additions  
  - HepB: 20 additions & 25 switches  
  - Hib: 24 switch coverage rate data would not impact the difference between additions and switches. |
| Comparison between GAVI and non-GAVI LMIC | • GAVI & non-GAVI LMICs are capable of achieving peak coverage within 2 years when introducing a Hib vaccine switch. | C  
  - Small sample sizes (4 GAVI and 7 non-GAVI evaluable LMIC introductions) limit the robustness of this conclusion. |
4. **SG2.3: VACCINE SUPPLY STABILITY**

4.1. **Introduction**

The third evaluation question is, “To what extent has GAVI improved the stability of global and country level vaccine supply?”

Ensuring stable global and country level vaccine supply is a difficult but critical challenge, especially in a market as large as the one GAVI has created. For example, in 2010 the birth cohort for all high income countries is estimated to be 12 million and for all non-GAVI-eligible middle income countries, 44 million. For GAVI-eligible countries (n=72), the 2010 birth cohort is expected to be 80 million or two- to seven-fold greater than non-GAVI middle and high income countries, respectively.

To protect GAVI-eligible countries against a single disease such as pneumonia, over 200 million vaccine doses are currently required to fully immunise an infant (i.e. three doses per treatment).

For a variety of reasons, the worldwide vaccine supply has been unstable, even for some products in high income countries. While the number of multinational vaccine producers worldwide has decreased (from 26 producing the U.S.-recommended childhood vaccines in 1967 to 5 producing these vaccines in 2004), the number of emerging country suppliers producing vaccines for global markets has increased. New suppliers, however, can be delayed or deterred from market entry by the complexity and cost of vaccine production, intellectual property protection, and the trends in increased regulatory quality assurance and control.

Over the past several years, the global community has seen that when suppliers are limited, manufacturing issues can create serious disruptions to supplies (e.g. the recent recall of a prequalified pentavalent vaccine).

Creating a secure and stable supply of GAVI-funded vaccines is critical for accelerating vaccine introduction. It is only through the combination of stable demand, secure supply, and affordable vaccine prices that the full impact of vaccination can be achieved – averting millions of deaths in countries with the greatest disease burden.

4.2. **Scope of the evaluation question**

This section evaluates GAVI’s role in improving the stability of vaccine supply from 2000–09 in GAVI-eligible countries.

The evaluation:

- Compared UNICEF’s product availability assessments and the number of available prequalified suppliers to GAVI doses approved and UNICEF doses shipped data to assess supply availability versus demand and to determine supply stability for YF and HepB- and Hib-containing vaccines.

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• Documented the number of available prequalified suppliers for pneumococcal and rotavirus vaccines.

• Documented historical supply-related events and information to provide insight on supply challenges, where appropriate.

• Reviewed country Annual Progress Reports to identify country level supply shortages.

• Conducted a comparative analysis of WHO prequalified suppliers before and after the formation of GAVI as an indicator of GAVI’s role in improving supply stability.

• Summarised others’ perceptions on the extent of GAVI’s impact on achieving supply stability (e.g. electronic survey, structured interviews)

4.3. Methodology

4.3.1. Overview

In 2005, a GAVI sponsored Supply Strategy Task Team defined a healthy supply market as one that ensured a “sustainable quantity of supply through a diverse supplier base.” For the purposes of this evaluation, stable supply is defined as having sufficient supply to meet demand, over time, with more than one supplier.

Ideally, this analysis would determine whether multiple suppliers provided adequate supply over time to meet actual demand for YF and HepB- and Hib-containing vaccines. Unfortunately, data for both the supply availability and demand component of the analysis were not available; therefore, proxy data was used.

For the supply availability analysis, the amount of supply capacity dedicated for use in GAVI markets would have been the preferred data. Given vaccine suppliers typically serve many markets with any given manufacturing facility, supply dedicated to GAVI markets will vary depending on market demand and attractiveness. The amount of supply offered to GAVI markets through UNICEF’s supply tendering process would have served as a good proxy for available supply, however, this data has not been made public for 2001–09.

The only supply availability data for this analysis was UNICEF’s product availability assessments. These assessments provide the end user a qualitative assessment of the product availability in each year of a three year tender period. UNICEF’s latest assessments for the 2004–06, 2007–09, and the 2010–12 procurement rounds were used. UNICEF’s assessments are documented as color-coded flags. Table 4.1 summarises the assessment option definitions.

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While supply availability is a necessary condition for supply stability, it is not sufficient. Therefore, this evaluation also examines the stability of supply as represented by the number of suppliers with prequalified products. Prequalified product data was obtained from the WHO prequalified vaccines website. The number of suppliers with prequalified products was further segmented into those who received UNICEF supply awards and those who did not. This data was only available from 2004 onward. Situations where there were suppliers who did not receive UNICEF supply awards were believed to be indicative of supply stability at a more global scale.

For the actual demand analysis, country specified demand would have been the preferred data. Country applications for each vaccine were examined, where available, but the demand data contained within these applications were typically inconsistent and/or difficult to interpret. The GAVI Secretariat recommended GAVI approved doses data be used in lieu of country application data. The approved doses data was used as the initial comparator for the supply data. However, GAVI approved doses were typically quite different than UNICEF shipped doses, even in situations where there were no supply constraints. For example, GAVI approved doses were:

- Significantly higher (1.3–2.3 times) or significantly lower (0.7 times) than the shipped doses for YF vaccine in years where there was adequate supply.
- Significantly higher (1.3–1.8 times) or lower (0.5–0.6 times) than the shipped doses for HepB monovalent vaccine in years where there was adequate supply.
- Significantly higher (1.2–3.1 times) than the shipped doses for HepB tetravalent vaccine in years where there was adequate supply.

Attempts to clarify these discrepancies with UNICEF and GAVI Secretariat staff were unsuccessful. As a result, both GAVI approved and UNICEF shipped doses were included in the evaluation to help interpret supply stability.

Finally, country-level supply shortages for YF and HepB- and Hib-containing vaccines were identified through a review of country Annual Progress Reports.

<table>
<thead>
<tr>
<th>Option</th>
<th>Assessment Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>▲</td>
<td>No established demand. Availability needs to be determined based on need.</td>
</tr>
<tr>
<td>▼</td>
<td>Very limited supply.</td>
</tr>
<tr>
<td>▶</td>
<td>Limited supply. Requires planning to ensure adequate supply.</td>
</tr>
<tr>
<td>▶▶</td>
<td>Supply exceeds current demand.</td>
</tr>
</tbody>
</table>

Table 4.1: Definitions for the UNICEF product availability assessment options

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132 Personal communication, GAVI Secretariat, March 2010.
133 Approved Doses Syringes and Safety boxes 5_01_10, provided by the GAVI Secretariat, February 2010.
The evaluation for pneumococcal and rotavirus vaccines was limited given these vaccines were not procured by UNICEF in the 2001-09 evaluation timeframe (per SG2.1: Gambia and Rwanda introduced PCV7 in 2009 and Nicaragua introduced rotavirus in 2006 through supplier donations and three additional Latin American countries introduced rotavirus through PAHO in 2008–09). Therefore, only data on the number of suppliers prequalified prior to 2010 were provided for these vaccines.

Qualitative information on the extent to which GAVI has improved the stability of global and country level supply was obtained from multiple sources, including:

- Responses from the electronic survey to the statement “GAVI has contributed to improving the stability of global and country level supply.” Responses (n=282) were analysed for both ‘as received’ (referred to as ‘raw’ data) and ‘adjusted’ data (adjusted by removing non-respondents from each statement).

- Responses (n=22) from consultations with current and past GAVI Board members to the statement “GAVI has contributed to improving the stability of global and country level supply.”

- Responses from 13 supplier representatives from six companies to two questions:
  - “In what ways does GAVI influence your vaccine development and manufacturing decisions?”
  - “How has GAVI influenced the entry of other new manufacturers?”

- Responses from the EPI manager electronic survey seeking feedback on any issues with vaccine supply under the GAVI NVS program.

- Relevant comments and insights generated from five country consultations.

The evidence sources used to evaluate this question are summarised in Table 4.2. This table includes the resources referenced for historical supply-related events and information on GAVI’s role in improving the stability of vaccine supply.

Table 4.2: Evaluation sources and descriptions for GAVI’s contribution to global supply stability

<table>
<thead>
<tr>
<th>Evidence source</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of documentation</td>
<td>• GAVI documents (e.g. Board meeting minutes and supportive documents, GAVI Phase I evaluation, GAVI approved doses)</td>
</tr>
<tr>
<td></td>
<td>• Vaccine licensure and WHO prequalification dates (e.g. national regulatory authority’s websites such as USFDA and EMEA; supplier websites, WHO websites)</td>
</tr>
<tr>
<td></td>
<td>• Vaccine product descriptions (e.g. product inserts, supplier websites)</td>
</tr>
<tr>
<td></td>
<td>• Vaccine product availability status (e.g. GAVI Alliance documents, country Annual Progress Reports, supplier documents, national regulatory authority websites, UNICEF product availability menus)</td>
</tr>
<tr>
<td>E-survey</td>
<td>Responses to one relevant statement from the electronic survey:</td>
</tr>
<tr>
<td></td>
<td>• GAVI has contributed to improving the stability of global and country level vaccine supply</td>
</tr>
</tbody>
</table>

61
Structured interviews included comments from:

- Current and ex-GAVI Board members with one question designed to solicit feedback on this evaluation statement (GAVI has contributed to improving the stability of global and country level vaccine supply)
- Supplier representatives from multinational and emerging country suppliers

Comments from the GAVI Secretariat were not included due to the perceived conflict of interest
Comments from other consultation interviews were not included due to minimal responses on this strategic goal

The EPI Manager electronic survey sought input on the question:

- Any issues with vaccine supply under GAVI NVS program

Country consultations resulted in ad hoc comments related to this question.

Meetings were requested with representatives from the GAVI Secretariat and UNICEF to seek input on the discrepancies between GAVI approved doses and UNICEF doses shipped when supply constraints were not the issue

4.3.2. Comparative analyses

To further evaluate the potential impact GAVI has had on improving vaccine supply, the number of WHO prequalified products in the market prior to the formation of GAVI (1999) was compared to the number of WHO prequalified products nine years after the start of GAVI (2009). The level of growth in the number of suppliers sheds light on GAVI’s possible role in improving the stability of supply, both for GAVI markets and globally.

4.3.3. Limitations

These analyses have limitations due to:

- Lack of quantitative supply and relevant demand information and inability to reconcile data from multiple sources.
- Lack of detail on the criteria that result in a particular UNICEF product availability assessment.
- Inconsistent prequalification dates for prequalified vaccines over time, e.g.
  - Unable to document early prequalification dates of products no longer provided to UNICEF markets.
  - Conflicting prequalification dates from different sources (e.g. for Institut Pasteur YF vaccine, one WHO document lists prequalification as 1999, while the WHO prequalification website lists it as 2001).\(^\text{136,137}\)
  - GSK’s Hib monovalent vaccine, prequalified in 1998, is listed as a liquid product rather than a lyophilised product in.


• Redesigned WHO website (went public in June 2010) that no longer provides access to certain information (e.g. GSK’s liquid/lyo pentavalent product information available in June 2010, but no longer available as of July 2010).

• Minimal information on country-level supply shortages due to incomplete APR data (437 cases of unavailable APRs or APRs with missing information).

• Limited qualitative insights from:
  o EPI manager electronic survey: participants only represented 30% of GAVI countries.
  o Small number of supplier interviews (n=6 suppliers) limited generalisability and did not allow for disaggregation by sector (emerging/multinational).
  o Limited country-level stakeholder responses due to only five country consultations (7% of total stakeholder countries in 4 out of 6 WHO regions).

4.4. Evaluation analysis

4.4.1. Yellow fever vaccine supply assessment

Historically, YF vaccine supplies have not met demand.\textsuperscript{138,139,140} Much of the early supply constraints were due to a single prequalified product from 1987-2001. In 2001, two additional products were prequalified and a forth product was prequalified in 2009. However, only two suppliers to date have been issued UNICEF awards since 2007.

To address the YF vaccine supply issues, GAVI established a non-pre-funded vaccine stockpile in 2000 that was to be used for outbreak control and preventative campaigns.\textsuperscript{141,142} This stockpile started at 2 million doses per year, but vaccine shortages and disruptions in immunisation were reported through 2002 due to unpredictable demand from outbreaks and limited supplies (the accumulated stockpile was actually used up within the first quarter of 2001). GAVI expanded the stockpile to 6 million doses per year in 2003 and expanded it again to 12 million doses per year in 2007. Nonetheless, supply fluctuations continued due to the uncertainty in outbreak-driven demand and the need for two of the four prequalified suppliers to first meet their national and regional demand before providing supplies to GAVI.\textsuperscript{143,144,145}

\begin{footnotesize}
\begin{enumerate}
\item \textsuperscript{138} Yellow Fever Stockpile Investment Case, submitted by the Yellow Fever Task Force to GAVI. December 2005.
\item \textsuperscript{140} Evaluation of the progress of Yellow Fever control in Africa and the use of GAVI/VF support, 16\textsuperscript{th} GAVI Board, Doc 18, 1 July 2005.
\item \textsuperscript{141} Evaluation of the progress of Yellow Fever control in Africa and the use of GAVI/VF support, 16\textsuperscript{th} GAVI Board, Doc 18, 1 July 2005.
\item \textsuperscript{142} Yellow Fever Investment Case, Continuation Proposal. Submitted by the Yellow Fever Initiative to the GAVI Alliance, May 2008.
\item \textsuperscript{143} UNICEF supply division conference call, January 29 2010.
\item \textsuperscript{145} Yellow Fever Investment Case, Continuation Proposal. Submitted by the Yellow Fever Initiative to the GAVI Alliance, May 2008.
\end{enumerate}
\end{footnotesize}
UNICEF began assessing product availability in 2004. Supply stability for 10 dose vials (the most frequently shipped presentation) was maintained from 2004 to 2008, but became more limited in 2009. In a 2010 UNICEF presentation, YF vaccine supply stability was described as ‘still fragile’ for the 2010–12 time period because of the funding uncertainty for campaign-driven demand.\(^{146}\)

With the exception of 2005-06, UNICEF shipped less doses than GAVI approved between 2004-08, even though supply was not constrained. The reasons for these discrepancies are unknown.

### 4.4.2. HepB mono- and tetravalent vaccine supply assessment

**HepB monovalent**

The first and second HepB monovalent vaccines were prequalified in 1987 and 1996, respectively, but minimal doses were shipped to low income countries prior to GAVI's inception in 2000.

Figure 4.2 shows the number of prequalified suppliers over time relative to UNICEF’s product availability assessment and GAVI approved and UNICEF shipped doses.

With the advent of GAVI financing support for HepB monovalent vaccines in 2000, demand quickly increased and the number of available suppliers increased from two to nine by 2009. Six of the nine prequalified suppliers received UNICEF awards in 2007–09.

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UNICEF’s product availability assessment confirmed that GAVI had created a stable market for HepB monovalent vaccines given supply exceeded demand. However, the demand for HepB monovalent vaccine decreased significantly between 2006–09, as GAVI-eligible countries began to adopt or switch to pentavalent vaccines. UNICEF no longer includes HepB monovalent vaccines in their GAVI product menus.\textsuperscript{147}

**HepB tetravalent**

The first HepB tetravalent vaccine was prequalified in 1998 and UNICEF reported in 2000 that HepB tetravalent supplies were not projected to meet 2001–03 demand.\textsuperscript{148} UNICEF shipped doses were approximately 10 percent below GAVI approved doses during this period, likely due to the supply shortage.

Figure 4.3 shows the number of prequalified suppliers over time relative to UNICEF’s product availability assessment and GAVI approved and UNICEF shipped doses.

A second supplier was prequalified in 2004, but only one supplier was issued a UNICEF award. Two additional suppliers were prequalified in 2006 and each received an award in the 2007–09 tender, but UNICEF product availability assessments indicated a ‘very limited’ or ‘limited’ supply situation until 2007. From 2007 onward, an excess in supplies was reported. This was due to an additional supplier award and a dramatic decrease in demand as countries switched to pentavalent vaccine or were instead provided HepB monovalent vaccine due to pentavalent supply shortages in previous years.\textsuperscript{149,150}

\textsuperscript{150} http://www.gavi.org/resources/15brd_P1vaccinesinP2.pdf (accessed 2 March 2010).
By the time the fifth HepB tetravalent vaccine was prequalified in 2007, demand had reached peak and declined to less than 1.5m doses by 2009. As with HepB monovalent vaccines, demand for HepB tetravalent vaccines decreased as countries switched to pentavalent vaccines. The potential supply now far exceeds demand and UNICEF has assumed ‘no established demand’ for HepB tetravalent vaccines from 2011 and beyond.151

4.4.3. Hib monovalent and tetravalent vaccines supply assessment

The first Hib monovalent vaccine was prequalified in 1997. The number of prequalified products slowly increased to five by 2008. This increase in suppliers was surprising given the lack of demand for this vaccine. UNICEF’s product availability assessment indicated ‘no established demand’ for Hib monovalent vaccines in 2004–06 and ‘limited supply’ or ‘very limited supply’ from 2007–09, in spite of the availability of five prequalified vaccines. Some suppliers have stated they prequalified a Hib monovalent vaccine in the hope of speeding up their pentavalent vaccine prequalification once licensed.152

The first Hib tetravalent vaccine was prequalified in 2002 and since then, only three products have been prequalified. Following initial vaccine introductions by Gambia, Moldova, PNG, and Zambia, the only GAVI-eligible country currently using a Hib monovalent or tetravalent vaccine is Bosnia & Herzegovina through 2011 and Moldova, which will receive GAVI funding through 2010, respectively.153

Like HepB mono- and tetravalent vaccines, GAVI’s funding for Hib-containing vaccines influenced new suppliers to enter the Hib mono- and tetravalent market. However, with the shift in focus to pentavalent vaccines, the supply and demand for these vaccines have

153 Timeframe of GAVI Support to Countries as of 30 Nov 2009, provided by the GAVI Secretariat, January 2010.
been minimal. UNICEF is forecasting ‘limited’ supplies and no demand beyond 2011 for Hib monovalent vaccines and ‘very limited’ supplies for Hib tetravalent through 2012.\(^{154}\)

### 4.4.4. Pentavalent vaccine supply assessment

The DTwP-HepB-Hib pentavalent vaccine is the preferred combination vaccine by GAVI and by GAVI-eligible countries. GAVI made the decision to support DTwP-combination vaccines based on programmatic ease and increased injection safety of introducing a combination vaccine into countries with weak immunisation systems.\(^{155}\)

Figure 4.4 shows the number of prequalified suppliers and suppliers receiving UNICEF awards over time, relative to UNICEF’s product availability assessment and GAVI approved and UNICEF shipped doses.

*Figure 4.4: Prequalified pentavalent vaccine suppliers over time relative to GAVI approved doses and UNICEF product availability assessments (first assessment for 1 dose vials, second assessment for 10 dose vials)*

The first Hib-containing pentavalent vaccine was prequalified in 1998 and was a combination of a liquid DTwP-HepB and a lyophilised Hib monovalent vaccine. In 2000, UNICEF reported that combination vaccine production may not meet demand from 2001 to 2003.\(^{156}\) Only about 10 million doses per year were approved and shipped through 2003 and supply became ‘very limited’ in 2004.

WHO prequalified the first fully liquid pentavalent vaccine in 2006 and, two years later, prequalified two additional liquid pentavalent products manufactured by emerging country suppliers (both in India). Despite the increase in available supply, UNICEF product availability assessments indicate ‘limited’ supply through 2009. This may be due, in part, to production problems at one pentavalent supplier.\(^{157}\) UNICEF has projected pentavalent

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supply should be adequate from 2010 onward.\textsuperscript{158} A second liquid/lyophilised pentavalent vaccine was prequalified in May 2010 and is now available in 1, 2, and 10 dose ampoules.\textsuperscript{159}

4.4.5. HepB- & Hib-containing vaccine country level supply shortage assessment

While care is taken by UNICEF to manage supply shortages, some shortages do occur. Country level shortages are documented in country-specific Annual Progress Reports (APRs). Figure 4.10 shows the annual APR-reported supply shortages by vaccine.\textsuperscript{160} It should be noted that 437 of the APRs required for this analysis were either not available or had missing information.

The seven vaccine shortages reported in 2003 represented 16\% of countries receiving GAVI-supported vaccine shipments that year of which 71\% were shortages in HepB tetravalent and pentavalent vaccines (5/7).\textsuperscript{161} From 2004–08, the reported shortages represented only 2.7\% of countries receiving vaccines during that time frame.\textsuperscript{162}

\textit{Figure 4.10: Number of country-level vaccine shortages reported each year}

![Number of country-level vaccine shortages reported each year](image)

In general, the most shortages were reported for HepB tetravalent and pentavalent vaccines. However, the shortages are not always attributed to a specific vaccine. Forty percent of the reported shortages (6/15) for 2003–08 did not identify the vaccine.

Given the small sample size, an assessment of GAVI’s value add regarding country supply shortages cannot be made.

4.4.6. Pneumococcal vaccine supply assessment

The first pneumococcal conjugate vaccine (PCV7) was first licensed in 2000, but not prequalified until 2009 (Figure 4.5).

\begin{itemize}
\item \textsuperscript{158} http://www.unicef.org/supply/files/Product_Menu_FEB_2010_published.pdf (accessed 15 April 2010).
\item \textsuperscript{159} http://www.who.int/immunisation_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html (accessed July 2010).
\item \textsuperscript{160} http://www.gavialliance.org/performance/country_results/index.php (accessed 18 February 2010).
\item \textsuperscript{161} http://www.gavialliance.org/performance/country_results/index.php (accessed 18 February 2010).
\item \textsuperscript{162} Ibid.
\end{itemize}
The significant delay between licensure and prequalification was largely due to the need to test the effectiveness of this vaccine in developing countries and to change the original single dose pre-filled syringe presentation to a single dose vial presentation, per WHO’s request. A second vaccine, the PCV10, was prequalified in 2009 and the PCV13 vaccine is expected to be prequalified in late 2010.

While it is too early to accurately assess the stability of pneumococcal vaccine supplies, demand for pneumococcal vaccines has been generated, in part, through the efforts of the PneumoADIP and the impact of the innovative AMC financing (see SG2.5). As a result, GAVI has already received commitments from GSK and Pfizer to supply 30 million doses annually for 10 years beginning in 2012 and 2013, respectively. For 2010-12, they have also committed to providing approximately 50 million doses to meet early demand. Therefore, no supply constraints are anticipated in the 2010-11 timeframe.

**4.4.7. Rotavirus vaccine supply assessment**

The very first rotavirus vaccine was licensed in 1998, but withdrawn a year later because of an increased risk of intussusception. It took an additional five years for the next rotavirus vaccine (GSK’s lyophilised Rotarix) to be licensed and another three years to be prequalified (Figure 4.6).

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However, for the first time the prequalification was for use in limited regions only (AMRO and EURO). A second regionally prequalified vaccine (Merck’s liquid RotaTeq) became available in 2008. For enteric vaccines, it was important to show evidence of effectiveness more broadly, especially in Africa and Asia, prior to prequalifying globally. The first global prequalification (GSK’s liquid Rotarix) occurred in 2009 and liquid RotaTeq is expected to receive global prequalification in 2010.

It is too early to tell whether the supply of rotavirus vaccines will be constrained given these products have yet to be introduced in GAVI-eligible countries (other than through donation or PAHO procurement). When the rotavirus investment case was completed in 2006, both multinational suppliers expressed interest in supplying rotavirus vaccine to GAVI, noting significant supply requirements would necessitate additional capital investments. In addition, the US National Institutes of Health granted a license for a bovine-human reassortment vaccine (BRV) to manufacturers in India, China, the United States, and Brazil. PATH is supporting BRV suppliers by providing financial support and scientific assistance for the Phase I and II clinical trials. If successful, these additional suppliers will increase GAVI market supply, further stabilising supply and creating the competitive forces that could potentially drive vaccine prices down.

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171 Accelerating the introduction of rotavirus vaccines into GAVI-eligible countries. Investment Case for GAVI Secretariat. Submitted by PATH’s Rotavirus Vaccine Program, October 2006.
4.5. Comparative analysis

4.5.1. WHO prequalified products pre- and post-GAVI

Since GAVI’s inception, the number of WHO prequalified YF and HepB- and Hib-containing vaccine products has increased significantly (Table 4.3).

Table 4.3: Number of underused WHO prequalified vaccine products in 1999 versus 2009

<table>
<thead>
<tr>
<th>Vaccine/Year</th>
<th>1999 (Pre-GAVI)</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow Fever</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>HepB monovalent</td>
<td>5(^1)</td>
<td>9</td>
</tr>
<tr>
<td>HepB tetravalent</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Hib monovalent</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Hib tetravalent</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Pentavalent(^2)</td>
<td>1</td>
<td>4(^3)</td>
</tr>
</tbody>
</table>

\(^1\)Includes three plasma-derived vaccines that have since been discontinued

\(^2\)Pentavalent vaccine in 1999 was a combination of HepB tetravalent (liquid) + Hib monovalent (lyophilized); pentavalent vaccines in 2009 include one liquid/lyophilised and three liquid forms

\(^3\)WHO has recently cancelled the Shantha pentavalent vaccine’s prequalification

The number of prequalified YF vaccines increased by three, the number of prequalified HepB mono- and tetravalent vaccines increased by eight, the number of Hib mono- and tetravalent vaccines both increased by five, and the number of pentavalent vaccines increased by three. Given GAVI-eligible country preference for pentavalent vaccines, the increase from one prequalified pentavalent vaccine in 1999 to four prequalified pentavalent vaccines in 2009 has been an important improvement in HepB- and Hib-containing vaccine supply.

Although an increase in the number of prequalified suppliers is important, the number and quantity of UNICEF awards is a more accurate assessment of supplier stability for GAVI markets. However, this analysis could not be included since this data is only available from 2004 onward.

4.6. Qualitative analyses

4.6.1. Electronic survey results

To assess the perception of key global stakeholders, responses to Statement “GAVI has contributed to improving the stability of global and country level vaccine supply” were evaluated.

As shown in Figure 4.7, over 75% of survey respondents strongly agreed or agreed, and less than 5% disagreed or strongly disagreed.
4.6.2. Structured interview results

GAVI Board Members

Of the 22 current and former GAVI Board members who participated in the structured interviews, 18 (81%) commented on vaccine supply. Six respondents (33%) thought GAVI should encourage new developing country suppliers to enter the market or thought that as new suppliers entered the market prices would decrease. Four respondents (22%) stated that GAVI should work with suppliers to reduce prices and/or work to increase the number of suppliers.

Suppliers

Of the 12 companies requested to participate, 13 staff members from six companies participated in interviews.

In response to the first question: “In what ways does GAVI influence your vaccine development and manufacturing decisions?”, three of the six companies stated the AMC process helped them assess the real market need for pneumococcal vaccines. The demand forecasts and the consultative process provided more clarity and allowed for better planning and decision-making. Three suppliers also stated that GAVI vaccine prioritisation has guided their vaccine development and/or capacity decisions.

Only four out of six suppliers responded to the second question: “In your opinion, how has GAVI influenced the entry of other new manufacturers?” Of the four responders, three believed that the existence of GAVI has encouraged more suppliers to prequalify vaccines for GAVI markets. One company stated that most suppliers had already
prequalified a vaccine, and therefore, had already entered the UNICEF market, but GAVI has created a better environment for ‘low cost’ manufacturers.

4.6.3. EPI manager survey results

Among the 23 respondents to the EPI manager survey, only 13 (57%) responded to the question asking whether their country had experienced supply issues. Eleven respondents (48%) indicated any issues experienced were either post-evaluation time frame (2010) or for a non-GAVI funded vaccine. Two respondents (8%) reported a shortage of yellow fever vaccine (year unspecified). One respondent commented this shortage was due to a shipment error, and the other commented the shortage was due to higher-than-anticipated wastage rates of vaccine with the 20-dose presentation.

4.6.4. Country visit results

Five country visits were conducted as a part of GAVI’s Phase II evaluation. While structured questions were not asked regarding GAVI’s role in improving vaccine supply, a variety of country-specific insights were generated from these country consultations.

Bangladesh

Bangladeshi officials requested DTwP-HepB vaccine, but due to a global supply shortage Bangladesh was given HepB monovalent vaccine in 2003. (The application for DTwP-HepB was submitted in April 2001.) Excluding this example, Bangladeshi interviewees reported no other supply issues.

Mali

No major issues were highlighted by the country stakeholders relating to vaccine availability and supply with the exception of some stock outs for unspecified traditional vaccines in 2009.

Nigeria

Nigerian officials reported no stock outs or other supply issues for YF vaccines. However, they did report stock outs with their HepB vaccine, which is currently procured without GAVI support.

Bolivia

Bolivian officials reported no supply issues with rotavirus vaccines.

Uzbekistan

Uzbek officials reported no supply issues with GAVI-supported vaccines.
4.7. Conclusions

GAVI has added value by improving supply stability for underused vaccines. This was a result of GAVI creating a more stable market that attracted an increased number of prequalified suppliers.

Although YF supply stability was improved from 2004-08, it was not sustained beyond 2008 and UNICEF projects continued supply instability for 2010–12. Despite the ongoing supply challenges, it was only after GAVI’s creation of a YF stockpile that infant immunisation became sustainable for countries. Vaccination coverage rates increased once countries had access to stockpiled vaccines and they no longer had to rely on infant-targeted doses for YF outbreak use (see SG2.1).174,175,176 However, these gains may be at risk if GAVI’s current funding gap is not resolved. The Board recently approved only $22m of the $180m requested for YF vaccines.177 Supplier perceptions of future financing shortfalls may lead to a reallocation of available supply or reduced production.178,179

GAVI improved supply stability for HepB mono- and tetravalent vaccines. However, demand for these vaccines has continually declined due to a shift to pentavalent vaccines.

For pentavalent vaccines, GAVI improved supply stability from 2005 onward and is expected to achieve supply stability for 2010 and beyond.

For pneumococcal vaccines, GAVI has added value by securing two 10-year commitments for 30m doses per year from both GSK and Pfizer beginning in 2012 and 2013, respectively. In addition, GAVI has secured approximately 50m doses total from these suppliers for use in the 2010–12 timeframe, which is predicted to be sufficient to meet 2010-11 demand. Supply beyond these initial commitments is still uncertain given AMC supply tenders are issued on an annual basis.

GAVI has not yet secured any supply commitments for rotavirus vaccine.

Responses from electronic surveys and stakeholder interviews provided additional qualitative feedback on GAVI’s value. The majority of respondents agreed that GAVI has had an impact on improving the stability of global and country level supplies.

The robustness of the conclusions included in this section are summarised in Table 4.4 based on a relative rating scale described in section 1.1.3 of the Introduction.

176 Yellow Fever Stockpile Investment Case, submitted by the Yellow Fever Task Force to GAVI. December 2005.
177 Personal communication, GAVI Secretariat, 22 July 2010.
Table 4.4: Relative robustness of the SG2.3 findings

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
</table>
| GAVI impact on stability of YF vaccine supply                          | • GAVI has improved YF vaccine supply stability from 2004–08.  
  - Three additional products have been prequalified since GAVI’s inception.  
  - UNICEF reports combined with product availability assessments indicate supply excess from 2004–08 (10 dose vial).  
  - UNICEF product availability assessment indicates ‘limited’ to ‘very limited’ supply in 2009 and ‘still fragile’ from 2010–12.                                                   | • Actual supply as defined by amount of supply offered through tendering process is unknown.  
  - UNICEF product availability assessments and number of prequalified suppliers were used as proxies.  
  • Criteria for defining UNICEF product availability classifications are unknown.  
  • Actual demand data is not available.  
  - Approved and shipped doses were used as proxies.  
  • Product availability assessments are inconsistent with approved vs. shipped dose data.  
  - Even though UNICEF declared supply excess, shipped doses were less than approved doses implying a supply shortage from 2004 – 2007.  
  • In 2009, four suppliers were prequalified but only two received UNICEF supply awards even though supply was characterised as very limited.  
  - Unknown if only two suppliers submitted bids.                                                                                                                                                                      | C                                                                                                                                                                                                                             |
| GAVI impact on supply stability of HepB mono- and tetravalent vaccines | • GAVI has achieved supply stability for HepB mono- and tetravalent vaccines.  
  - The number of prequalified HepB monovalent suppliers increased from two to nine since GAVI’s inception.  
  - The number of prequalified HepB tetravalent suppliers increased from one to five since GAVI’s inception.  
  - UNICEF product availability assessments indicated supply excess of HepB mono- and tetravalent vaccines from 2004 and 2007 onward, respectively.  
  • However, due to the shift to pentavalent vaccines, there is now very limited demand for both products.                                                                                                             | • Same supply, UNICEF product availability assessments, and demand limitations apply, as with YF conclusions.  
  • Product availability assessments are inconsistent with approved vs. shipped dose data for HepB monovalent and tetravalent.  
  - Even though UNICEF declared supply excess for HepB monovalent from 2004-09, shipped doses were less than approved doses implying a supply shortage.  
  - Shipped doses for HepB tetravalent were approximately equivalent to approved doses from 2004-06 when UNICEF product availability assessments indicated very limited or limited supply.  
  - Even though UNICEF declared supply excess for HepB tetravalent from 2007-09, shipped doses were less than approved doses.                                                                                     | C                                                                                                                                                                                                                             |
**Evaluation question SG2.3:** To what extent has GAVI improved the stability of global and country level vaccine supply?

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
</table>
| GAVI impact on supply stability of pentavalent vaccines | • Three additional products have been prequalified since GAVI’s inception.  
• UNICEF product availability assessment indicates improvement from ‘very limited’ supply in 2004 to ‘limited’ supply from 2005 onward.  
• UNICEF has projected adequate supply in 2010-12. | C  
• Same supply, UNICEF product availability assessments, and demand limitations as YF.  
• Product availability assessment inconsistent with approved vs. shipped dose data for pentavalent.  
• Shipped doses for pentavalent were approximately equivalent to approved doses from 2004-07 when UNICEF product availability assessment indicated very limited or limited supply. |
| GAVI impact on supply stability of pneumococcal vaccines | • GAVI has secured two 10-year commitments for 30m doses per year beginning in 2012 and 2013.  
• GAVI has also secured and these initial commitments is still uncertain. | A  
• The two suppliers have agreed to provide ~31m doses for 2010–11 demand.  
• AMC supply contracts are in place with both suppliers to provide 30m doses each per year for up to 10 years beginning in 2012 and 2013. |
| GAVI impact on supply stability of rotavirus vaccines | • GAVI has not yet secured any supply commitments for rotavirus vaccine. | A  
• No supply contracts in place. |
5. **SG2.4: VACCINE AFFORDABILITY**

5.1. **Introduction**

The fourth Strategic Goal 2 evaluation question is, “To what extent has GAVI made vaccines and related technologies more affordable?”

The formation of GAVI was expected to leverage the power of a global purchasing pool for GAVI-eligible countries to create greater and more stable demand, which in turn would lead to greater supplier competition, improved production economies of scale and ultimately, low-priced vaccines. These expected low priced vaccines would in turn, enable countries to sustain immunisation programs after the termination of donor financing support.\(^1\)\(^2\),\(^3\) Because vaccine prices are an important driver of vaccine adoption decisions by countries and vaccine financing decisions by GAVI, reductions in vaccine prices are key to accelerated vaccine introduction and sustained immunisation in GAVI countries.\(^2\),\(^3\),\(^4\)

5.2. **Scope of the evaluation question**

This section evaluates the extent to which GAVI has made vaccines more affordable. GAVI’s impact on the affordability of related technologies (i.e. INS) is included in the SG1 evaluation section, and thus will not be addressed here. In addition, a wider analysis of GAVI’s contribution to ‘sustainability,’ of which price is clearly an important part, is contained in the SG3.

GAVI defines affordability as a vaccine “price that countries can eventually finance in a sustainable manner”.\(^5\) Determining what is an ‘affordable price’ to countries will require analyses beyond the scope of this evaluation and would be dependent on a variety of factors, such as when GAVI financing ends, country GNI and health expenditure, and the global economy (although SG3 does refer to 1% of public health expenditures as an appropriate benchmark for vaccine expenditures). Therefore, this analysis focuses on the extent to which GAVI has achieved vaccine price reductions over time, thereby making GAVI funded vaccines more affordable to the countries it serves.

This evaluation:

- Summarised GAVI’s supply strategy principles in order to generate insights on how GAVI intended to make vaccines more affordable over time.

- Compared market characteristics of size (infant population) and income level served (low vs. middle income countries) between GAVI and PAHO to develop insights on potential purchasing power and tiered pricing.

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\(^1\) GAVI Board meeting minutes, October 1999.
\(^3\) Milstien J, Cohen JC, Olsen JT. An evaluation of the GAVI Alliance efforts to introduce new vaccines via the Accelerated Development and Introduction Plans (ADIPs) and the Hib Initiative. HSLP, February 2007.
\(^4\) GAVI Alliance, Doc 9, 16th GAVI Board, Supply Strategy for GAVI/VF Vaccines, 6 July 2005, D Strombom.

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Doc # AF-9 Vaccine market development, GAVI Board meeting 6-7 December 2005.
• Examined weighted average UNICEF vaccine prices for GAVI markets over time (2001–10) and corresponding trends in vaccine supply and demand for YF and HepB- and Hib-containing vaccines to determine GAVI’s impact on vaccine affordability.
  
  o Compared GAVI UNICEF vaccine prices to non-GAVI UNICEF vaccine prices and PAHO prices to develop insights on vaccine price trends relative to purchasing power.
  
  o Compared 2010 pneumococcal and rotavirus vaccine prices to PAHO and US public market prices, where possible.

• Conducted a comparative analysis to provide insight on vaccine ‘affordability’ in GAVI-eligible countries.
  
  o Compared current country costs for routine non-GAVI EPI vaccines to costs for GAVI-funded underused and new vaccines.

• Summarised others’ perceptions on the extent of GAVI’s impact on making vaccines more affordable (e.g. electronic survey, structured interviews)

5.3. Methodology

5.3.1. Overview

The current evaluation is intended to include data from 2001–09, however, at GAVI’s request, 2010 data has been included, where available.

To understand how GAVI has impacted vaccine affordability, UNICEF vaccine prices for GAVI markets were obtained from publicly available sources and reported as weighted average prices.\(^ 186,187,188,189\) Since documentation on UNICEF’s award process, specific supplier negotiations and prices, and the method for allocating share among the available suppliers is not publicly available, insights on price changes over time were limited, but included where possible.

Vaccine price dynamics are complex and related to supplier competition, supply, and demand. As described in SG2.3, an accurate assessment of supply cannot be determined without knowing supply capacity or supply offered to UNICEF/GAVI markets for each vaccine. Therefore, UNICEF’s product availability assessments and the number of prequalified products were used as proxies for ‘supply’ (see SG2.3 for details).\(^ 190,191\)

\(^{186}\) UNICEF Product Menus for Vaccines Supplied for GAVI:
  


For country demand, GAVI approved doses and UNICEF shipped doses were used as proxies in the absence of other more reliable data (see section SG2.3).\textsuperscript{192,193}

Insights on vaccine affordability were also obtained from three qualitative sources:

- Responses from the electronic survey to the statement “GAVI has made vaccines and related technologies more affordable to countries.” Responses (n=282) were analysed for both ‘as received’ (referred to as ‘raw’ data) and ‘adjusted’ data (adjusted by removing non-respondents from each statement).

- Responses (n=22) from consultations with current and past GAVI Board members to the statement “GAVI has made vaccines and related technologies more affordable to countries.”

- Relevant comments and insights generated from five country consultations.

The evidence sources used to evaluate this question are summarised in Table 5.1.

\textit{Table 5.1: Evaluation sources and descriptions for the vaccine price affordability analysis}

<table>
<thead>
<tr>
<th>Evidence source</th>
<th>Description</th>
</tr>
</thead>
</table>
| Review of documentation | • Tiered pricing principles  
• Vaccine prices (e.g. UNICEF product menus, PAHO newsletters, Center for Disease Control and Prevention (CDC) historical prices)  
• Actual doses shipped by UNICEF to GAVI-eligible countries  
• Market size and characteristics (e.g. UN birth cohort and World Bank income classifications) |
| E-survey               | The e-survey sought input to the question: “GAVI has made vaccines and related technologies more affordable to countries.”                          |
| Structured Interview   | Structured interviews sought input from current and ex-GAVI Board members to the question: “GAVI has made vaccines and related technologies more affordable to countries”  
• Comments from the GAVI Secretariat were not included due to the perceived conflict of interest  
• Comments from other structured interviews were not included due to the limited number of relevant comments |
| EPI manager survey     | The EPI manager survey did not seek input on this question.                                                                                   |
| Country consultations  | Country consultations resulted in \textit{ad hoc} comments related to this question.                                                           |

\textsuperscript{199} \url{http://www.unicef.org/supply/index_gavi.html} (accessed 22 July 2010).
\textsuperscript{192} Approved Doses Syringes and Safety boxes 5_01_10, provided by the GAVI Secretariat, February 2010.
\textsuperscript{193} \url{http://www.unicef.org/supply/index_gavi.html} (accessed 22 July 2010).
Meetings, teleconferences, and e-mail communications were requested from the GAVI Secretariat, UNICEF Supply Division, and PAHO to seek input on:

- YF vaccine price increases
- HepB tetravalent vaccine price increases between 2003-06
- Pentavalent price increase between 2003–04
- Procurement Reference Group function and accomplishments
- Most appropriate UNICEF prices to use in the analysis when multiple or conflicting sources were available
- Most appropriate PAHO prices to use in the analysis

5.3.2. Comparative analyses

To determine if GAVI added value by leveraging its market power when negotiating vaccine prices, historic pricing dynamics in GAVI markets were compared to the historic pricing dynamics in PAHO and non-GAVI UNICEF markets (UNICEF currently procures immunisation supplies for 80 – 100 countries). These comparisons were made on the same vial sizes for all vaccines except pentavalent vaccines, where two different pentavalent presentations are the only products offered in the UNICEF product menus for GAVI countries during this evaluation period (2 dose liquid/lyophilised product and 1 dose liquid product).

To determine market size differences, the infant population for GAVI and PAHO markets were assessed based on the 2010 infant cohort as forecasted in the UN Population database. The infant population associated with non-GAVI UNICEF markets could not be assessed due to lack of information on the exact countries comprising the non-GAVI UNICEF market.

The GAVI infant vaccine market included all GAVI-eligible countries except Somalia (n=71). Somalia was excluded because it is not eligible to apply for vaccines given its DTP3 coverage rate is below the required 50 percent level. The PAHO infant vaccine market included countries that currently purchase vaccines through PAHO’s Revolving Fund with the exception of the six GAVI-eligible Latin American countries (excluded to avoid double counting) and the seven PAHO countries that lacked birth cohort data (total population representing less than 1% of the PAHO market).

The differences in country income level across the two markets were also assessed to aid in the interpretation of results. The income level assessment was based on World Bank country income classifications for 2009.

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5.3.3. Counterfactual analyses

No counterfactual analyses were conducted for this evaluation question. Non-GAVI vaccines (e.g. BCG, DTP, OPV) were inappropriate for generating vaccine price reduction insights given these vaccines have been available at commodity prices for many years. More recent vaccines are either not yet used in developing country public markets (e.g. zoster vaccine) or do not yet have sufficient developing country pricing data for evaluation (e.g. JE).

Biological drugs were not considered as a counterfactual because these products are used primarily in high and upper middle income countries (e.g. chemotherapy) and have very different public market characteristics. Small molecule drugs currently used in developing country public markets (e.g. anti-retrovirals) are also not relevant counterfactuals since small molecules are easier to manufacture (i.e. lower cost of goods) and are already sold at generic prices in developing countries.

5.3.4. Limitations

These analyses have limitations due to:

- Lack of vaccine price data for every vaccine in every year (e.g. missing HepB monovalent (10 dose), and YF vaccine prices for 2001–04).

- Different vaccine prices from different sources (UNICEF and GAVI)
  - GAVI dashboard prices contain WAP that do not match with data provided by UNICEF (vaccine prices and shipped doses by presentation), for example:
    - 2009 YF WAP listed at $0.77/dose which should be $0.81/dose (73% doses shipped were 10 dose vials).
    - 2010 pentavalent WAP listed at $2.85/dose vs. UNICEF’s WAP listed at $3.01/dose for liquid and $2.95/dose for liquid/lyo.
  - UNICEF prices were used because prices were provided by both vaccine type and presentation.

- Inaccurate or inconsistent WHO product information (e.g. GSK’s liquid/lyo pentavalent vaccine prequalified in 1998, but listed as a liquid vaccine in June).

- Redesigned WHO website (went public in June 2010) that no longer provides access to certain information (e.g. GSK’s liquid/lyo pentavalent product information no longer available as of July 2010).

- Different vaccine presentation availability in different markets could not be made due to different vial sizes (e.g. a direct comparison between PAHO and UNICEF pentavalent vaccines from 2001–06).

- Affordability being assessed based on vaccine price alone, ignoring costs associated with vaccine introduction and uptake (e.g. shipping, cold storage, tariffs, human resources).
• Use of proxy data for actual supply and demand data.

• Inconsistent information between UNICEF’s GAVI market product menu and actual UNICEF shipped doses by vaccine type, formulation and presentation, e.g.
  o YF product menu lists WAP for 5 and 10 dose vials only, yet UNICEF documents indicate 5, 10, and 20 dose vials were shipped to countries.
  o One dose lyophilised and 2 dose liquid presentations were included in the doses shipped data in 2008–09, but these presentations have not been prequalified.

• Lack of data regarding UNICEF vaccine price negotiations and procurement decisions that would enable a more thorough understanding of the weighted average price dynamics.

• Lack of access to additional documentation or information that may clarify inconsistencies and ambiguities.

• Limited qualitative insights from:
  o EPI manager electronic survey: participants only represented 30% of GAVI countries.
  o Small number of supplier interviews (n=6 suppliers) limited generalisability and did not allow for disaggregation by sector (emerging/multinational).
  o Limited country-level stakeholder responses due to only five country consultations (7% of total stakeholder countries in 4 out of 6 WHO regions).

5.4. Evaluation analysis

5.4.1. GAVI pricing strategy review

During the design of GAVI in 1999, the Proto-Board defined a procurement strategy that:

• Seeks the lowest effective price for the purchase of these vaccines for the eligible countries;

• Is based on the principle of open, competitive tendering through UNICEF Supply Division;

• Explores a competitive negotiation mechanism with producers of new vaccines to help bring these vaccines to the poorest populations at the earliest possible time; and

• Expresses its gratitude to the pharmaceutical industry for making efforts to make these vaccines available at the lowest possible prices.198

198 1st GAVI Board meeting, 28 October 1999.
From the beginning, low vaccine prices were regarded as a key GAVI goal. A number of studies and activities have been funded by GAVI to update its procurement principles and create supply strategies that could help guide vaccine procurement. A historic summary of GAVI procurement and supply activities is shown in Figure 5.1.

**Figure 5.1: History of GAVI Alliance procurement and supply activities**

A 2002 Mercer study concluded that serious shortcomings and inefficiencies were experienced during the first round of GAVI-financed vaccine procurement. As a result of this study, GAVI’s procurement ‘principles’ were updated and approved in 2004. These refined principles recognised the need for:

- A focus on GAVI’s principle of vaccine stability (ensuring sustainable supply of quality, affordable vaccines) by supporting a diversified supplier base;
- Efficiency of supply with the greatest affordability;
- Transparency with industry and across Alliance partners;
- Effective product-specific procurement strategies and tools to account for market conditions;
- Exploration of longer term arrangements and guaranteed minimum volumes in making awards;
- Encouraging the entry of new suppliers.

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200 Doc AF.7 Supply Strategy. GAVI Board meeting 6-7 December 2005.
The 2004 principles again placed an emphasis on an affordable GAVI supply. These procurement principles were updated again in 2005 (now called ‘procurement objectives’) and used to guide the Supply Strategy Task Team in its development of a Hib- and HepB-containing supply strategy. The 2005 procurement objectives were focused on:

- Ensuring a healthy market: ensuring the sustainable quantity of supply through a diverse supplier base;
- Selecting products and presentations that best meet the need of client countries;
- Achieving a long-term affordable price that countries can eventually finance in a sustainable manner.

At this time, it was recognised that simply increasing demand would not necessarily lead to decreased vaccine prices and that price was dependent on a number of variables, including supply capacity, number of suppliers, changes in product type, and financing. The recommended supply strategy for HepB and Hib-containing vaccines stated that the aim of a supply strategy was to “assure a reliable supply of high-quality vaccines in the presentations and volumes needed to meet developing country demand, at affordable, sustainable prices.”

Upon approval of the 2005 supply strategy for Hib and HepB containing vaccines, the task team was to develop “a detailed procurement strategy and implementation plan...that gives explicit recognition to agreed objectives and proposed suitable methodologies for achieving them.” However, an implementation plan was not delivered to the Board in 2007 and no documentation of the development of an implementation plan to achieve the procurement objectives or the aim of the supply strategy has been found.

GAVI has also not conducted or sponsored any studies to fully understand the cost and market driven determinants of vaccine prices. This type of study should be a fundamental component of any future supply and/or pricing strategy.

In 2010, the Programme and Policy Committee (PPC) proposed to comprehensively revise GAVI’s supply and procurement strategy for GAVI’s current portfolio of vaccines. This strategy is not expected to be delivered to the Board for approval until early 2011. The GAVI Phase I evaluation noted that progress in managing supply and pricing was limited and represented a missed opportunity. Unfortunately, the opportunity to put in place a strategy to address ways to lower vaccine prices has also been missed in Phase II.

The result of not having put in place a specific plan for reducing vaccine prices has been a continued reliance on natural market forces to lower vaccine prices. This evaluation focuses on the impact natural market forces have had for reducing vaccine prices. Where possible, this analysis seeks to understand GAVI’s role in vaccine pricing for GAVI markets.

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201 Doc AF.7 Supply Strategy. GAVI Board meeting 6-7 December 2005.
202 Personal communication, GAVI Secretariat, 22 July 2010.
5.4.2. Yellow fever vaccine price analysis

Historically, multiple YF vaccine presentations have been prequalified and available to UNICEF markets (i.e. 5, 10, 20, and 50 dose vials). However, from 2003 onward, when UNICEF information was available on YF vaccines for GAVI markets, only the 5 and 10 dose vials were offered in these markets.

Figure 5.2 provides the WAP per dose for 5 and 10 dose vials of lyophilised YF vaccine in UNICEF/GAVI markets over time.

For both presentations, vaccine price has increased steadily over time, with 2010 prices at $0.69/dose for 5 dose vials and $0.90/dose for 10 dose vials. The WAP for 5 dose vials increased by $0.11/dose (19%) between 2004–10 while the 10 dose vial increased by $0.10/dose (12%) over the same time period. A more accurate assessment of the true increase in price over time was not possible due to missing price data for 2001-03. However, the non-GAVI UNICEF prices in 2002 were $0.45/dose for 5 dose vials and $0.63/dose for 10 dose vials, indicating a 2002–10 price increase of 53% and 43% for 5 and 10 dose vials, respectively.

To understand the potential drivers associated with these price increases, the price dynamics were compared to the supply and demand dynamics during this timeframe. Only the 10 dose YF vaccine presentation was examined since the majority of GAVI-eligible countries receive the 10 dose vial presentation (> 65%).

Figure 5.3 shows the relationship among vaccine price, supplier, and demand dynamics. Given there has been an increase in the number of prequalified products over time, and a more stable YF vaccine market due to GAVI’s funding of routine infant immunisation and a stockpile for outbreaks and preventive campaigns, one might expect prices to have declined, or at least stabilised over time. However, in this case, supplier characteristics must be considered before drawing any pricing dynamic conclusions.

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Currently, two of the four YF vaccine suppliers are state-owned suppliers who are mandated to first meet national and then regional demand before providing YF vaccines to UNICEF markets. This results in available supply from these manufacturers being highly uncertain and often limited. Consequently, UNICEF must procure a greater portion of the required supplies from the highest priced supplier. This has been a major contributor to the lack of YF vaccine price decline in GAVI markets.

Going forward, growing concerns about the availability of sufficient donor financing to support YF vaccine procurement for these markets may result in reduced supply capacity or supply reallocation to other markets. Should these concerns become reality, prices may continue to increase as GAVI moves into Phase III. It is unclear at this time what strategies GAVI will put in place to mitigate the risk of continued price increases.

5.4.3. HepB mono- and tetravalent vaccine price analysis

HepB monovalent

Historically, UNICEF has offered five different HepB monovalent presentations. However, the 20 dose vial size was not offered after 2003. It is important to note HepB monovalent vaccines were not funded in GAVI Phase II, and as of 2010, are no longer offered in UNICEF’s product menu to GAVI countries.

Figure 5.4 provides the WAP per dose over time for each of the HepB monovalent vaccine presentations.

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206 Personal communication, UNICEF Supply Division, January 2010.
207 Yellow Fever Investment Case, Continuation Proposal. Submitted by the Yellow Fever Initiative to the GAVI Alliance, May 2008.
Figure 5.4: HepB monovalent vaccine price per dose for all vial sizes in GAVI markets

As shown, the 10 dose presentation is currently the least expensive vaccine, priced at approximately 55% to 80% of the other vaccine presentations ($0.05-$0.15/dose less) as of 2009. From 2001–10 (2004–09 for 10 dose), there has been a decline in price for every presentation type. These price declines are summarised in Table 5.2.

Table 5.2: HepB monovalent vaccine price declines 2001–09

<table>
<thead>
<tr>
<th>Presentation (doses per vial)</th>
<th>HepB monovalent 2001–09 price decline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$/dose</td>
</tr>
<tr>
<td>1 dose</td>
<td>$0.35</td>
</tr>
<tr>
<td>2 dose</td>
<td>$0.30</td>
</tr>
<tr>
<td>6 dose</td>
<td>$0.22</td>
</tr>
<tr>
<td>10 dose</td>
<td>$0.09</td>
</tr>
<tr>
<td></td>
<td>(2004-09 only)</td>
</tr>
</tbody>
</table>

To understand the potential drivers associated with these price declines, the price dynamics were compared to the supply and demand dynamics during this timeframe. Only the 10 dose presentation was examined since the majority of GAVI-eligible countries received the 10 dose vial presentation.209

Figure 5.5 shows the relationship among vaccine price, supplier, and demand dynamics.

The price changes over time are likely due to natural market forces, in this case:

- Supplier competition driving prices downward as the number of WHO prequalified products increased from 3 in 2001 to 9 in 2010.
- Over supply due to the decrease in demand since 2006 when GAVI stopped financing HepB monovalent vaccines (post Phase I) in lieu of Hib-containing pentavalent vaccines.

Figure 5.5: Relationship among price, number of prequalified products, and demand (shipped doses) for HepB monovalent vaccines

The majority of the HepB monovalent doses in 2009 (nearly 70%) were shipped to India, as the majority of other GAVI countries introduce or switch to the pentavalent vaccine.210

HepB tetravalent

For HepB tetravalent vaccines, a 10 dose liquid presentation was available from 2001–09. This presentation will not be offered after 2010. A 2 dose liquid presentation was listed on the UNICEF/GAVI product menu from 2006–09, but was not included in the 2010 product menu.211

Figure 5.6 provides the WAP per dose for both HepB tetravalent vaccine presentations.

Figure 5.6: HepB tetravalent vaccine price per dose for all vial sizes in GAVI markets

The 2-dose presentation price has remained steady from 2006–09, and is likely due to limited supplies from a single supplier and limited demand for this product (≤ 58,000 doses in 2006–08). Price for the 10 dose presentation has increased and decreased over time, with an overall 37%, or $0.41/dose decline since 2001.

To understand the potential drivers associated with these price changes, the price dynamics were compared to the supply and demand dynamics during this timeframe. Only the 10 dose HepB tetravalent presentation was examined since the majority of GAVI-eligible countries received the 10 dose vial presentation (> 99%). Figure 5.7 shows the relationship among vaccine price, supplier, and demand dynamics.

Figure 5.7: Relationship among price, number of prequalified products, and demand (shipped doses) for HepB tetravalent vaccines

The price decline in 2007 was likely due to price competition and declining demand expectations as the number of WHO prequalified products increased as suppliers also began to anticipate the decline in demand due to the market shift toward pentavalent vaccines. The rationale for the price increase from 2003 to 2006 is less obvious, especially since the second prequalified product was from an emerging supplier.

5.4.4. Evaluation analysis: Hib mono- and tetravalent vaccine price analysis

Historically, UNICEF has offered three Hib monovalent and two Hib tetravalent presentations. However, neither vaccine will be included in the UNICEF/GAVI product menu beyond 2011.

As shown in Figures 5.8 and 5.9, the prices for both Hib mono- and tetravalent vaccines have increased over time. Since the demand for Hib mono- and tetravalent vaccines has been minimal (≤135,000 and ≤1.1m annual doses, respectively), these vaccines have only been included in this evaluation for completeness.

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Given GAVI's focus on pentavalent vaccines and the limited demand for these vaccines, GAVI would not be expected to focus on reducing Hib mono- and tetravalent vaccine prices.

5.4.5. Pentavalent vaccine price analysis

The first pentavalent vaccine was composed of liquid DTwP-HepB and lyophilised Hib monovalent vaccine. This liquid/lyophilised product was offered in 2 dose vials. The first fully liquid pentavalent vaccine was WHO prequalified in 2006 and became available to GAVI markets in 2007.

As shown in Figure 5.10, pentavalent vaccine prices did not drop significantly until 2010. The price of the liquid/lyophilised pentavalent vaccine started at $3.50/dose in 2001 and decreased in the second and third year of the first tender (2001–03). At the start of the second tender (2004), the price increased to $3.65/dose then decreased to $3.60/dose for the remaining two years (2005–06).
The 2004 increase in price was due to the lone supplier needing to accelerate their return on investment in anticipation of the liquid pentavalent vaccine eroding the lyophilised formulation market.\textsuperscript{214} Recently, the liquid/lyophilised price has decreased to $2.95/dose (2010). An additional supplier has recently prequalified a liquid/lyophilised pentavalent vaccine in multiple vial sizes (SII in 2010), so the weighted average price of this vaccine formulation is expected to decline further.\textsuperscript{215}

In 2007, a fully liquid presentation was prequalified in a 1 dose presentation with a price of $3.75/dose. In 2008, two emerging suppliers prequalified liquid pentavalent vaccines and the price began to decline as a result of market competition. The 2010 WAP is now $3.01/dose which is a 20\% reduction from 2007.

These price declines are summarised in Table 5.3. As shown, significant price reductions are now occurring in 2010.

\textbf{Table 5.3: Pentavalent vaccine price declines 2001–09}

<table>
<thead>
<tr>
<th>Formulation (doses per vial)</th>
<th>Pentavalent price declines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Through 2009</td>
</tr>
<tr>
<td></td>
<td>$/dose</td>
</tr>
<tr>
<td>Liquid/lyophilised (2 dose vial)</td>
<td>$0.00 (2001–09)</td>
</tr>
<tr>
<td>Liquid (1 dose vial)</td>
<td>$0.34 (2007–09)</td>
</tr>
</tbody>
</table>

To understand the potential drivers associated with these price declines, the price dynamics were compared to the supply and demand dynamics during this timeframe. Figure 5.11 shows the relationship among vaccine price, supplier, and demand dynamics.

\textsuperscript{214} Personal communication, UNICEF Supply Division, June, 2010.

\textsuperscript{215} \url{http://www.who.int/immunisation_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html}, (accessed 22 July 2010)
Throughout GAVI Phase I, a single supplier was serving the pentavalent market. With no supplier competition or pressure from the global community to lower vaccine prices, this supplier was able to maintain a relatively constant price per dose between 2004–09.\textsuperscript{216,217} When the first liquid vaccine became available in 2007, the price per dose was higher than the liquid/lyophilised product despite the elimination of a costly lyophilisation step. This higher price was likely due to a combination of the higher costs associated with a 1 versus 2 dose vial and a single supplier market for the preferred liquid formulation.

For the liquid pentavalent vaccine, the natural market forces that typically drive vaccine prices down began to emerge in 2008 when two additional liquid pentavalent vaccine products were prequalified. Liquid pentavalent vaccine prices declined 9\% through the 2009 evaluation period, and declined 20\% by 2010. UNICEF projects further declines through 2012.

How long it will take to achieve commodity-level prices for pentavalent vaccines and what that price will be is still highly uncertain. It is unclear at this time what strategies GAVI will put in place to accelerate pentavalent price decline, but the incentive to do so is significant as demand for this vaccine exceeds all other GAVI vaccines.\textsuperscript{218}

5.5. **Comparative analyses**

5.5.1. **GAVI and PAHO market analysis**

To determine if GAVI has made vaccines more affordable, GAVI vaccine prices should not only be examined in isolation, but in comparison to other relatively large vaccine markets. The most relevant markets for comparison purposes are the non-GAVI UNICEF and PAHO markets. The non-GAVI UNICEF market is comprised of 80–100 countries,


\textsuperscript{218} \url{http://www.unicef.org/supply/index_gavi.html} (accessed 22 July 2010).
including the current 72 GAVI countries, and represents the overall buying power of UNICEF. Given the non-GAVI UNICEF market contains middle income countries, higher prices relative to GAVI markets alone would be expected based on tiered pricing principles.

The PAHO markets represent the buying power of the PAHO Revolving Fund. Given this market is also comprised of a large number of middle income countries, it too would be expected to procure higher priced vaccines relative to UNICEF/GAVI, both due to relative market size and income level distribution.

To better understand the differences between these markets, the size of the infant vaccination market (birth cohort) was assessed and further classified by country income level. Population data for the non-GAVI UNICEF market was not obtainable, therefore, Table 5.4 summarises the size of the UNICEF/GAVI and PAHO markets in 2010 and how these market are distributed by country income classification. The PAHO infant vaccine market includes countries that currently purchase vaccines through PAHO’s Revolving Fund, with the exception of the six GAVI-eligible PAHO countries.

Table 5.4: UNICEF and PAHO market characteristics

<table>
<thead>
<tr>
<th>Market Characteristics</th>
<th>GAVI Birth cohort (millions)</th>
<th>PAHO Birth cohort (millions)</th>
<th>Non-GAVI Birth cohort (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Middle</td>
<td>80</td>
<td>0% (6M infants)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Lower Middle</td>
<td>60% (48M infants)</td>
<td>15% (1M infants)</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>40% (32M infants)</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

GAVI’s infant vaccine market is 11 times larger (73m infants more) than PAHO’s. In addition, 40% of the GAVI market is in low income countries, while the majority of the PAHO market is in upper middle income countries (85%). The significant size and income level differences between these two markets was expected to drive the greater purchasing power of UNICEF, resulting in greater volume discount and lower vaccine prices for GAVI markets.

5.5.2. Yellow fever vaccine prices in comparator markets

Figure 5.12 provides the weighted average price for 5 dose vials of YF vaccine in UNICEF/GAVI, non-GAVI UNICEF (represented as UNICEF), and PAHO markets.

UNICEF/GAVI prices are generally equivalent to UNICEF prices except for 2010 when the UNICEF/GAVI price is slightly higher than the UNICEF price ($0.69/dose versus $0.66/dose, respectively).

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The rationale for the difference in these 2010 prices is not clear, but it’s expected that GAVI demand will exceed the 2.5m doses projected for non-GAVI UNICEF markets given 2009 GAVI demand exceeded 4m doses.\textsuperscript{221} Therefore, it is unclear why UNICEF was able to secure a lower price and why this price was not also offered to GAVI markets.

From 2004–09, PAHO prices are higher than UNICEF/GAVI, with the exception of 2007, when prices are roughly equivalent. In 2004–05, PAHO prices are approximately 10% higher ($0.07/dose) than UNICEF/GAVI prices and in 2008–09, approximately 5% greater ($0.04/dose). Prices in both PAHO and GAVI markets have increased overall between 2005–10.

The lower UNICEF/GAVI prices relative to PAHO are likely explained by the supplier landscape. PAHO YF vaccine supplies are sourced from a single Brazilian supplier, whereas UNICEF procures YF vaccines from multiple suppliers (Brazil, France, Senegal, and Russia).

Figure 5.13 provides the weighted average YF vaccine price for 10 dose vials in UNICEF/GAVI, UNICEF, and PAHO markets.

UNICEF/GAVI prices are generally equivalent to UNICEF prices except for 2009 when the UNICEF/GAVI price is slightly higher than the UNICEF price ($0.87/dose versus $0.86/dose, respectively). The one cent per dose difference was not considered material for this comparative analysis.

\textsuperscript{221} http://www.unicef.org/supply/files/Product_Menu_update_31_May.pdf (accessed 22 July 2010).
PAHO prices relative to UNICEF/GAVI prices vary widely between 2004–09. In 2004–05, PAHO prices are approximately 10% higher ($0.07/dose) than UNICEF/GAVI prices and from 2006–09, PAHO prices are 10-20% lower ($0.10 - $0.18/dose) than UNICEF/GAVI prices. Information explaining the erratic nature of PAHO pricing for the 10 dose vial was not available. Therefore, it is not possible to evaluate UNICEF/GAVI relative to PAHO on prices for the 10 dose YF vaccine.

5.5.3. HepB mono- and tetravalent vaccine prices in comparator markets

HepB monovalent

PAHO prices were not available for the 2, 6 and 10 dose vial presentation for HepB monovalent vaccines, therefore, one dose vials were the only type of vaccine compared in this analysis.

Figure 5.14 provides the weighted average HepB monovalent vaccine price for one dose vials in UNICEF/GAVI, UNICEF, and PAHO markets.

UNICEF prices are slightly lower than UNICEF/GAVI market prices in 2002–03, equivalent from 2004–06, and $0.13/dose higher (48%) from 2007–10. The drivers of these price differences are unclear. An analysis of projected doses in UNICEF markets versus shipped doses to GAVI markets was attempted to understand the role demand might have played in the price differences. However, the data could not be reconciled in any given year (e.g., projected doses in UNICEF markets, which included projected GAVI doses, were less than the actual GAVI doses shipped).222,223

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PAHO prices were generally lower than UNICEF/GAVI prices, except in 2004 ($0.01/dose difference) and in 2009, when they are equivalent. Since PAHO procures only 1 dose HepB monovalent presentations for all infant vaccinations, the lower prices are likely due to the higher demand relative to UNICEF/GAVI markets where the demand for one dose vials was small (< 2.8m annually from 2001–09).  

**HepB tetravalent**

Figure 5.15 provides the weighted average prices for a 10 dose HepB tetravalent vaccine in UNICEF/GAVI and UNICEF non-GAVI markets. A comparison to the PAHO market could not be made because PAHO does not procure HepB tetravalent vaccines.

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The UNICEF 10 dose vial price was essentially equivalent to the UNICEF/GAVI price from 2002-05 except in 2003 when the UNICEF/GAVI price was $0.05/dose less (5%) than UNICEF.

### 5.5.4. Pentavalent vaccine prices in comparator markets

Figure 5.16 provides the weighted average pentavalent vaccine price for multiple presentations in UNICEF/GAVI, UNICEF, and PAHO markets.

**Figure 5.16: Pentavalent vaccine price per dose for multiple presentations in comparator countries**

A 2 dose liquid/lyophilised UNICEF product offered from 2002-05 was comparable to UNICEF/GAVI prices except in 2003 when the UNICEF/GAVI price was 3% lower ($0.10/dose).

PAHO and UNICEF/GAVI price comparisons for the liquid/lyophilised product were not possible because of differences in presentation. PAHO markets procure 1 dose presentations and UNICEF/GAVI procures 2 dose presentations. The one dose PAHO prices are likely higher than the 2 dose UNICEF/GAVI prices because of the cost of the vial. PAHO prices for the one dose liquid formulation were 4-12 percent ($0.14 to $0.42/dose) higher than UNICEF/GAVI prices from 2007-09. PAHO prices were not available for 2010.

### 5.5.5. New vaccine prices in comparator markets

While it is too early to evaluate vaccine prices over time for the new vaccines, it is worth pointing out that both pneumococcal and rotavirus vaccine prices are or will be priced significantly less than in high and middle income markets. This is the principle of ‘tiered pricing,’ where suppliers price their vaccines according to country income levels (i.e. the ability of the country to pay). For example, in 2009, the single dose HepB monovalent vaccine was priced at $9.50-$10/dose in the US public market compared to $0.27/dose in...
Even for a vaccine that has been licensed for nearly 30 years, the low income market price is only 3% of the price in high income markets.

**Pneumococcal vaccines**

An innovative financing mechanism, the Advanced Market Commitment (AMC), is being piloted on pneumococcal vaccine introduction in GAVI markets (see SG3 for details on the AMC and GAVI’s role). This mechanism provides an upfront subsidy payment to suppliers in exchange for a 10-year commitment to supply pneumococcal vaccines at a price of $3.50 or less per dose. The upfront subsidy is paid from a $1.5 billion fund created through donations from seven donors and results in a price to suppliers of $7.00 per dose during the subsidy period, typically 2-3 years depending on actual demand.

Although direct price comparisons between high and low income public markets cannot be made for pneumococcal vaccines because of the presentation differences (high income markets use pre-filled syringes), the price differences are still significant. GAVI market prices are 4-5% of US public market prices ($66.44/dose to $91.75/dose for PCV7 and PCV13, respectively). The $3.50/dose GAVI price ceiling for any AMC eligible pneumococcal vaccine is also 16% or $21.75 per dose lower than the 2009 PAHO price for the PCV7 vaccine. This price difference currently represents the largest price difference between vaccines introduced in both GAVI and PAHO markets.

Although pneumococcal vaccines will be priced significantly lower than in other markets, it is too early to know if GAVI-eligible countries will be able to afford this vaccine once GAVI financing support is no longer available. To mitigate the risk of delayed introduction or unsustainable pneumococcal vaccine programs due to country financial constraints, GAVI will need to work closely with vaccine suppliers to identify how best to incentivise these suppliers to offer these vaccines at a price well below the current $3.50 per dose price ceiling.

**Rotavirus vaccines**

Rotavirus vaccine prices have yet to be negotiated by UNICEF so price comparisons cannot be made. However, it is worth noting that these vaccines currently cost $59.18/dose ($177.54/treatment) and $83.75/dose ($167.50/treatment) in US public markets compared to approximately $16.00/treatment in PAHO markets ($5.50/dose for the 3 dose vaccine and $7.90/dose for the 2 dose vaccine). PAHO prices are approximately 10% of the cost in the US public market. It is expected that UNICEF will be able to negotiate a lower price than PAHO for GAVI markets.

Rotavirus vaccines will likely face the same affordability challenges as pneumococcal vaccines once GAVI financing support is no longer available. To mitigate the risk of delayed introduction or unsustainable rotavirus vaccine programs due to country financial constraints, GAVI will also need to work closely with rotavirus vaccine suppliers to identify

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227 Ibid.

how best to incentivise these suppliers to offer their vaccines at a price that will be affordable to this market.

5.5.6. Country affordability analysis

“Affordability” is defined by GAVI as a “price that countries can eventually finance in a sustainable manner.” While a more in-depth discussion on affordability is provided in the SG3 evaluation, this analysis compares the amount countries are currently paying for their non-GAVI supported vaccines to what they would be paying if they were also fully responsible for the price of their GAVI vaccines.

In 2010, the total country cost to fully immunise an infant against BCG, measles, and polio (non-GAVI funded vaccines) is approximately $0.78.\(^\text{229}\) As shown in Table 5.5, with GAVI funding of the underused vaccines, adding YF and pentavalent vaccines now costs a country $1.38 to fully immunise an infant with BCG, measles, polio, pentavalent (DTwP-HepB-Hib), and YF vaccines. However, without GAVI funding, the cost to fully immunise an infant with these vaccines would increase to $10.50, which is a 7.8-fold increase over the current cost to country. It is unlikely countries would be able to afford this level of cost increase once GAVI funding is no longer available. Therefore, GAVI will need to successfully define and implement strategies to significantly reduce underused vaccine prices in Phase III.

Table 5.5: 2010 cost to fully immunise an infant with underused vaccines in a GAVI-eligible country

<table>
<thead>
<tr>
<th>Vaccine (presentation)</th>
<th>Doses required</th>
<th>2010 Cost of fully immunised infant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WAP/dose(^1)</td>
<td>Non-GAVI funded vaccines</td>
</tr>
<tr>
<td>BCG (20ds)</td>
<td>1</td>
<td>$0.05</td>
</tr>
<tr>
<td>MCV (10ds)</td>
<td>1</td>
<td>$0.23</td>
</tr>
<tr>
<td>tOPV (10ds)</td>
<td>3</td>
<td>$0.17</td>
</tr>
<tr>
<td>Penta (1ds)</td>
<td>3</td>
<td>$2.94</td>
</tr>
<tr>
<td>YF (10ds)</td>
<td>1</td>
<td>$0.90</td>
</tr>
</tbody>
</table>

\(^1\)2010 UNICEF non-GAVI and GAVI WAP
\(^2\)Assumes $0.15/dose co-pay for each vaccine per dose

As countries introduce pneumococcal vaccines with GAVI funding, the cost to fully immunise an infant increases to $1.83 (assuming a country co-pay of $0.15/dose). However, as shown in Table 5.6, country immunisation costs without GAVI funding would cost $21.21 for a fully immunised infant given current prices. This is a greater than 11-fold increase in country immunisation costs per infant.

Table 5.6: 2010 cost to fully immunise an infant with underused and pneumococcal vaccines in a GAVI country

<table>
<thead>
<tr>
<th>Vaccine (presentation)</th>
<th>Doses required</th>
<th>WAP/dose(^1)</th>
<th>2010 Cost of fully immunised infant</th>
<th>Country immunisation costs with GAVI funding</th>
<th>Country immunisation costs without GAVI funding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Non-GAVI funded vaccines</td>
<td>GAVI-funded vaccines</td>
<td></td>
</tr>
<tr>
<td>BCG (20ds)</td>
<td>1</td>
<td>$0.05</td>
<td>$0.78</td>
<td>-</td>
<td>$1.83</td>
</tr>
<tr>
<td>MCV (10ds)</td>
<td>1</td>
<td>$0.23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tOPV (10ds)</td>
<td>3</td>
<td>$0.17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penta (1ds)</td>
<td>3</td>
<td>$2.94</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YF (10ds)</td>
<td>1</td>
<td>$0.90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumo (1ds)</td>
<td>3</td>
<td>$3.50</td>
<td></td>
<td>$1.05</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) 2010 UNICEF non-GAVI and GAVI WAP
\(^2\) Assumes $0.15/dose co-pay for each vaccine per dose

While GAVI has worked hard on behalf of developing countries to negotiate a low price for pneumococcal vaccines, these prices may not be affordable to many GAVI-eligible countries once GAVI financing support is no longer available.\(^{290}\)

5.6. Qualitative analyses

5.6.1. Electronic survey results

Among the 20 statements in the electronic survey, only one was designed to solicit feedback on GAVI’s impact on the affordability of vaccines and related technologies. Responses to the statement: “GAVI has made vaccines and related technologies more affordable to countries.” are summarised in Figure 5.17.

\(^{290}\) Evaluation team estimate.
Slightly less than 70% of survey respondents strongly agreed or agreed with this statement, while 6% disagreed or strongly disagreed. This statement did not make a distinction between affordability based on the actual vaccine price versus affordability based on the required country co-pay. Therefore, conclusions based on these results would be questionable.

Sixty-two respondents to the electronic survey provided additional ad hoc comments on this topic. These responses were summarised into overarching themes. Table 5.7 summarises these comments by the themes that represented at least 10% of the comments provided.

Table 5.7: E-survey qualitative response feedback themes for question 14 – ‘GAVI has made vaccines and related technologies more affordable to countries’

<table>
<thead>
<tr>
<th>Response Theme</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAVI support and co-financing have made vaccines more affordable to countries</td>
<td>15</td>
</tr>
<tr>
<td>Sustainability is an issue/long-term affordability is unclear</td>
<td>13</td>
</tr>
<tr>
<td>Modest decline in prices/not as much decline as expected</td>
<td>9</td>
</tr>
</tbody>
</table>

While the most frequent comment was that GAVI support has made vaccines more affordable to GAVI-eligible countries, the next most frequent comment was that sustainability remains a concern. The last theme representing at least 10% of the comments suggested GAVI vaccine price declines were modest or less than expected.

5.6.2. Structured interview results

Of the 22 current and former GAVI Board members who participated in the structured interviews, 17 (77%) commented on GAVI's impact on vaccine price. Nine of these 17 (52%) commented specifically that GAVI could have done more to reduce vaccine prices
and/or that it is not clear why GAVI was able to reduce vaccine prices. The 8 remaining respondents (47%) spoke more generally about how vaccine prices did not decrease as much as expected. Four respondents noted that the price of some HepB-containing vaccines had declined, but two of those four questioned whether GAVI had anything to do with the decline. Three respondents commented that GAVI (either itself or through its partners) should work to encourage emerging suppliers to enter the low income vaccine market. Several other respondents noted the vaccine market had a limited number of suppliers.

At some point during their structured interviews, 11 of the current and former GAVI Board members commented on the issue of vaccine sustainability at the country level, saying either that GAVI could do more on this issue or that there were many unknowns around sustainability.

5.6.3. Country visit results

Five country visits were conducted as a part of GAVI’s Phase II evaluation. While structured questions were not asked regarding GAVI’s role in making vaccines more affordable, a variety of country-specific insights were generated from these country consolidations.

Bangladesh

Bangladeshi stakeholders commented that Bangladesh has successfully met its co-financing payments so far. Bangladeshi interviewees noted without GAVI support and the co-financing system, it would not have been able to cover the cost of introducing monovalent HepB and pentavalent vaccines. Bangladeshi stakeholders did report substantial concern regarding its ability to fully fund these vaccines in the absence of GAVI. They felt GAVI could do more to support emerging market manufacturers to enter the market, which would lead to lower vaccine prices. Bangladeshi stakeholders said specifically it would be helpful if the pentavalent vaccine price declined from approximately $3 per dose to $1.80 per dose.

Bolivia

Bolivian stakeholders made no relevant comments regarding the price of underused vaccines.

Mali

Malian stakeholders made no relevant comments regarding the price of underused vaccines.

Nigeria

Nigerian stakeholders noted the relatively high prices of pentavalent and pneumococcal vaccines and acknowledged they would find it difficult to fund these vaccines without GAVI financial support.
Uzbekistan

Uzbek stakeholders noted that pentavalent vaccine continues to be too expensive for the government to fund on its own, and some country stakeholders noted the limited price reduction in the vaccine thus far.

5.7. Conclusions

The results of this SG2.4 evaluation are consistent with previous evaluations and documentation that concluded creating a large and stable market for vaccines was not sufficient for realizing rapid reduction in vaccine prices. Although price reductions have been achieved for some GAVI supported vaccines, the most widely used vaccines have not become affordable for countries over the course of GAVI's first 10 years.

Although GAVI did attract three additional YF vaccine suppliers to the market by 2009, YF vaccine prices increased 12-19% over the 2004–10 timeframe and by greater than 40-50% over 2002 non-GAVI UNICEF prices. Prices may increase further if GAVI's current funding gap is not resolved, as the GAVI Board recently approved only $22m of the $180m requested for YF vaccines. Supplier perceptions of continued financing shortfalls may lead to further price increases.

GAVI has probably improved the affordability of HepB-containing vaccines. GAVI also attracted four additional HepB monovalent and four additional HepB tetravalent vaccine suppliers to the market by 2009. HepB monovalent vaccine prices for all presentations and HepB tetravalent vaccine prices for the 10 dose presentation declined by 32-56% and by 37% respectively between 2001–09 (2004–09 for the 10 dose HepB monovalent vaccine). Ordinarily it might be reasonable to conclude that the additional suppliers attracted by GAVI would have contributed to the observed price reductions. However, the entry of the new suppliers also coincided with a significant decline in demand for these vaccines as GAVI-eligible countries adopted or transitioned to the pentavalent vaccine. Therefore, it is difficult to attribute these price declines to GAVI actions.

GAVI also attracted three additional pentavalent vaccine suppliers to the market between 2004–09. The price of the liquid/lyophilized formulation did not decline through 2009, however, a 16% decrease did occur in 2010. This decline was likely driven by decreased demand due to the increased liquid formulation supply. Additional price reductions are expected once the second liquid/lyophilized product enters the market (prequalified in May 2010).

The liquid pentavalent vaccine formulation, introduced in 2007, declined in price by 9% between 2007–09 and by 20% through 2010. The presence of three liquid pentavalent vaccine suppliers by 2008 drove the price declines.

Although GAVI can be credited with attracting additional suppliers to the pentavalent vaccine market, the price declines to date have been driven by competitive market forces. While any declines in price do make the vaccine more affordable to GAVI-eligible countries, the declines to date are not sufficient to make the vaccine affordable in a sustained way once GAVI financing support is no longer available.
For pneumococcal and rotavirus vaccines, the GAVI price is either far lower or expected to be far lower than high income public market prices. While much effort has gone into appropriately pricing these vaccines for low income markets, these vaccine prices are unlikely to be sustainable for most countries without continued GAVI funding (see additional perspective on affordability in the SG3 evaluation).

The expectation has been and remains that GAVI would put strategies in place to make vaccines more affordable for GAVI-eligible countries beyond what could be achieved by natural market forces. The fact that this has not happened in Phase II, especially after it was identified as a major issue after Phase I, is a clear failure by GAVI. This failure is either the result of a lack of prioritization of this objective or a lack of understanding about what does and could drive vaccine price declines.

Overall, our judgement is that vaccine pricing has been an area of weak performance by GAVI. In reaching this conclusion, we recognise that:

- The ability to achieve price reductions is affected by a wide range of cost and market factors, which may not easily be in GAVI (or UNICEF’s) control; and

- Without GAVI financing, countries would not be able to introduce and take to scale critically important and impactful vaccines.

The primary failure in our view is that GAVI has not been sufficiently proactive in understanding the nature of price drivers for its key vaccines or in working with suppliers to maximise price reductions through explicit strategies. Given the complexity of these markets, we cannot say what the results of a more proactive approach would have been, but it is clear that relying on natural market forces to reduce vaccine prices can be a slow process.

The robustness of the conclusions included in this section are summarised in Table 5.8 based on a relative rating scale described in section 1.1.3 of the Introduction.

Table 5.8: Relative robustness of SG2.4 findings

<table>
<thead>
<tr>
<th>Evaluation question SG2.4: To what extent has GAVI made vaccines and related technologies more affordable?</th>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role of GAVI supply strategy in improving affordability</td>
<td>• Although GAVI supply and procurement strategy documents have emphasised the need for ‘affordable’ vaccines, GAVI has not had a plan in place during Phase 1 or Phase 2.</td>
<td>A</td>
<td>• Information comes from reliable sources (e.g., previous GAVI evaluations, GAVI Board documents, and GAVI procurement documents).</td>
</tr>
<tr>
<td></td>
<td>• GAVI intends to submit a supply strategy in 2011 that is expected to include a plan to address vaccine pricing.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAVI’s impact on YF vaccine affordability</td>
<td>• GAVI has not improved YF vaccine affordability.</td>
<td>A</td>
<td>• Data comes from reliable sources (e.g. UNICEF</td>
</tr>
<tr>
<td></td>
<td>– GAVI WAP for 5- and 10-dose vials</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Evaluation question SG2.4: To what extent has GAVI made vaccines and related technologies more affordable?

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analyses</strong></td>
<td><strong>Findings</strong></td>
<td><strong>Robustness</strong></td>
</tr>
</tbody>
</table>
| **GAVI’s impact on HepB monovalent and tetravalent vaccine affordability** | • GAVI has improved HepB monovalent vaccine affordability.  
  - Prices for 10 dose HepB monovalent decreased by 32% from 2004-09.  
  - The number of prequalified suppliers increased to nine by 2008.  
  - Demand decreased to 12m doses by 2009 (without India) due to pentavalent preference.  
  • GAVI has improved HepB tetravalent vaccine affordability.  
  - The price of the 10 dose HepB tetravalent presentation decreased by 37% from 2004-09.  
  - The number of prequalified suppliers increased to five by 2007.  
  - Demand decreased to 1m doses by 2009 due to pentavalent preference. | A  
  • Data comes from reliable sources (e.g. UNICEF product menus).  
  • Missing 2001-03 prices will not change conclusions. |
| **GAVI’s impact on pentavalent vaccine affordability** | • WAP of pentavalent vaccine has only recently decreased, but GAVI has not yet made this vaccine ‘affordable’.  
  - Single supplier exists for GAVI market through 2006.  
  - Two suppliers supplying GAVI market by 2008.  
  - Liq/lyo presentation WAP did not decline from 2001-09 ($3.50/dose) but recently declined 16% to $2.95/dose in 2010.  
  - Liquid presentation WAP started higher than liq/lyo presentation in 2007 ($3.75/dose) and decreased 20% to $3.01/dose in 2010. | A  
  • Data comes from reliable sources (e.g. UNICEF product menus).  
  • Comparisons limited due to 2-dose liq/lyo and 1-dose liquid formulations, but will not change conclusion |
| **GAVI’s impact on pneumococcal vaccine affordability** | • Through the AMC, GAVI has secured pneumococcal vaccine prices that are significantly lower than middle- or high- | A  
  • Data comes from reliable sources (e.g. AMC supply |
**Evaluation question SG2.4:** To what extent has GAVI made vaccines and related technologies more affordable?

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>income markets.</td>
<td></td>
</tr>
<tr>
<td>GAVI’s impact on rotavirus vaccine affordability</td>
<td>• Rotavirus vaccine prices cannot be evaluated since UNICEF has not yet negotiated a price for GAVI countries.</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>Data comes from reliable sources (GAVI Secretariat, UNICEF).</td>
</tr>
<tr>
<td>GAVI’s impact on country-level vaccine affordability</td>
<td>• It is unlikely GAVI countries can afford underutilised or new vaccines once GAVI financing support ends.</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>• The cost of fully immunising an infant with YF and pentavalent vaccines will increase &gt; 7-fold.</td>
<td>Data comes from reliable sources (e.g. UNICEF product menus, GAVI Phase II financing policy).</td>
</tr>
<tr>
<td></td>
<td>• The cost of fully immunising an infant with YF, pentavalent, and pneumococcal vaccines will increase &gt; 11-fold.</td>
<td>• Limited country input, but all relevant comments have been consistent.</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>
6. **SG2.5: EVIDENCE BASE FOR NEW VACCINE INTRODUCTION**

6.1. **Introduction**

The fifth evaluation question under SG2 is: “To what extent has GAVI contributed to the advancement of the evidence base required for countries to address the policy decision related to the introduction of new vaccines?”

Experts have stated that disease burden, vaccine safety and effectiveness, cost effectiveness data, and country vaccination infrastructure are believed to be helpful for vaccine introduction decisions.\(^{231,232,233}\) Even though studies on disease burden and vaccine safety and effectiveness are important, these studies have not routinely been conducted in low-income countries.\(^{234}\)

GAVI has funded organisations chartered with advancing the evidence base for YF, Hib-containing, pneumococcal, and rotavirus vaccines to support their accelerated introduction into GAVI-eligible country immunisation programs. This section reviews GAVI’s contribution to the advancement of the evidence base required for countries to make an informed vaccine introduction decision.

6.2. **Scope of the evaluation question**

This section evaluates GAVI’s role in advancing the evidence base required for countries to make a vaccine introduction decision. The evaluation:

- Examined the extent to which GAVI advanced the evidence, based on the results of two recent evaluations
- Summarised major contributions to the evidence base from GAVI-funded ADIPs and Initiatives
- Summarised others’ perceptions on the timeliness and accuracy of GAVI’s demand forecasts (e.g. structured interviews)

6.3. **Methodology**

6.3.1. **Overview**

Unlike the other SG2 evaluation questions, contributions made to the evidence base are difficult to analyse quantitatively. Therefore, a qualitative analysis approach has been taken for this evaluation question. The qualitative analyses are based on publicly available information, including two recent comprehensive evaluations on the GAVI-funded ADIPs and Hib Initiative and on GAVI’s Phase I performance.


\(^{232}\) An evaluation of the GAVI Alliance efforts to introduce new vaccines via the Accelerated Development and Introduction Plans (ADIPs) and the Hib Initiative. HSLP, February 2007.


Two recent evaluations, one on the GAVI-funded PneumoADIP, Rotavirus Vaccine Program (RVP), and Hib Initiative and the other on GAVI’s Phase I performance, examined the extent to which GAVI advanced the evidence base required for countries to address policy decisions related to new vaccine introduction.\textsuperscript{235,236}

To expand on these findings, an additional review of GAVI’s contributions to YF, Hib-containing, pneumococcal, and rotavirus vaccines was conducted using a country information readiness framework developed with the input of 24 global health experts.\textsuperscript{237} Criteria in this framework included sufficient data on disease burden, vaccine safety and effectiveness, vaccine cost effectiveness, and programmatic feasibility data. This evidence-based framework incorporated data from journal articles and other publicly available documentation from the GAVI-funded ADIPs (PneumoADIP, RVP) and Hib Initiative, the Yellow Fever Initiative, the Accelerated Vaccine Initiative (AVI), and WHO websites.\textsuperscript{238,239,240,241,242,243} The complete set of framework components provides the structure for the evaluation data summary (see Table 6.2).

HepB was not included in this evaluation because the GAVI Secretariat did not fund evidence-base creation activities for hepatitis B.

The qualitative responses from the general electronic survey on GAVI’s role in advancing the evidence base (n=282) were reviewed and consolidated by overarching theme, as were qualitative responses from the EPI manager electronic survey on the types of information provided by members of GAVI (n=23).

Results from structured interviews with 22 current and past GAVI Board members were also included. These respondents were asked to comment on the extent GAVI contributed to the advancement of the evidence base required for countries to address the policy decision related to introduction of new vaccines. Findings from the country visits were also summarised for inclusion in the evaluation.

Nine members from the GAVI-funded PneumoADIP, GAVI-funded RVP and GAVI-funded Hib Initiative were interviewed. They addressed what GAVI had done well and what it could have done better to further the evidence base required by countries when making vaccine adoption decisions. These interviews are referred to as “targeted interviews.”

The evidence sources used to evaluate this question are summarised in Table 6.1.

\textsuperscript{235} An evaluation of the GAVI Alliance efforts to introduce new vaccines via the Accelerated Development and Introduction Plans (ADIPs) and the Hib Initiative. HSLP, February 2007.
\textsuperscript{238} http://www.pneumoadip.com/ (accessed 14 May 2010).
\textsuperscript{239} http://www.rotavirusvaccine.org/ (accessed 14 May 2010).
\textsuperscript{241} http://www.who.int/mediacentre/factsheets/fs100/en/ (accessed 17 May 2010).
Table 6.1: Evaluation sources and descriptions for GAVI’s contribution to the evidence base

<table>
<thead>
<tr>
<th>Evidence source</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review documentation of</td>
<td>• Prior evaluations (e.g. GAVI Phase I and ADIPs)</td>
</tr>
<tr>
<td></td>
<td>• Documentation on the evidence base (e.g. GAVI-funded PneumoADIP, RVP, Hib Initiative; AVI literature, publications, websites)</td>
</tr>
<tr>
<td>E-survey</td>
<td>The e-survey sought input to the question “GAVI has provided countries with the evidence required to address the policy decisions related to the introduction of new vaccines”</td>
</tr>
<tr>
<td>Structured interviews</td>
<td>Structured interviews included comments from current and ex-GAVI Board members on a question designed to solicit feedback on GAVI’s contribution to the evidence base</td>
</tr>
<tr>
<td></td>
<td>• Comments from the GAVI Secretariat were not included due to potential perception of a conflict of interest</td>
</tr>
<tr>
<td></td>
<td>• Comments from other global consultation interviews were not included due to minimal responses on this strategic goal</td>
</tr>
<tr>
<td>EPI manager survey</td>
<td>The EPI manager electronic survey sought input to the question “types of information received from members of GAVI regarding vaccines available for introduction with GAVI support”</td>
</tr>
<tr>
<td>Country Consultations</td>
<td>Country consultations resulted in ad hoc comments related to this question</td>
</tr>
<tr>
<td>Information/data gathering meetings</td>
<td>Meetings were requested with representatives of the GAVI-funded ADIPs and Hib Initiative and one non-GAVI funded vaccine program (Meningitis Vaccine Project (MVP)), to seek input on what GAVI had done well and what it could have done better to further the evidence base required by countries when making vaccine adoption decisions</td>
</tr>
</tbody>
</table>

6.3.2. Limitations

These analyses have limitations due to:

- The reliance on qualitative data to evaluate the question.
- Low participation in the EPI manager electronic survey (24% response).
  - Only 30% of GAVI countries represented.
- EPI manager input and perspective limited by short-term tenure.
- Targeted interviews representing a small number of individuals, most of whom may have had a conflict of interest given that GAVI provided funding for the activities being evaluated (excludes comments made by MVP members).
6.4. Qualitative analyses

6.4.1. Review of documentation: prior evaluations

A comprehensive evaluation of the GAVI-funded ADIPs and the GAVI-funded Hib Initiative was conducted by HLSP in 2007. This evaluation found the ADIPs and Hib Initiative successful in “compiling the disease burden data to support the introduction of the vaccines, advocating for their use”.\(^{244}\) The report explicitly outlined contributions to the evidence base, including development of sound disease burden data, communications and advocacy to key stakeholders on their respective diseases and vaccines, cost effectiveness work, and encouragement for additional manufacturers to enter the market.

The review concluded by recognising the accomplishments of the GAVI-funded ADIPs in accelerating introduction of both pneumococcal and rotavirus vaccines and facilitating decision making for Hib vaccines. This review also compared the ADIPs to two other similar programs (the Meningitis Vaccine Project and the Japanese Encephalitis Project) and found the vaccine programs effective, regardless of their funding source.

The GAVI Phase I performance evaluation conducted by Abt Associates also reviewed the work of the ADIPs. The report concluded the ADIPs “successfully advocated for the use of pneumococcal and rotavirus vaccines, as well as funding for pneumococcal vaccine.”\(^{245}\)

The results of both ADIP evaluations concluded these organisations contributed significantly to generating the critical evidence needed by country decision makers. Examples of the evidence generated by these organizations are summarised in Table 6.2.

\(\text{Table 6.2: GAVI-funded activities by criteria used by countries when making vaccine introduction decisions}\)

<table>
<thead>
<tr>
<th>Key evidence-base components</th>
<th>Yellow Fever</th>
<th>Hib</th>
<th>Pneumococcal</th>
<th>Rotavirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Burden Data</td>
<td>• Yellow Fever Initiative-funded case-based yellow fever surveillance in 19 African countries</td>
<td>• Hib Initiative-funded regional surveillance in Africa and Eastern Mediterranean Region</td>
<td>• PneumoADIP-funded surveillance activities in over 56 countries in Africa, Asia, the Western Pacific region, the Eastern Mediterranean region, and Latin America</td>
<td>• RVP-funded regional surveillance and disease burden assessment networks in Latin America, Africa, the Middle East, Asia, and Europe</td>
</tr>
</tbody>
</table>

\(^{244}\) An evaluation of the GAVI Alliance efforts to introduce new vaccines via the Accelerated Development and Introduction Plans (ADIPs) and the Hib Initiative. HSLP, February 2007.

<table>
<thead>
<tr>
<th>Key evidence-base components</th>
<th>Yellow Fever</th>
<th>Hib</th>
<th>Pneumococcal</th>
<th>Rotavirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Safety &amp; Effectiveness Data</td>
<td>• Yellow Fever Initiative-funded monitoring of vaccine quality and safety and support of operational research</td>
<td>• Hib Initiative-funded research studies in 16 GAVI-eligible countries on impact of vaccine</td>
<td>• AVI-funded short-term vaccine effectiveness study in one country</td>
<td>• RVP-funded Phase III clinical trials in Asia and Africa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• AVI-funded post-marketing safety monitoring in two countries</td>
</tr>
<tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• AVI-funded post-marketing safety monitoring in two countries</td>
</tr>
<tr>
<td>Vaccine Cost-Effectiveness Data</td>
<td>• GAVI Yellow Fever Investment Case includes comprehensive vaccine cost-effectiveness data</td>
<td>• Hib Initiative-funded development of a cost-effectiveness tool for country use</td>
<td>• PneumoADIP-funded study on the cost-effectiveness of vaccination in GAVI-eligible countries</td>
<td>• AVI funded assessment on economic impact of introduction in one country</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• AVI-funded creation, maintenance, and country training on tools enabling cost-effectiveness analysis</td>
</tr>
<tr>
<td>Programmatic Feasibility Data</td>
<td>• WHO discussions on routine immunisation, outbreak control, and preventative campaigns</td>
<td>• WHO &amp; UNICEF conducted regional and country calls to discuss programmatic introduction issues</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 6.4.2. GAVI’s financial contributions

For YF, Hib-containing, pneumococcal, and rotavirus vaccines, GAVI funded consortiums to carry out activities related to advancing the evidence base. The funding for each is summarised below.\(^{246}\)

- PneumoADIP ($57.8m total)
  - Initial 2003-07 budget: $30m
  - 2008 extension activities: $11.2m

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\(^{246}\) Doc #AF.3 – AVI update & ADIPs/WHO budget extensions, GAVI Alliance & Fund joint EC meeting - 6 May 2008.
Surveillance activities extension: $16.6m

- Rotavirus Vaccine Program ($53.7m total):
  - Initial 2003-07 budget: $30m
  - Clinical trials: $15m
  - 2008 extension activities: $8.8m

- Hib Initiative:
  - Initial 2005-09 budget: $37m
  - 2008 extension activities: $1.17m

- Yellow Fever Initiative launched in 2007 with a $58m contribution from GAVI

- AVI launched in 2009 with a $99.6m budget ($49M for AVI and $50.6M for special studies) to continue the work of PneumoADIP and RVP and to serve as a platform to support the introduction of future vaccines

GAVI did not fund an ADIP-like organisation to accelerate introduction of HepB vaccines, however, they did provide financial assistance to WHO to develop lab surveillance and conduct serosurveys for hepatitis. In addition, WHO has provided vaccination recommendations and vaccine introduction guidelines.

These five GAVI-funded organisations were launched to provide, among other things, the evidence-base required to make informed vaccine introduction decisions. This level of financial resources focused on advancing the evidence base had not occurred prior to the formation of GAVI. All five organisations have relied on a partnership model, where unique skills and complementary expertise motivate focus on a diverse set of activities to generate the necessary evidence.

**PneumoADIP**

GAVI's funding of PneumoADIP was intended to expedite the development of pneumococcal vaccines and accelerate their introduction in developing countries. As part of this effort, PneumoADIP funded activities to generate the evidence needed for introduction of pneumococcal vaccines and to disseminate the evidence via communications and advocacy initiatives. To generate evidence, Pneumo ADIP:

- Quantified the pneumococcal disease burden
PneumoADIP, along with WHO, provided technical and financial support to establish surveillance networks in the South Asian (SEARO), Latin American (PAHO), Eastern Mediterranean (EMRO), and Western Pacific (WPRO) regions. These regional networks communicated data to partners, including ministries of health, multilateral organisations, and donors supporting vaccination.

PneumoADIP also worked with WHO to develop official estimates of the global pneumococcal disease burden, including information on which serotypes are most common in different regions.

- **Estimated vaccine impact**
  
  - PneumoADIP created the Asian Field Site Initiative to identify and develop sites for vaccine impact studies in Asia. The studies conducted at these sites provided policymakers in Asia with the evidence they needed to make decisions regarding the introduction of pneumococcal vaccines.

- **Calculated cost-effectiveness**
  
  - PneumoADIP funded a cost-effectiveness study to provide policymakers with the information they needed to secure the necessary financial investment for introducing pneumococcal vaccines.

In conjunction with generating the evidence required to introduce new vaccines, PneumoADIP also supported efforts to communicate the evidence to decision makers. These activities included:

- **Raising disease and vaccine awareness in the global media**
  
  - A study commissioned by PneumoADIP found the organisation raised awareness of pneumococcal disease and the impact of vaccination through the number of media campaigns it conducted, including traditional and web-based media, documentaries, and newsletters.

- **Conducting regional workshops**
  
  - In conjunction with the Hib Initiative, PneumoADIP hosted workshops in Africa and Asia to inform policymakers about pneumococcal disease and vaccination impact.

- **Raising disease and vaccine awareness with experts**
  
  - PneumoADIP, in collaboration with the Sabin Vaccine Institute, convened a council of experts to raise awareness about pneumococcal disease and advocate at a high level in all regions for adoption of pneumococcal vaccines.

- **Developing an investment case to accelerate pneumococcal vaccine introduction**

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255 GAVI Alliance Investment Case: Accelerating the introduction of pneumococcal vaccines into GAVI-eligible countries. Submitted by GAVI's PneumoADIP, October 2006.
PneumoADIP developed the investment case for GAVI support for pneumococcal vaccines, including forecasting demand for the vaccines to estimate financial costs to GAVI and countries and calculate the associated health impact of those investments.

Rotavirus Vaccine Program

GAVI's funding of RVP was intended to expedite the development of rotavirus vaccines and accelerate their introduction in developing countries. In partnership with the WHO and CDC, RVP activities included:

- Supporting vaccine development
  - Provided financial support and worked closely with Merck and GSK to conduct key clinical trials for rotavirus vaccines in South Africa and Bangladesh.
- Advancing the evidence base for rotavirus disease burden
  - Established surveillance networks that included at least 40 countries.
- Estimating the cost-effectiveness of rotavirus vaccination
  - Estimated the cost-effectiveness of rotavirus vaccination at the global, regional, and country levels.
- Advocating for rotavirus vaccine adoption in Latin America and Eastern Europe
  - Worked in partnership with the Sabin Vaccine Institute to accelerate the adoption of rotavirus vaccines into Latin American countries.
  - Held meetings in Eastern Europe to provide disease and vaccine information to country decision-makers.
- Creating advocacy materials
  - Researched effective messaging strategies for rotavirus vaccine introduction advocacy and disseminated and developed other information and learning tools.
- Developing an investment case to accelerate rotavirus vaccine introduction
  - Developed the investment case for GAVI support for rotavirus vaccines, including forecasting demand for the vaccines to estimate financial costs to GAVI and countries and calculate the associated health impact of those investments.

256 Doc #AF.6 – Accelerated Vaccine Introduction. GAVI Alliance and Fund Board Meeting, 15 June 2008.
257 Accelerating the introduction of rotavirus vaccines into GAVI-eligible countries. Investment Case for GAVI Secretariat, submitted by PATH's Rotavirus Vaccine Program, October 2006.
258 http://www.rotavirusvaccine.org/clinicalresearch.htm
259 An evaluation of the GAVI Alliance efforts to introduce new vaccines via the Accelerated Development and Introduction Plans (ADIPs) and the Hib Initiative. HSLP, February 2007.
**Hib Initiative**

For underused vaccines, GAVI’s recognition of the delay in introduction resulted in funding to increase the evidence base for Hib-containing vaccines. The GAVI-funded Hib Initiative played a significant role in:

- Estimating the burden of Hib disease
  - Developed a surveillance protocol and establish surveillance sites in the European and African regions and India.

- Securing a global recommendation for use of Hib vaccines
  - Contributed to the development of an updated WHO Position Paper in November 2006 that recommends vaccination in all countries, regardless of evidence of disease burden.
  - Worked with WHO regional offices to disseminate the new WHO position to 64 GAVI-eligible countries

- Estimating the cost-effectiveness of Hib vaccination
  - Summarised all available data on cost-effectiveness of Hib vaccination to ensure this key information for vaccine introduction decision-making was compiled in a single location.

- Advocating at the country level
  - Worked directly with countries to promote the adoption of Hib vaccines.
  - Focused on large countries to maximise impact (Bangladesh, Mozambique, and Pakistan).

- Raising disease and vaccine awareness at the global level
  - Raised awareness through traditional and web-based media, documentaries, and newsletters.

**Yellow Fever Initiative**

For YF vaccines, GAVI’s recognition of the delay in introduction also resulted in funding to increase the evidence base for YF vaccine introduction. The Yellow Fever Initiative is a joint collaboration between WHO and UNICEF with the participation of national governments. They work to secure global vaccine supply and vaccinate people at high risk. Through their work, better surveillance systems have been established in 19 African countries. In addition, the Yellow Fever Initiative has been working with suppliers to build more capacity and to increase the number of prequalified suppliers.

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260 An evaluation of the GAVI Alliance efforts to introduce new vaccines via the Accelerated Development and Introduction Plans (ADIPs) and the Hib Initiative. HSLP, February 2007.
In late 2008, the activities of PneumoADIP and RVP were transitioned to AVI, a group run by a cross-functional management team including the GAVI Secretariat, WHO, UNICEF, PATH, John Hopkins University, and the US Center for Disease Control. AVI was designed to reduce the time and costs related to pneumococcal, rotavirus, and future vaccine introduction. AVI is expected to work in a coordinated way across vaccines with the objective of standardising the work to accelerate the introduction of new vaccines. AVI has a range of evidence base activities it plans to complete over the course of its existence. These planned activities include:

- Generating health and economic impact data to support the introduction decision, developing and implementing costing tools for comparative cost effectiveness analysis, and providing countries with a tool kit to make assessments themselves.

- Funding special studies related to the optimisation of dosing and delivery schedules, including a landscape analysis of PCV dosing schedules, an understanding of the impact of breastfeeding and age of administration on the immunogenicity of rotavirus vaccine, mathematical modelling of rotavirus and pneumococcal transmission patterns to identify optimal vaccine schedules, characterise the dynamics of herd immunity, and evaluate potential unintended consequences of vaccine introduction.

- Advocating adoption of pneumococcal and rotavirus vaccines with a focus on generating the evidence required for introduction in large countries.

6.4.3. Electronic survey results

Among the 20 statements included in the electronic survey, one statement directly addressed GAVI’s contribution to the evidence base: “GAVI has provided countries with the evidence required to address the policy decisions related to the introduction of new vaccines”. The survey results are summarised in Figure 6.1.

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265 AVI Workplan, provided by the GAVI Secretariat, May 2010.
Figure 6.1: E-survey choice responses to question 15 - ‘GAVI has provided countries with the evidence required to address the policy decisions related to the introduction of new vaccines’ (282 responses, of which 260 were non-blank)

Approximately 65% of the electronic survey respondents agreed or strongly agreed with the statement, while only 7% of respondents disagreed or strongly disagreed with the statement.

Seventy-seven respondents to the electronic survey provided additional ad hoc comments on this topic. These responses were summarised into overarching themes. Table 6.3 summarises these comments by the themes that represented at least 10% of the comments provided.

Table 6.3: E-survey qualitative response feedback themes for question 15 - ‘GAVI has provided countries with the evidence required to address the policy decisions related to the introduction of new vaccines’

<table>
<thead>
<tr>
<th>Response Theme</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>The evidence base had been provided by GAVI partners including WHO, UNICEF, and the GAVI-funded ADIPs</td>
<td>24 (31%)</td>
</tr>
<tr>
<td>More work needed to be done and more evidence-based work at the country level was needed</td>
<td>12 (16%)</td>
</tr>
<tr>
<td>Provided examples of evidence provided by GAVI and its partners that had helped countries make decisions about vaccine introductions</td>
<td>11 (14%)</td>
</tr>
</tbody>
</table>

6.4.4. Structured interview results

GAVI Board Members

Among the 22 current and past Board members who participated in the structured interviews, 55% (12) commented on GAVI’s contribution to the evidence base. Seven thought GAVI had successfully contributed to the evidence base and four thought GAVI had been somewhat successful. One respondent commented that this was primarily the
responsibility of Alliance partners, WHO and UNICEF. Twelve respondents did not provide a response to this question.

**ADIPs and Hib Initiative members**

Telephone interviews with nine respondents who had been members of the ADIPs and the Hib Initiative were carried out during March 2010. Those interviewed were asked to comment on what GAVI had done well and what it could have done better to further the evidence base required by countries when making vaccine adoption decisions. These comments are provided for insight only since the ADIP and Hib Initiative interviewees have a potential conflict of interest in evaluating GAVI, given GAVI was the funding source for these organizations.

The majority of respondents felt strongly that GAVI had provided the resources necessary to expand the evidence base and noted this level of funding had never been available prior to 2000. The respondents highlighted the types of activities these resources supported, including:

- Clinical trials that generated evidence on vaccine performance.
- Surveillance at the global, regional, and country level.
- Development of cost-effectiveness models.
- Increased vaccine awareness among key policy makers.
- Identification and dissemination of lessons learned.

Respondents noted the significant value that resulted from the linking of research, surveillance, communications, and advocacy activities in their particular disease areas. Respondents also believed GAVI helped energise people and organisations so they could move forward in a more coordinated fashion.

Many respondents believed the creativity and innovation that occurred in the early stages of the ADIPs were because of GAVI’s “light touch.” This hands-off approach allowed the ADIPs to be nimble and respond to perceived research and communication needs quickly. Several respondents thought that in the last two years, GAVI’s management style had swung toward a more intensive management and control of indicators of progress; the feeling expressed was this had slowed the progress GAVI would have otherwise made with regard to expanding the evidence base. Respondents thought some of this occurred during the transition from the ADIPs to AVI and that AVI was still trying to find its mandate. Respondents noted GAVI’s recent financial situation meant there was an increased focus on fundraising and worried this would stall progress on advancing the evidence base for new vaccines.

### 6.4.5. EPI manager survey results

Twenty-two of 23 EPI managers responded to the EPI manager electronic survey on what information was provided for the vaccines available for introduction with GAVI support by members of GAVI. Table 6.4 summarises these comments by frequency of mention.
Table 6.4: Overarching themes on EPI manager response to the types of information GAVI provides on its vaccines

<table>
<thead>
<tr>
<th>Response Theme</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Said they had been provided information by partners</td>
<td>16</td>
</tr>
<tr>
<td>Disease burden data provided (most commonly specified response)</td>
<td>9</td>
</tr>
<tr>
<td>Vaccine product profile data provided</td>
<td>6</td>
</tr>
<tr>
<td>Cost-effectiveness data provided</td>
<td>4</td>
</tr>
<tr>
<td>Vaccine cost data provided</td>
<td>3</td>
</tr>
</tbody>
</table>

Overall, 50% of the responses included an adjective such as “good”, “valuable”, or “wide” when describing the type of information received, although lack of an adjective in no way implied the information was not considered valuable. In three cases, EPI managers noted the information disseminated for pneumococcal and rotavirus vaccines was an improvement over information provided for pentavalent vaccine.

6.4.6. Country visit results

Five country visits were conducted as a part of GAVI’s Phase II evaluation. While structured questions were not asked regarding GAVI’s contribution to the advancement of the evidence required for country decision-making regarding vaccine introduction, a variety of country-specific insights were generated from these country consolidations.

Bangladesh

Bangladeshi stakeholders reported that GAVI Alliance support for HepB and Hib disease burden assessments and associated health impact calculations led to government support for vaccine introduction. Bangladeshi officials noted this support for disease surveillance was provided primarily by WHO.

Mali

Malian stakeholders reported GAVI’s support to help make the decision to adopt vaccines played an important role in the introduction of the pentavalent vaccine.

Nigeria

Nigerian stakeholders did not comment on the evidence base provided by GAVI.

Bolivia

Bolivian stakeholders reported on several evidence based activities provided by GAVI partners that helped with the decision to introduce rotavirus vaccine and that aided in the continued assessment of rotavirus introduction. GAVI helped by providing support for experts on burden of disease assessments (through PAHO) and analysis of surveillance data prior to introduction. Bolivian officials also credited the rotavirus introduction with improvements in the diarrheal surveillance system, including strengthening the capabilities for microbiological diagnosis, increasing the number of sentinel centres (some directly
funded by GAVI), and developing stronger networks with the National University and other partners. A GAVI value-add has been the additional resources provided for improved surveillance of other diseases.

Uzbekistan

Uzbek stakeholders commented they received evidence-based information from both national (Paediatrics Institute) and GAVI (WHO) sources prior to new vaccine introduction.

6.5. Conclusions

The evaluation confirmed the significant value GAVI has added by advancing the evidence base required for country policy decisions related to the introduction of YF, Hib-containing, pneumococcal, and rotavirus vaccines. Significant contributions were made to the evidence base for disease burden, vaccine safety and effectiveness, cost-effectiveness, and programmatic feasibility through the GAVI-funded Yellow Fever Initiative, Hib Initiative, PneumoADIP, and RVP. WHO was also highlighted as a major provider of evidence to inform country decision-making.

Less evidence is available on AVI’s contributions to building the evidence base, however, this is not surprising given AVI only began its work in 2009.

The majority of electronic survey respondents agreed GAVI had contributed to the evidence base for countries to make vaccine introduction decisions; the majority of responding EPI managers named the evidence base information they had received from GAVI and found it valuable. Of the responding Board members, a majority perceived GAVI had been successful or somewhat successful in advancing the evidence base. Additionally, a majority of the targeted interviewees believed GAVI had financed projects that significantly advanced the evidence base.

The robustness of the conclusions included in this section are summarised in Table 6.5 based on a relative rating scale described in Section 1.1.3 of the Introduction.

Table 6.5: Relative robustness of the SG2.5 findings

<table>
<thead>
<tr>
<th>Issue/Theme</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAVI contribution to the evidence base for YF vaccine introduction</td>
<td>• Through monetary contribution to Yellow Fever Initiative, GAVI has made contributions to advance the evidence base for YF vaccine introduction.</td>
<td>B • Conclusion was obtained from desk review only. • Qualitative interviews did not mention Yellow Fever Initiative, so results could not be triangulated.</td>
</tr>
<tr>
<td>GAVI contribution to the evidence base for HepB-containing vaccine introduction</td>
<td>• Through WHO recommendations and vaccine introduction guidelines, GAVI has made contributions to advance the evidence for HepB-containing</td>
<td>B • Conclusion was based on desk review only. • Interviews did not mention HepB evidence base, and so results could not be</td>
</tr>
</tbody>
</table>
**Evaluation Question SG2.5:** To what extent has GAVI contributed to the advancement of the evidence base required for countries to address the policy decision related to the introduction of new vaccines?

<table>
<thead>
<tr>
<th>Issue/Theme</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
<tbody>
<tr>
<td>vaccine introduction.</td>
<td>triangulated.</td>
<td></td>
</tr>
</tbody>
</table>

**GAVI contribution to the evidence base for Hib-containing vaccine introduction**
- Through the GAVI-funded Hib Initiative, GAVI has made substantial contributions to the evidence base for Hib vaccine introduction.
- Conclusion was based on desk review, previous evaluations, and interview results.
- All evidence sources were in agreement.

**GAVI contribution to the evidence base for pneumococcal vaccine introduction**
- Through the GAVI-funded PneumoADIP, GAVI has made substantial contributions to the evidence base for pneumococcal vaccine introduction.
- It is too early to tell what the AVI contributions have been.
- Conclusion was based on desk review, previous evaluations, and interviews.
- All evidence sources were in agreement.

**GAVI contribution to the evidence base for rotavirus vaccine introduction**
- Through the GAVI-funded RVP, GAVI has made substantial contributions to the evidence base for rotavirus vaccine introduction.
- It is too early to tell what the AVI contributions have been.
- Conclusion was based on desk review, previous evaluations, and interviews.
- All evidence sources were in agreement.
7. **SG2.6: VACCINE DEMAND FORECASTS**

7.1. **Introduction**

The final question under SG2 is: “To what extent has GAVI developed and used vaccine demand forecasts that are accurate and timely?”

Vaccine demand forecasts are an important input into many types of decisions, including how much vaccine to procure for a specified time frame, how much donor support would be required to finance a vaccine, what type of donor financing would be most appropriate for a particular vaccine, and whether to develop a new vaccine.²⁶⁶,²⁶⁷

7.2. **Background**

Early in GAVI’s existence, analyses from McKinsey and Mercer identified credible demand forecasts as the key motivator for industry involvement in developing countries.²⁶⁸,²⁶⁹ Both strategic demand forecasts for products in development and supply chain forecasts for licensed products were highlighted as necessary components for a comprehensive supply picture.

Supply chain forecasts, commonly called supply forecasts, are developed for products on the market or close to market launch, and the forecast typically spans 18 months to 3 years. Supply forecasts are used to inform manufacturing scheduling decisions and supply procurement decisions. In the global health sector, supply forecasts are used routinely by the UNICEF Supply Division (UNICEF) for its vaccine supply tendering process.

In contrast, strategic demand forecasts generally span 15 years or more and are created for products typically five or more years from launch. This long-term forecast is critical for evaluating the risk and return associated with large vaccine-related investments. For example, a strategic demand forecast will provide suppliers the insight on overall market size needed to make investment decisions on product development and manufacturing capacity. In the global health sector, strategic demand forecasts are also important for informing donor vaccine financing support decisions.

The GAVI Alliance employs both types of forecasts. The first demand forecasts for YF, HepB-, and Hib-containing vaccines were created by a supply subgroup of the GAVI Financing Task Force. These forecasts were developed in 2000 to inform GAVI’s initial procurement round (2001–03).²⁷⁰ A Mercer study conducted in 2002 found these forecasts suffered from substantial inaccuracies.²⁷¹ As a result, the GAVI Board recommended the Alliance adopt a multi-disciplinary project management approach to forecasting and procurement across program, supply, and finance.²⁷² The Vaccine Provision Project (VPP)

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was thus chartered to address the shortcomings and inefficiencies observed during the first round of GAVI-financed vaccine procurement and was piloted on GAVI forecasting and procurement over the 2004–06 time frame.

During the pilot, UNICEF was responsible for supply issues and WHO was responsible for program issues, including the development of forecasts to inform UNICEF’s supply tender for the 2004 – 2006 procurement round. The WHO, along with UNICEF and the GAVI Secretariat, created a Delphi panel-based model to develop the forecast.

The VPP Pilot produced mixed results and was ultimately abandoned in favour of a UNICEF-driven procurement approach, but it was concluded that strategies recommended in the Mercer study were applied to a large extent and considerable progress had been made toward establishing credible and predictable demand.273 For the remainder of Phase I and for all of Phase II, WHO has been responsible for developing forecasts for YF and HepB- and Hib-containing vaccines for use in the UNICEF procurement process.

GAVI first began its use of strategic demand forecasts with the advent of vaccine investment cases in 2005. For pneumococcal and rotavirus vaccines, GAVI initially relied on strategic demand forecasts developed by the ADIPs for their investment cases. The forecasts were created using a methodology developed by PneumoADIP, which was formally vetted with and accepted by vaccine industry representatives and global health sector experts.274 These forecasts provided the foundation for GAVI’s vaccine financing decisions.

As the GAVI Alliance moved away from investment cases in lieu of developing a five-year investment strategy in 2008, it recognised the need for an integrated demand forecast that took into account the many new vaccines becoming available to developing country markets.275 Vaccine-specific forecasts that for the most part ignored competing vaccine-preventable disease product impacts would not be appropriate when making vaccine portfolio investment decisions. The development of an integrated demand forecast that would more accurately reflect country adoption decision-making across 10 or more vaccine programs was quite complex and required significant input from numerous vaccine program teams, as well as WHO, CDC, GAVI, and UNICEF. The resulting forecast was considered aggressive, but was approved for use in the GAVI vaccine investment strategy analysis by a diverse set of global health sector experts.276

As the GAVI-funded ADIPs and the Hib Initiative reached the end of their planned life spans, GAVI’s Accelerated Vaccine Initiative (AVI) assumed responsibility for forecasting pneumococcal and rotavirus demand in the short-term and for all GAVI current or potential future vaccines in the longer term.277 One of the major benefits of this new system was that it would ensure forecast variables are based on the same assumptions across all vaccines.

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AVI’s demand forecasting methodology was not provided for this evaluation, but forecast assumptions provided with AVI’s pneumococcal and rotavirus vaccine forecasts imply these forecasts incorporate New & Underutilised Vaccines Implementation (NUVI) team input for near-term introduction forecasting and expected country application success rates to predict longer-term introductions. The vaccine forecasts also incorporate assumptions on how soon these vaccines can be introduced relative to the introduction of another vaccine (e.g. pneumococcal vaccine introduction separated from other introductions by 24 months unless documented data implies otherwise, rotavirus introduction at least 24 months after pentavalent introduction).

The AVI forecast for pneumococcal vaccines has been used to inform the UNICEF call for offers that was issued as part of the AMC in September 2009. UNICEF has not yet issued a tender for rotavirus vaccines.

The GAVI Alliance has continually worked to improve its vaccine demand forecasting methodologies, processes, and tools for vaccines within its current and potential future vaccine portfolios. Given this level of focus and resource investment, it is important to evaluate whether these forecasts have been timely and accurate for their intended purpose.

### 7.3. Scope of the evaluation question

This evaluation section examines vaccine demand forecasts and seeks to determine whether they were timely and accurate. The evaluation includes YF, HepB monovalent and tetravalent, Hib-containing pentavalent, pneumococcal, and rotavirus vaccines. The demand for Hib mono- and tetravalent vaccines was minimal; therefore, these vaccines were not included in the evaluation.

The analyses focused on forecasted versus actual demand at an aggregate rather than a country-by-country level, as the aggregate variance would have the greatest impact on GAVI Alliance partners and key stakeholders.

For underused vaccines, the evaluation covers the period 2001–09. For new vaccines, the evaluation extends beyond 2009 to enable an assessment of forecasted demand relative to projected demand based on actual country adoptions and approved GAVI applications. The evaluation:

- Documented the GAVI application and vaccine procurement process to inform the selection of demand forecasts for use in this evaluation.
- Compared demand forecast data for YF, HepB monovalent and tetravalent, and pentavalent vaccines to available forecast data, quantity procured, and shipped doses to the GAVI approved doses to determine variances.
- Compared demand forecast data for pneumococcal and rotavirus vaccines to actual country adoptions, and projected adoptions based on approved GAVI applications to determine variances.

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278 AVI Pneumo ver 1.0 and 1.1 PowerPoint slides, provided by AVI, 25 January 2010.
280 Approved Doses Syringes and Safety boxes 5_01_10, provided by the GAVI Secretariat, February 2010.
• Sought input from WHO, UNICEF, and the GAVI Secretariat on the use and perceived accuracy of the demand forecasts.
• Sought input from suppliers on the use, timeliness, and accuracy of GAVI demand forecasts.

Comparative analyses could not be conducted because independently developed forecasts for the same vaccine in the same market for the same timeframe were not available. Comparisons between the accuracy of forecasts for different vaccines could be made, but meaningful insights could not be drawn from these comparisons.

Details on developing country demand forecasting methodologies employed by WHO or UNICEF prior to GAVI or the accuracy of these forecasts in predicting demand for vaccines not introduced by GAVI were not available for use in a counterfactual analysis. No other counterfactual analysis approach was identified.

7.4. Methodology

7.4.1. Overview

To determine whether GAVI Alliance efforts have resulted in timely and accurate demand forecasts requires agreement on the definition of these terms. GAVI-approved definitions for these terms were not available.

For this evaluation, a timely demand forecast was assumed to be available at the time it can provide the most value to the end user. Timeliness was based on when the forecast was made available to the end user and whether the end user perceived the forecast to have been “in time” for its intended use.

An accurate demand forecast is one that is within an acceptable level of variance given the specific purpose for which it is being used. However, the acceptable variance range is likely to be different for different end users. For example, a manufacturer with the ability to produce 50m doses may perceive a ± 5m dose variation between forecast and actual demand acceptable compared to a supplier with the ability to supply only 10m doses.

The acceptable level of variance is also expected to differ depending on the type of demand forecast evaluated. In general, the variance should be less for supply forecasts than for strategic demand forecasts given they typically account for demand 18–36 months into the future and given they are developed based on direct input from countries via conversations with WHO and UNICEF Supply Division. For strategic demand forecasts, the variance would be expected to be higher than with supply forecasts given these forecasts are much longer term and typically based on minimal, if any, direct country input.

7.4.2. Current GAVI Application and Vaccine Procurement Process

Figure 7.1 summarises GAVI’s current country application and vaccine procurement process.
Figure 7.1: GAVI Application and Vaccine Procurement Process

[Diagram of vaccine procurement process]

286 Personal communication, UNICEF, 03 May 2010.
As described in the figure, demand for YF and HepB- and Hib-containing vaccines are forecasted by WHO on an annual basis, with quarterly updates. These forecasts are based on country application data and other factors.\textsuperscript{287} WHO shares these forecasts with UNICEF to inform the vaccine procurement process and annual UNICEF forecast updates (however, UNICEF does not use the WHO YF forecast for its procurement forecasting process).\textsuperscript{288} UNICEF receives the WHO forecasts, and then conducts its own country-by-country review, and based on review outcomes, updates the forecast, as appropriate. The updated forecast is incorporated into the tender RFP or is used to inform UNICEF’s annual forecast update to suppliers.

The RFP is issued to suppliers, who rely on the forecast to develop supply bids for the tender period. The aggregate supplier bids are referred to as the offered supply. These bids are reviewed by the relevant Procurement Reference Group (PRG) which makes supply award recommendations to UNICEF. Based on the offered supply and expected demand, UNICEF awards firm contracts and good faith/non-binding long-term arrangements (LTAs) to some or all of the suppliers participating in the procurement round.

UNICEF issues annual supply forecast updates to suppliers to manage expectations relative to the LTAs. UNICEF procures doses from awarded suppliers, as needed, and suppliers ship the doses to countries per UNICEF guidance.

Based on this process, five types of demand forecasts are appropriate for inclusion in this evaluation. These are summarised in Table 7.1. However, the UNICEF 3-year RFP tender forecasts are confidential and were not provided for this evaluation.

Table 7.1: Demand forecasts appropriate for inclusion in the evaluation

<table>
<thead>
<tr>
<th>Demand Forecast</th>
<th>End User</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO 10-20 year country demand forecast</td>
<td>UNICEF</td>
<td>Inform vaccine procurement process</td>
</tr>
<tr>
<td>AVI Demand Forecasts</td>
<td>UNICEF</td>
<td>Inform vaccine procurement process</td>
</tr>
<tr>
<td>UNICEF 3 year RFP tender forecast</td>
<td>Suppliers</td>
<td>Inform supplier bids</td>
</tr>
<tr>
<td>UNICEF Original LTA Amount</td>
<td>Suppliers</td>
<td>Inform suppliers of the amount of supply UNICEF may procure</td>
</tr>
<tr>
<td>UNICEF annual forecast update</td>
<td>Suppliers</td>
<td>Inform supplier planning decisions relative to LTA</td>
</tr>
</tbody>
</table>

Ideally, the WHO and UNICEF annual supply forecasts would be compared to actual country demand, but as documented in SG2.3, actual demand data was not available. The GAVI Secretariat recommended approved doses data be used as a proxy for actual demand. While this data was used as requested, it is not clear how GAVI approved doses

\textsuperscript{287} Estimates for VF 2001-2011, Excel spreadsheets provided by WHO, March 2010.

\textsuperscript{288} Personal communication, UNICEF, 26 April 2010.
influenced the supply forecasting or procurement process and therefore, comparisons with procured and shipped doses were also included for comparison purposes (Figure 7.2).

Figure 7.2: Role of GAVI Approved Doses in Vaccine Demand Forecast and Procurement Process (simplified procurement process representation based on Figure 7.1)

7.4.3. Underused vaccines analysis methodology

Annual WHO demand forecasts for YF and HepB- and Hib-containing vaccines were provided for 2003–08, with the exception of 2005. Data for UNICEF’s supplier LTAs, annual forecast update to suppliers, and quantity procured were not provided for this evaluation, however, UNICEF pre-tender meeting PowerPoint presentations for YF, HepB tetravalent, and pentavalent vaccines are publicly available.289,290 The required UNICEF data for these vaccines was approximated from the graphics included in these PowerPoint presentations. A pre-tender meeting presentation for HepB monovalent data was not available, therefore, this demand forecast could only be compared to GAVI doses approved and UNICEF doses shipped.

The analysis was conducted by UNICEF procurement round. These rounds were initiated in 2000 (covering 2001–03), 2003 (covering 2004–06), and 2006 (covering 2007–09). The 2009 tender round (covering 2010–12) was not evaluated because complete award data for the tender period are not yet available.291 The evaluation only included WHO forecasts developed for years in which a UNICEF procurement round was initiated (e.g. 2006 WHO forecast used for the 2006 UNICEF procurement round evaluation).

The data required for the evaluation of YF and HepB- and Hib-containing vaccines compared to data that could be obtained is summarised in Table 7.2.

Table 7.2: Availability of data required for demand forecast analysis for YF, HepB monovalent, HepB tetravalent, and pentavalent vaccines

<table>
<thead>
<tr>
<th>Data Required</th>
<th>Availability Status</th>
<th>Data Obtained</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAVI Financing Task Force Supply Subgroup 2001-03 Demand Forecast</td>
<td>Not Available</td>
<td>• Forecast not available from WHO, UNICEF, or GAVI Secretariat</td>
</tr>
<tr>
<td>UNICEF 3-year RFP tender forecast</td>
<td>Not Available</td>
<td>• Confidential information</td>
</tr>
<tr>
<td>Supplier bids (i.e. aggregate offered supply)</td>
<td>Not Available</td>
<td>• Not publically available for 2001–09</td>
</tr>
<tr>
<td>UNICEF LTA Awards</td>
<td>Partially Available</td>
<td>• Required data approximated from graphics included in publically available pre-tender meeting PowerPoint presentations • Available for YF (2003–09) and HepB tetravalent and pentavalent vaccines only (2001–08)</td>
</tr>
<tr>
<td>UNICEF annual forecast to suppliers</td>
<td>Partially Available</td>
<td>• Required data approximated from graphics included in publically available pre-tender meeting PowerPoint presentations • Available for YF (2007–08) and HepB tetravalent and pentavalent vaccines only (2002–08)</td>
</tr>
<tr>
<td>GAVI doses approved</td>
<td>Available</td>
<td>• Data provided by GAVI Secretariat(^{293})</td>
</tr>
<tr>
<td>UNICEF quantities procured</td>
<td>Partially Available</td>
<td>• Required data approximated from graphics included in publically available pre-tender meeting PowerPoint presentations • Available for YF (2003–08) and HepB tetravalent and pentavalent vaccines only (2001–08)</td>
</tr>
<tr>
<td>UNICEF doses shipped</td>
<td>Available</td>
<td>• Shipped doses publicly available on UNICEF website and provided by UNICEF in Excel spreadsheets</td>
</tr>
</tbody>
</table>

7.4.4. New vaccines analysis methodology

Because there have only been limited GAVI-eligible country introductions of pneumococcal (n=2) and rotavirus vaccines (n=4) as of June 2010, demand forecasts developed by the PneumoADIP and the Rotavirus Vaccine Program for their GAVI

\(^{292}\) Personal communication, WHO, March 2010.

\(^{293}\) Approved Doses Syringes and Safety boxes 5_01_10, provided by the GAVI Secretariat, February 2010.
investment cases and their subsequent updates, as well as the AVI SDF v1.0 forecast were compared to actual and projected demand.

Actual demand was based on AVI projected doses for countries that have already introduced pneumococcal and rotavirus vaccines and projected demand was based on AVI projected doses given GAVI application approvals, conditional approvals, and approvals requiring clarification. Applications requiring resubmission were not included in the projected demand forecast.

The data required for the evaluation of pneumococcal and rotavirus vaccines compared to data that could be obtained is summarised in Table 7.3.

Table 7.3: Availability of data required for demand forecast analysis for pneumococcal and rotavirus vaccines

<table>
<thead>
<tr>
<th>Data Required for Analysis</th>
<th>Availability Status</th>
<th>Data Obtained</th>
</tr>
</thead>
</table>
| GAVI Investment Case Demand Forecasts | Available | • Pneumococcal IC submitted October 2006 (SDF v1.0) \(^{295}\)  
• Rota IC submitted October 2006 (SDF v1.0) \(^{296}\) |
| Demand forecast updates | Available | • Available and included in the evaluation  
  - Pneumococcal IC SDF v2.0 (distributed Jan. 2008)  
  - AVI pneumococcal vaccine SDF v1.0  
  - AVI rotavirus vaccine SDF v1.0  
• Available, but not used in the evaluation \(^{297}\)  
  - AVI pneumococcal vaccine SDF v0.0, v0.1, v1.1  
  - AVI rotavirus vaccine SDF v1.1 |
| ‘Actual’ demand based on actual and projected demand | Partially Available | • GAVI data for countries that have already introduced pneumococcal or rotavirus vaccines  
  • GAVI data for applications cited as ‘approved, approved with clarification, and conditional approval’ |
| UNICEF supplier awards | Partially Available | • First round AMC award quantities for pneumococcal vaccines \(^{298}\) |
| UNICEF shipments | Partially Available | • Shipped doses publicly available on UNICEF website and provided by UNICEF in Excel Spreadsheet for pneumococcal vaccines; no rotavirus vaccines have been shipped through UNICEF for GAVI \(^{299}\) |

7.4.5. Demand forecast accuracy and timeliness assessment methodology

The quantitative analyses conducted for this evaluation provide an assessment of the variance between forecast and actual data. Because there are currently no indicators that define the level of acceptable variance, the assessment of accuracy relied on a qualitative

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\(^{294}\) Approved Doses Syringes and Safety boxes 5_01_10, provided by the GAVI Secretariat, February 2010.

\(^{295}\) GAVI Alliance Investment Case: Accelerating the introduction of pneumococcal vaccines into GAVI-eligible countries. Submitted by GAVI’s Pneumococcal ADIP, October 2006.

\(^{296}\) Accelerating the introduction of rotavirus vaccines into GAVI-eligible countries. Investment Case for GAVI Secretariat. Submitted by PATH’s Rotavirus Vaccine Program, October 2006.

\(^{297}\) Personal communication, AVI, June 2010.


assessment of accuracy based on end user feedback. End user feedback was also the method for assessing the timeliness of demand forecasts.

A summary of the key GAVI Alliance partners and stakeholders who have developed and used vaccine demand forecasts are provided in Table 7.4.

Table 7.4: Forecast developer and user summary

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Forecast Developer</th>
<th>Forecast User (Purpose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YF</td>
<td>WHO</td>
<td>• Provided to UNICEF, but not used by UNICEF</td>
</tr>
<tr>
<td></td>
<td>UNICEF</td>
<td>• UNICEF (supplier tendering process)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Industry (tender response)</td>
</tr>
<tr>
<td>HepB- &amp; Hib-</td>
<td>WHO</td>
<td>• UNICEF (supplier tendering process)</td>
</tr>
<tr>
<td>containing</td>
<td></td>
<td>• Industry (tender responses)</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>PneumoADIP (2003–08)</td>
<td>• Industry (capacity strategy decisions)</td>
</tr>
<tr>
<td></td>
<td>AVI (2009–Present)</td>
<td>• UNICEF (supplier tendering process)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GAVI Secretariat/Board (financing decisions; ongoing financial management)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>GAVI’s RVP (2004–2008) &amp;</td>
<td>• Industry (capacity decisions)</td>
</tr>
<tr>
<td></td>
<td>GAVI’s AVI (2009–Present)</td>
<td>• UNICEF (supplier tendering process)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GAVI Secretariat/Board (financing decisions and ongoing financial management)</td>
</tr>
</tbody>
</table>

Given the underutilised vaccine demand forecasts are delivered to end users as part of the vaccine procurement process, these forecasts were assumed to have been delivered in a timely fashion. For new vaccine demand forecasts, delivery through the vaccine procurement process was also assumed to have been timely. Therefore, only vaccine suppliers were asked to comment on the timeliness of the applicable demand forecasts.

WHO, UNICEF, and the GAVI Secretariat were contacted to gain their perspective on demand forecast accuracy. WHO suggested UNICEF and GAVI were better positioned to comment. UNICEF stated forecast accuracy data was provided in its annual reports to the GAVI Alliance. This accuracy data was found for unspecified vaccines in the 2003 and 2008 annual reports and has been included in the current evaluation. No references to forecast accuracy were found in the 2001, 2002, 2004–07, or 2009 annual reports. The GAVI Secretariat was not available for comment.

Structured interviews that included questions on demand forecast timeliness and accuracy were conducted with 13 staff members from six different multinational and emerging suppliers. Relevant information from these interviews is included in the analysis.

The evidence sources used to evaluate this question are summarised in Table 7.5.

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300 Personal communication, WHO, 14 April 2010 and 17 June 2010.
301 Personal communication, UNICEF, 10 May 2010.
Table 7.5: Evidence sources and descriptions for the extent to which the GAVI Alliance has developed and used vaccine demand forecasts that are accurate and timely

<table>
<thead>
<tr>
<th>Evidence source</th>
<th>Description</th>
</tr>
</thead>
</table>
| Review of documentation                | • Previous GAVI evaluations  
• Supply chain and strategic demand forecasts (e.g. investment cases, WHO forecasts, AVI forecasts)  
• Actual doses approved and doses supplied (e.g. GAVI Secretariat documents, UNICEF Supply Division data)  
• Country expression of interest letters and submitted, pending, approved applications (e.g. GAVI Independent Review Committee documentation) |
| E-survey                               | The electronic survey did not seek input on this question.                                                                                   |
| Structured interviews                  | Only the structured interviews with vaccine suppliers sought input on this question.                                                        |
| EPI manager survey                     | The EPI manager electronic survey did not seek input on this question.                                                                        |
| Country visits                         | Country consultations did not seek input on this question.                                                                                   |
| Information / data gathering meetings  | Meetings were requested with representatives from the GAVI Secretariat, WHO, UNICEF Supply Division, and vaccine suppliers to learn:  
• How demand forecasts are used within their organisations (i.e. what decision-making process do the forecasts support)  
• Which demand forecasts are used for these purposes (i.e. who developed the demand forecast)  
• How have they benefitted from GAVI Alliance-partner developed demand forecasts  
• Whether GAVI Alliance partner-developed demand forecasts were timely and accurate enough for its needs |

7.4.6. Analysis limitations

These analyses have limitations due to

- Unavailable UNICEF RFP tender forecasts.
- Unavailable UNICEF supply chain forecast for YF vaccines.
- Incomplete forecast data for HepB monovalent, HepB tetravalent, and pentavalent vaccines.
- Use of PowerPoint presentation graphics to approximate UNICEF LTA awards, annual forecast update to suppliers, and doses procured.
- Lack of data to explain variances between WHO forecasts and UNICEF LTA awards, including UNICEF RFP tender forecasts and offered supply.
- Minimal, if any, input on forecast accuracy from GAVI Alliance partners.
• Limited supplier response to requested interviews (only six of nine suppliers responded to e-mail requests for interviews) and limited specific information provided by suppliers on the ‘accuracy and timeliness’ of the demand forecasts.

7.5. Evaluation analysis

7.5.1. YF vaccine demand forecast accuracy assessment

Although WHO provides UNICEF with an annual YF vaccine demand forecast, UNICEF has relied on the YF vaccine investment case forecast (developed by WHO) for outbreak response and campaign vaccine procurement and on UNICEF’s annual country-by-country forecasting exercise for routine vaccine procurement. Where available, UNICEF’s original LTA amount and annual forecast to suppliers was compared to GAVI approved dose to assess the accuracy of these forecasts.

Figure 7.3 summarises the relevant vaccine procurement data for UNICEF’s first three YF vaccine procurement rounds. Variances relative to GAVI doses approved are shown in Table 7.6.

Figure 7.3: YF demand forecasts versus actual demand proxies for UNICEF’s 1st-3rd procurement rounds

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303 Personal communication, UNICEF, April 2010.
In general, the accuracy of the demand forecasts relative to GAVI doses approved varied widely (20% to over 500%), although the variance of the LTA forecasts improved from Round 1 to Round 3. In all cases, the demand forecasts were higher than what had been approved by GAVI, for unknown reasons.

The quantity procured was higher than GAVI approved doses in all years except 2007. The rationale for why procurement would be 1.2 to nearly 6-fold higher than GAVI approved doses was not uncovered.

The variances between doses shipped and GAVI doses approved were erratic and in most years, fewer doses were shipped than were approved. This was true even in years where there was adequate or excess YF vaccine supply. In addition, from 2004–08, 50-75% less doses were shipped than procured. Although some of this variance might be attributed to the timing of shipments, timing alone would not account for the large variance from one year to the next.

### 7.5.2. HepB monovalent demand forecast accuracy assessment

WHO provides UNICEF with an annual HepB monovalent vaccine demand forecast, which UNICEF then modifies based on a country-by-country assessment. These forecasts were available for the second and third procurement rounds. Information on UNICEF’s procurement forecasts was not available for this vaccine. Therefore, the WHO forecast could only be compared to GAVI approved doses and UNICEF doses shipped.

Figure 7.4 summarises the relevant vaccine procurement data for UNICEF’s first three HepB monovalent vaccine procurement rounds. Variances relative to doses approved are shown in Table 7.7.
The only comparison that could be made in the first procurement round based on these data was the difference between doses shipped and doses approved. As shown, more doses were shipped than approved in 2001 and fewer doses shipped than approved in 2002 and 2003. However, based on an earlier evaluation by Mercer, the ‘uptake’ of HepB monovalent was only 11% of the amount awarded to suppliers.304 This difference was attributed to two large countries that preferred to delay HepB introduction until pentavalent vaccine supplies were available.

In the second round, the WHO forecasts were much higher (1.8–2.5-fold) than the approved doses and the doses shipped were approximately 20-30% lower than the doses approved.

In the third round, the WHO forecast was much lower compared to the second round. This was primarily due to the exclusion of China (2007) and because GAVI stopped its support for HepB monovalent vaccines in lieu of combination vaccines in Phase II.305 The WHO forecast in this time period was 19% of doses approved in 2007, 87% in 2008, and

50% in 2009. As shown, the variance of the WHO forecast and approved doses ranged from 13%–81%.

In general, the accuracy of these HepB monovalent forecasts did not improve over time, however, it was difficult to draw conclusions about the accuracy of the WHO forecasts without knowing the UNICEF RFP tender forecasts, the LTA awards, the annual forecast updates, or the actual quantities procured.

### 7.5.3. HepB tetravalent demand forecast accuracy assessment

WHO provides UNICEF with an annual HepB tetravalent vaccine demand forecast, which UNICEF then modifies based on a country-by-country assessment. These WHO forecasts were available for the second and third procurement rounds. UNICEF original LTA awards, annual forecast update to suppliers, and actual quantities procured were available for 2002–08. Therefore, only the LTA awards and annual update to supplier forecasts were compared to the GAVI approved doses for 2002–03. For 2004–08, the WHO and the previous forecasts were compared to the approved doses.

Figure 7.5 summarises the relevant vaccine procurement data for UNICEF’s first three HepB tetravalent vaccine procurement rounds. Variances relative to doses approved are shown in Table 7.8.

*Figure 7.5: HepB tetravalent demand forecasts versus actual demand proxies for UNICEF’s 1st-3rd procurement rounds*
Table 7.8 Summary of variances relative to GAVI doses approved by UNICEF procurement round for HepB tetravalent vaccines

<table>
<thead>
<tr>
<th>Forecast</th>
<th>Variance relative to GAVI doses approved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Round 1</td>
</tr>
<tr>
<td></td>
<td>2001</td>
</tr>
<tr>
<td>WHO forecast</td>
<td>-</td>
</tr>
<tr>
<td>Original LTA Amount</td>
<td>487%</td>
</tr>
<tr>
<td>Annual Forecast Update</td>
<td>-</td>
</tr>
<tr>
<td>Doses Procured</td>
<td>108%</td>
</tr>
<tr>
<td>Doses Shipped</td>
<td>99%</td>
</tr>
</tbody>
</table>

In the first procurement round, UNICEF’s original LTA amounts were higher than doses approved (0.6 to 6-fold). This was also the first tender period where doses shipped were approximately equal to doses approved. The adjustments between UNICEF’s LTA awards and the annual forecast to suppliers were likely driven by the supply shortage in the 2001–03 time period (see SG2.3).

In the second procurement round, the WHO forecasts were 1.4–3.3-fold higher than doses approved. However, in most years, the LTA forecast and the updated forecasts were more accurate but still had variances of -36% to 66%, depending on the year. In this procurement round, the doses procured and shipped were within 85% of doses approved. These variances may have been a result of supply shortages from 2004–06.

In the third procurement round, the WHO forecasts were progressively higher than doses approved (0.9 to 8-fold) whereas the LTA and updated forecasts were consistently less than the doses approved (10%–30%). The quantities procured during this period were approximately 55-80% of doses approved, even though UNICEF indicated supply excess during this period.

The accuracy of the HepB tetravalent forecasts shows no improvement over time, although 2009 LTA and updated forecast data could change this perception. The lack of improvement by round could be due to the difficulty in predicting demand as countries switched from HepB mono- and tetravalent vaccines to pentavalent vaccines.

7.5.4. Pentavalent vaccine demand forecast accuracy assessment

WHO provides UNICEF with an annual pentavalent vaccine demand forecast, which UNICEF then modifies based on a country-by-country assessment. These WHO forecasts were available for the second and third procurement rounds. UNICEF original LTA awards, annual forecast update to suppliers, and actual quantities procured were available for 2002–08. Therefore, only the LTA awards and annual update to supplier forecasts were compared to the GAVI approved doses for 2002–03. For 2004–08, the WHO and the previous forecasts were compared to the approved doses.
Figure 7.6 summarises the relevant vaccine procurement data for UNICEF’s first three pentavalent vaccine procurement rounds. Variances relative to quantities procured and doses approved are shown in Table 7.9.

**Figure 7.6: Pentavalent demand forecasts versus actual demand proxies for UNICEF’s 1st-3rd procurement rounds**

![Graph showing demand forecasts and actual demand for UNICEF’s pentavalent vaccines over three procurement rounds.](image)

**Table 7.9 Summary of variances relative to GAVI doses approved by UNICEF procurement round for pentavalent vaccines**

<table>
<thead>
<tr>
<th>Forecast</th>
<th>Round 1</th>
<th>Round 2</th>
<th>Round 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2001</td>
<td>2002</td>
<td>2003</td>
</tr>
<tr>
<td>WHO forecast</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Original LTA Amount</td>
<td>571%</td>
<td>(15%)</td>
<td>98%</td>
</tr>
<tr>
<td>Annual Forecast Update</td>
<td>-</td>
<td>(32%)</td>
<td>19%</td>
</tr>
<tr>
<td>Doses Procured</td>
<td>101%</td>
<td>(15%)</td>
<td>(1%)</td>
</tr>
<tr>
<td>Doses Shipped</td>
<td>86%</td>
<td>(4%)</td>
<td>2%</td>
</tr>
</tbody>
</table>

In the first procurement round, UNICEF’s original LTA amounts varied from greater than 6-fold (2001) to 15% less (2002). The updated forecasts were slightly better overall, but still varied widely. In 2001, doses procured and doses shipped exceeded doses approved by approximately 2-fold.

In the second procurement round, the WHO forecasts varied from slightly underestimating approved doses in 2004 to overestimating approved doses by up to 2.2-fold in 2005. The LTA amounts were higher than the doses approved, but the annual updated forecasts were
closer to approved doses (within 2-25%). Except for 2004, the doses procured and shipped were nearly identical to the doses approved.

In the third procurement round, the WHO forecasts progressively increased as country demand increased. The WHO forecast was still 1.7-fold higher than the doses approved in 2007, but was within 5%-15% in 2008 and 2009, respectively. The LTA forecast was approximately 90% of approved doses in 2007, but was only 67% of approved doses in 2008. The annual forecast to suppliers was within 12% of approved doses for 2007-08. Both the quantities procured and the doses shipped during this period varied by up to 26% of the doses approved.

The pentavalent vaccine forecasts did not consistently improve over time. However, the annual updated forecasts have been fairly accurate (within ~30%) across all procurement rounds.

7.5.5. Pneumococcal vaccine demand forecast accuracy assessment

Unlike YF, HepB- and Hib-containing vaccines, pneumococcal vaccines will be procured through UNICEF based on AMC procurement principles. These principles allow suppliers to bid up to the demand that is forecasted five years into the future. UNICEF will award 10-year contracts to the successful bidders instead of 3-year contracts. The AMC contracts require suppliers to make available a set number of doses for 10-years. AVI is responsible for publishing the 5-year demand forecasts.

This evaluation examines three strategic demand forecasts:

- PneumoADIP’s GAVI Investment Case strategic demand forecast (PneumoADIP SDF v1.0) developed in 2006
- PneumoADIP’s updated SDF v2.0 developed in 2007
- AVI’s demand forecast (AVI SDF v1.0) issued in November 2009

These forecasts were compared to the projected demand based on approved GAVI applications (approvals, conditional approvals, and approvals with clarification) according to the latest numbers provided by AVI. Figure 7.7 summarises the forecast and projected demand data.

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307 GAVI Alliance Investment Case: Accelerating the introduction of pneumococcal vaccines into GAVI-eligible countries. Submitted by GAVI’s PneumoADIP, October 2006.
309 AVI Pneumo ver 1.0 and 1.1 PowerPoint slides, provided by AVI, 25 January 2010.
310 Personal communication, AVI, Feb-Jun 2010.
PneumoADIP’s initial investment case demand forecast (SDF v1.0) was based on a model developed by PneumoADIP which included input from international global health experts on country introduction timing. This forecast preceded the AMC and was based on the assumption that PCV7 would not be used in GAVI-eligible countries, and therefore, demand was dependent on the prequalification of PCV10 and PCV13. The updated PneumoADIP SDF v2.0 forecast assumed limited use of PCV7 starting in 2008, followed by the introduction of PCV10 and PCV13 in 2010 and 2013, respectively. SDF v2.0 also incorporated updated UN population data, updated WHO coverage rate forecasts, and new country adoption information based on 34 letters of intent received from GAVI-eligible countries in response to GAVI’s call for expressions of interest in pneumococcal vaccines.\textsuperscript{311}

The AVI forecast used in this evaluation (v1.0) does not take into account the updated GAVI eligibility policy. Such a forecast does exist (v1.1), but AVI requested it not be used in this evaluation. The AVI v1.0 forecast includes the two countries that introduced PCV7 through supplier donation in 2009 and assumes at least 19 other countries will introduce a pneumococcal vaccine in the 2010–11 timeframe based on approved GAVI applications.

As shown, the PneumoADIP demand forecasts are within 20% of the projected demand based on approved GAVI applications.\textsuperscript{312,313}

\textsuperscript{312} New Vaccine Introduction Project. The Bill & Melinda Gates Foundation, 2007.
\textsuperscript{313} Weekly Epidemiological Record (2007) 82(12):93–104.
The AVI forecast is similar to the PneumoADIP forecast in 2010 (within 20% of projected demand) but 1.5-fold higher than the projected demand in 2011. This is likely due to an AVI assumption that additional applications would be approved in 2009 and 2010. Additional applications were not approved due to delays resulting from GAVI’s current financing gap.

It is too early to tell the true ‘accuracy’ of these forecasts, however, it is assumed that the timeliness of these forecasts have been good since the PneumoADIP SDF v1.0 forecast was used by GAVI to make its investment decision for pneumococcal vaccines and the AVI forecasts are updated semi-annually as part of the established AMC procurement process.\(^\text{314}\)

### 7.5.6. Rotavirus vaccine forecast versus actual and expected applications

Rotavirus vaccines will be procured through the same process used for YF and HepB- and Hib-containing vaccines. The UNICEF 3-year RFP tender will be based on the latest AVI forecast. UNICEF has not yet completed a procurement round for rotavirus vaccines.

This evaluation examines two demand forecasts:

- RVP’s GAVI Investment Case strategic demand forecast developed in 2006\(^\text{315}\)
- AVI’s rotavirus vaccine SDF v1.0\(^\text{316}\)

These forecasts were compared to the projected demand based on approved GAVI applications (approvals, conditional approvals, and approvals with clarification) according to the latest numbers provided by AVI.\(^\text{317}\) Figure 7.8 summarises the forecast and projected demand data.


\(^{316}\) AVI Rota ver 1.0 and 1.1 PowerPoint slides, provided by AVI, 25 January 2010.

\(^{317}\) Personal communications, AVI, Feb-Jun 2010.
The initial RVP investment case forecast assumed AMRO and EURO countries would introduce a rotavirus vaccine between 2007 and 2010 based on regional prequalification for the rotavirus vaccines in 2007. This forecast also assumed the rotavirus Phase III trials in Africa and Asia would be completed in 2009, WHO would recommend use in African and Asian countries in 2009, and countries would introduce beginning in 2010. The actual global recommendation for rotavirus vaccination was issued one year earlier than projected in the investment case. The major difference between the RVP forecast and the projected demand is the fewer number of AMRO and EURO countries that introduced a rotavirus vaccine by 2010 (67% of AMRO countries and 0% of EMRO countries). This discrepancy has resulted in a 13-fold higher forecast relative to 2011 projected demand and a nearly 40-fold higher than projected demand for 2012–14.

The AVI forecast did not make the same assumptions regarding the AMRO and EURO countries, hence the AVI forecast was significantly lower than RVP’s through 2011. AVI was similar to RVP in its 2012–14 forecast, where each forecast predicted faster uptake than currently projected based on approved GAVI applications. Similar to the RVP forecast, the AVI forecast is approximately 40-fold higher than projected over this timeframe. The variances associated with the 2012–14 timeframe are likely due to:

- The current GAVI funding gap delaying approval of new applications.
- The recent introduction of pentavalent vaccine in Eastern Europe, which is perceived to have created a delay in rotavirus vaccine introduction into GAVI-eligible EURO countries.

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319 Ibid.

320 Personal communication, AVI, Feb–June 2010.

It is too early to tell the true ‘accuracy’ of these forecasts, however, it is assumed the forecasts have been timely given the RVP investment case forecast was used by GAVI to make its investment decision for rotavirus vaccines and the AVI forecasts are updated semi-annually for use in financial and procurement planning processes.322

7.5.7. Qualitative analysis results

Structured interviews with forecast end users were conducted to assess the ‘accuracy’ and ‘timeliness’ of the vaccine forecasts from their perspective.

Suppliers

Six suppliers stated in interviews that the demand forecasts provided by the GAVI Alliance were very helpful for planning purposes. These suppliers were involved with YF, HepB-, and Hib-containing vaccines. In addition, suppliers acknowledged that the GAVI-funded PneumoADIP and GAVI-funded Rotavirus Vaccine Program had often used strategic demand forecasts in discussions with suppliers. These forecasts were perceived to have motivated additional supplier capacity to help meet demand for both pneumococcal and rotavirus vaccines in GAVI-eligible countries.323

UNICEF

UNICEF referred the evaluation team to the forecast accuracy assessments included in their Annual Reports.324 According to these Annual Reports, the UNICEF-created supply forecast for Hib had “close to 90% accuracy”325 in 2008 and the 5-year rolling forecast for unspecified vaccines “exceeded 80% accuracy in 2003”326. References to forecast accuracy were not found in the 2001, 2002, 2004, 2005, 2006, or 2009 Annual Reports. The 2007 Annual Report was not available.

GAVI Secretariat

GAVI Secretariat staff did not respond to multiple requests to discuss the timeliness and accuracy of the forecasts.327

7.6. Conclusions

GAVI has added value by delivering timely forecasts for use across its partners and with suppliers (WHO forecasts produced for UNICEF, UNICEF forecasts produced for suppliers, and GAVI-funded ADIP and AVI forecasts produced for GAVI and UNICEF). The process for creating and updating demand forecasts is well established for the underused vaccines, and has recently been established for the new vaccines.

322 Personal communication, AVI, Feb-Jun 2010.
324 Personal communication, UNICEF, 10 May 2010.
327 Personal communication, AVI, Apr-May 2010.
Determining the accuracy of the demand forecasts was more challenging. For underused vaccines, the evidence suggests the variance between WHO forecasted and approved doses (used as a proxy for demand) has not improved over the three procurement rounds, regardless of vaccine. The UNICEF LTAs and annual updated forecasts were more accurate than the WHO forecasts for HepB tetravalent and pentavalent vaccines and have improved over time for YF vaccines.

Independent of the demand forecasts, it was unclear why significant variation between GAVI approved doses and UNICEF procured doses and shipped doses was seen. While small variations can be expected based on changes in shipping dates and amounts, it is unclear why these different measurements of ‘demand’ are not more similar.

*Table 7.10: Summary of SG2.6 conclusions and associated robustness*

<table>
<thead>
<tr>
<th>Evaluation Question SG2.6: To what extent has GAVI developed and used vaccine demand forecasts that are accurate and timely?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Issue/Theme</strong></td>
</tr>
<tr>
<td>Timeliness of underused and new vaccine demand forecasts</td>
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<tr>
<td>Accuracy of YF vaccine demand forecasts</td>
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<tr>
<td>Accuracy of HepB monovalent vaccine demand forecasts</td>
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</table>
**Evaluation Question SG2.6:** To what extent has GAVI developed and used vaccine demand forecasts that are accurate and timely?

<table>
<thead>
<tr>
<th>Issue/Theme</th>
<th>Findings</th>
<th>Robustness</th>
</tr>
</thead>
</table>
| **Accuracy of HepB tetravalent vaccine demand forecasts** | • The accuracy of the WHO forecasts varied widely (variances up to 712%) across the first and second procurement rounds.  
• The accuracy of the LTA and annual updated forecasts were much better than the WHO forecasts (variance from -28% to 66%). | C.  
• Missing WHO, LTA and annual updated forecast data.  
• Little input from GAVI partners on what constitutes an “accurate” forecast.  
• Lack of actual demand data to explain variances.  
- Doses approved used as a proxy, but varied inconsistently with procured and shipped doses. |
| **Accuracy of pentavalent vaccine demand forecasts** | • The accuracy of the WHO forecasts varied less than for YF and HepB tetravalent vaccines (variance -4% to 118%) across the second and third procurement rounds.  
• The accuracy of the LTA and annual updated forecasts from 2002–09 were slightly better than the WHO forecasts (variance from -43% to 98%). | C.  
• Missing WHO, LTA and annual updated forecast data.  
• Little input from GAVI partners on what constitutes an “accurate” forecast.  
• Lack of actual demand data to explain variances.  
- Doses approved used as a proxy, but varied inconsistently with procured and shipped doses. |
| **Accuracy of pneumococcal vaccine demand forecasts** | • Too early to evaluate the accuracy of the forecasts. | -  
• Actual demand data over time not yet available. |
| **Accuracy of rota vaccine demand forecasts** | • Too early to evaluate the accuracy of the forecasts. | -  
• Actual demand data over time not yet available. |
8. SUMMARY AND CONCLUSIONS FOR SG2

8.1. Results achieved on SG2.1

*To what extent has GAVI accelerated the uptake of underused and new vaccines?*

GAVI has added value by accelerating YF vaccine introduction into YF endemic countries.

- The cumulative number of countries introducing YF increased from 46% to 86% since GAVI’s inception.
- The average number of country introductions per year increased by 38% post GAVI.
- The counterfactual analysis indicated earlier adoption than expected for 2 – 6 more countries.
- In addition, GAVI stockpile funding mitigated use of infant vaccines for outbreak control, thereby improving vaccination coverage rates and immunisation program sustainability.

GAVI has added significant value by accelerating HepB-containing vaccine introduction.

- The cumulative number of countries introducing HepB-containing vaccines has increased from 29% to 97% since GAVI’s inception.
- The average number of country introductions per year increased 3-fold post GAVI.
- The counterfactual analysis indicated earlier adoption than expected for 23 – 34 more countries.

GAVI has added significant value by accelerating Hib-containing vaccine introduction, especially after 2007.

- The cumulative number of countries introducing Hib-containing vaccines has increased from 7% to 83% since GAVI’s inception.
- Average number of country introductions per year increased greater than 10-fold post GAVI.
- Counterfactual analysis indicated earlier adoption than expected for 48 – 52 more countries.

GAVI has added value by accelerating pneumococcal vaccine demand based on approved GAVI applications (n=21; 2 introduced, 19 awaiting introduction).

- It is too soon to know GAVI’s actual impact on accelerated introduction, but accelerated introduction may be at risk due to the current funding gap and new eligibility policy.

GAVI has not accelerated rotavirus vaccine demand or introduction.
• Current projections based on actual introductions (n=4) and approved applications (n=6) indicate rotavirus vaccine introduction could be slower than previous GAVI-funded vaccine introductions.

• Only 6% of GAVI countries are projected to introduce within 5 years of the GAVI funding decision (14% within 5 years of the global WHO recommendation) compared to 80%, 49%, and 13% of remaining YF, HepB-, and Hib-containing introductions, respectively, and compared to 30% of projected pneumococcal vaccine introductions over the same five year funding timeframe.

8.2. Results achieved on SG2.2

To what extent have countries introducing underused and new vaccines been able to take them to scale quickly, i.e. achieve full scale coverage?

GAVI’s current model of providing countries with the financial and technical support to prepare for and introduce a vaccine appears to be effective.

• For YF vaccines, >80% of countries reached peak coverage within 3 years.
• For HepB-containing vaccines, >80% of countries reached peak coverage within 2 years.
• For Hib-containing vaccines, nearly 90% of countries reached peak coverage within 2 years.

Time to peak coverage was longer for vaccines considered additions vs. vaccines considered switches.

• Median time to peak for HepB monovalent vaccine additions was 2 years and 3 years for YF vaccines.
• Median time to peak for HepB and Hib tetravalent and pentavalent vaccine switches was 1 year.

Because GAVI’s current model is to provide countries with the financial and technical support to prepare for and introduce a vaccine and then rely on countries to introduce the vaccines to scale, GAVI was not expected to accelerate time to peak coverage. Therefore, GAVI’s current model of providing countries with the financial and technical support to prepare for and introduce a vaccine appears to be effective.

8.3. Results achieved on SG2.3

To what extent has GAVI improved the stability of global and country level vaccine supply?

GAVI has added value by creating a more stable vaccine market, resulting in an increase in the number of WHO prequalified suppliers post-GAVI. This has improved supply stability or led to the achievement of supply stability for the majority of the underused vaccines.

GAVI has added value by creating a more stable market for YF vaccines, but supply stability has worsened since 2008.
• Three additional products have been prequalified since GAVI’s inception.
• UNICEF reports combined with product availability assessments indicate improvements from 2000 – 2007.
• UNICEF product availability assessment indicates limited to very limited supply from 2008 onward.

GAVI has achieved supply stability for HepB mono- and tetravalent vaccines because of the entry of more suppliers and the decline in demand.

• The number of prequalified HepB monovalent suppliers increased from two to nine since GAVI’s inception.
• The number of prequalified HepB tetravalent suppliers increased from one to five since GAVI’s inception.
• UNICEF product availability assessments indicated supply excess of HepB mono- and tetravalent vaccines from 2004 and 2007 onward, respectively.
• However, due to the shift to pentavalent vaccines, there is now very limited demand for both products.

GAVI focused on creating a market for pentavalent vaccines, therefore, it did not focus on creating supply stability for Hib mono- and tetravalent vaccines.

GAVI has added value by creating a more stable market for pentavalent vaccines through 2009, and supply stability is expected for 2010 and beyond.

• Three additional products have been prequalified since GAVI’s inception.
• UNICEF product availability assessment indicates improvement from very limited supply in 2004 to limited supply from 2005 onward.
• UNICEF has projected adequate supply for 2010-12.

GAVI has added value by creating an attractive market for pneumococcal vaccine suppliers.

• GAVI has secured two 10-year commitments for 30m doses per year from both GSK and Pfizer beginning in 2012 and 2013, respectively.
• GAVI has secured approximately 50m doses total from these suppliers for use in the 2010-12 timeframe, which is predicted to be sufficient to meet 2010-11 demand.
• Supply beyond these initial commitments is still uncertain given AMC supply tenders are issued on an annual basis.

GAVI has not yet secured any supply commitments for rotavirus vaccine.
8.4. Results achieved on SG2.4

To what extent has GAVI made vaccines and related technologies more affordable?

Overall, there was little evidence to suggest that GAVI has added value by making vaccines more affordable.

Although GAVI supply and procurement strategy documents have emphasised the need for ‘affordable’ vaccines, GAVI has not put a plan in place to address vaccine pricing and has relied on natural market forces to drive vaccine price declines.

GAVI has not improved YF vaccine affordability.

• GAVI weighted average price for 5- and 10-dose vials increased by 19% and 13% between 2004 and 2010, respectively.
• This price increase occurred even though the number of prequalified products increased from two to four.
• This price increase occurred even though UNICEF reported supply excess for the 10 dose presentation from 2004-08, which represents the majority (66-77%) of shipped doses.

GAVI has improved HepB monovalent vaccine affordability; however, there is little demand for this vaccine.

• Prices for 10 dose HepB monovalent decreased by 32% from 2004-09.
• The number of prequalified suppliers increased to nine by 2008.
• Demand decreased to 12m doses by 2009 (without India) due to pentavalent preference.

GAVI has improved HepB tetravalent vaccine affordability; however, there is little demand for this vaccine.

• The price of the 10 dose HepB tetravalent presentation decreased by 37% from 2004-09.
• The number of prequalified suppliers increased to five by 2007.
• Demand decreased to 1m doses by 2009 due to pentavalent preference.

GAVI has only recently decreased pentavalent vaccine prices, but GAVI has not yet made this vaccine affordable.

• Single supplier for GAVI market through 2006.
• Two suppliers supplying GAVI market by 2008.
• Liq/lyo presentation WAP did not decline from 2001-09 ($3.50/dose), but recently declined 16% to $2.95/dose in 2010.
• Liquid presentation WAP started higher than liq/lyo presentation in 2007 ($3.75/dose), and decreased 20% to $3.01/dose in 2010.
For pneumococcal and rotavirus vaccines, the GAVI price is either far lower or expected to be far lower than high income public market prices. While much effort has gone into getting these vaccines appropriately priced for lower income markets, these vaccine prices will not be sustainable for most countries without continued GAVI funding.

GAVI has not actively addressed strategies for reducing vaccine prices throughout Phase I or Phase II. It is critically important that GAVI prioritise this effort as newer and more expensive vaccines enter GAVI’s portfolio.

8.5. Results achieved on SG2.5

To what extent has GAVI contributed to the evidence base required for countries to address the policy decision related to the introduction of new vaccines?

The evaluation confirmed the significant value GAVI has added by advancing the evidence base required for country policy decisions related to the introduction of YF, Hib-containing, pneumococcal, and rotavirus vaccines. Significant contributions were made to the evidence base for disease burden, vaccine safety and effectiveness, cost-effectiveness, and programmatic feasibility through the GAVI-funded Yellow Fever Initiative, Hib Initiative, PneumoADIP, and RVP. WHO was also highlighted as a major provider of evidence to inform country decision-making.

8.6. Results achieved on SG2.6

To what extent has GAVI developed and used vaccine forecasts that are accurate and timely?

GAVI has added value by delivering timely forecasts for use across the partners and with suppliers (WHO forecasts produced for UNICEF, UNICEF forecasts produced for suppliers, and GAVI-funded ADIP and AVI forecasts produced for GAVI and UNICEF). The process for creating and updating demand forecasts is well established for the underused vaccines, and has been recently established for the new vaccines.

Determining the accuracy of the forecasts was more challenging. For underused vaccines, the evidence suggests the variance between WHO forecasted and approved doses (used as a proxy for demand) has not improved over time, regardless of vaccine.

- For YF vaccines, the accuracy of the LTA forecasts varied widely (up to 500%) across the procurement rounds, but appear to have improved over time.
- For HepB monovalent vaccines, WHO forecasts varied widely (variances from -81% to 159%) across the first and second procurement rounds.
- For HepB tetravalent vaccines, WHO forecasts varied widely (variances up to 712%) across the first and second procurement rounds.
  - The accuracy of the LTA and annual updated forecasts were much better than the WHO forecasts (variance from -28% to 66%)
• For pentavalent vaccines, WHO forecasts varied less than for YF and HepB tetravalent vaccines (variance -4% to 118%) across the second and third procurement rounds.
  o The LTA and annual updated forecasts from 2002-09 were slightly better than the WHO forecasts (variance from -43% to 98%)

It is too soon to evaluate the accuracy of the new vaccine forecasts (pneumococcal and rotavirus vaccines).

### 8.7. Results achieved on SG2

Based on this evaluation, GAVI has been only partially achieved its SG2 goal. Table 8.1 summarises the extent to which GAVI’s second goal has been met.

**Table 8.1: Contribution by the SG2 programs to the goal**

<table>
<thead>
<tr>
<th>Accelerated the uptake and use of underused and new vaccines and associated technologies and improved vaccine supply stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔️ GAVI has played an important role in accelerating the introduction of YF, HepB and Hib vaccines.</td>
</tr>
<tr>
<td>❓ GAVI has played an important role in accelerating the demand of pneumococcal vaccines, but it is unclear whether introduction will be accelerated.</td>
</tr>
<tr>
<td>❌ It is too soon to say whether GAVI has accelerated the introduction of rotavirus vaccines, but based on current AVI projections, rota introduction is expected to be slower than other GAVI vaccine introductions.</td>
</tr>
<tr>
<td>✔️ The findings show GAVI-eligible countries are capable of quickly taking vaccine programs to scale.</td>
</tr>
<tr>
<td>✔️ ❌ GAVI has improved the stability of YF supply through 2007, but supply stability has worsened from 2008 onward.</td>
</tr>
<tr>
<td>✔️ GAVI has improved the stability of pentavalent vaccines through 2009 and is expected to achieve supply stability for 2010 and beyond.</td>
</tr>
<tr>
<td>✔️ GAVI has secured pneumococcal vaccine supply sufficient to meet 2010–11 demand and to meet a significant proportion of demand from 2012–22.</td>
</tr>
<tr>
<td>❏ GAVI has not yet secured any supply commitments for rotavirus vaccine.</td>
</tr>
<tr>
<td>❏ GAVI has not yet made YF vaccines more affordable to countries.</td>
</tr>
<tr>
<td>❏ GAVI has just recently improved the affordability of pentavalent vaccines, but more is needed to ensure these vaccines are affordable to countries in the absence of GAVI.</td>
</tr>
<tr>
<td>✔️ GAVI has played an important role in the advancement of the evidence base required for country policy decisions.</td>
</tr>
<tr>
<td>✔️ GAVI has delivered timely forecasts for underused and new vaccines for use across the partners and with suppliers.</td>
</tr>
<tr>
<td>❓ The accuracy of the underused vaccine demand forecasts varies widely</td>
</tr>
</tbody>
</table>