ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

Annual Report

1 April 2013 – 31 March 2014

Prepared by the GAVI Alliance Secretariat

Contents

Abbreviations

AMC	Advance Market Commitment
DTP	Diphtheria, Pertussis, Tetanus
FOC	Firm Order Commitment
GAVI	GAVI Alliance
GAVI Secretariat	GAVI Alliance Secretariat
IAC	Independent Assessment Committee
IPD	Invasive Pneumococcal Disease
IRC	Independent Review Committee
M&E	Monitoring and Evaluation
PATH	Program for Appropriate Technologies for Health
PCV	Pneumococcal Conjugate Vaccine
PROWG	Pneumo & Rota Operational Working Group
PSA	Provisional Supply Agreement
PSF	Product Summary File
PQT	WHO Prequalification Team
SDF	Strategic Demand Forecast
TPP	Target Product Profile
UNICEF	United Nations Children's Fund
VI-TAC	Vaccine Implementation Technical Advisory Consortium
WHO	World Health Organization
WUENIC	WHO/UNICEF Estimates of National Immunisation Coverage

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Executive Summary

Supply and Demand

The pilot Advance Market Commitment (AMC) for pneumococcal vaccines is now in its fourth year of implementation and significant progress has been made. During the 2013 – 2014 reporting period, the third Call for Supply Offers was successfully concluded. Two new supply agreements were signed, for periods of 11 years each (including dose provision in the AMC capacity development period), bringing the total number of supply agreements under the AMC programme to six. In addition to the annual supply commitment achieved under these new agreements, additional supply was also secured for delivery in the short term for 2013 to 2015. Noticeably, the first reduction in the tail price under AMC to below US $3.50/dose will likely contribute to a total savings of US $157 million over the lifetime of the agreements.

With the six supply agreements, the total contracted supply amount through 2024 now amounts to 1.46 billion doses. Out of the US $1.5 billion AMC funds, the two suppliers that have pre-qualified pneumococcal vaccines have been allocated US $1.095 billion of the funds. Twenty-seven percent of the AMC funds remain available.

On the demand side, the uptake of pneumococcal vaccines has been unprecedented. During this reporting period, sixteen additional AMC-eligible countries have introduced this vaccine, bringing the total number of introductions to date to 40. Fifteen other countries that have been approved for GAVI support are expected to introduce in the coming two years. Despite the remarkable performance in terms of the number of introductions, some delays in introductions have been registered as a result of a number of factors. These include global supply constraints, insufficient human resource capacity at the country level to manage competing priorities, delays in expanding cold chain capacity, political issues and organisational changes in countries, and delays in making funding available at national and/or sub-national levels for pre-introduction activities. Drawing from lessons gathered from introductions to date, GAVI Alliance is strengthening the coordination mechanism among partners, identifying and addressing bottlenecks in funding disbursements, and deploying refined tools to assist countries in their pre-introduction activities.

Based on Strategic Demand Forecast (SDF) v8.0 which was approved after the 2013 procurement cycle, GAVI Secretariat, in consultation with UNICEF SD, decided to not issue a fourth Call for Supply Offers for the procurement of pneumococcal vaccines in 2014. The need for the next tender will be re-assessed later in 2014 based on SDF v9.0 and the outcomes of the next rounds of New Vaccines Support applications to the GAVI Secretariat.

Monitoring and Evaluation

AMC progress continues against selected indicators as shown in Table 1. The continued scale up of PCV vaccines is forecasted to result in the prevention of 1.5 million deaths by 2020.

Table 1. Selected non-confidential indicators for AMC progress tracking (based on calendar year view)

	2009	2010	2011	2012	2013	2014*
Objective 1: To accelerate the development of pneumococcal vaccines that meet developing country needs.						
Cumulative number of AMC eligible TPP vaccines	0	2	2	2	2	2
Cumulative number of AMC registered manufacturers who have made their registration public	0	4	4	4	5	5

	2009	2010	2011	2012	2013	2014*
Objective 2: To bring forward the availability of effective pneumococcal vaccines for developing countries.						
Annual number of doses of TPP vaccine procured under AMC by year (in millions)	0	7	36	58	58	-
Objective 3: To accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers.						
Cumulative number of countries that have applied for GAVI support for PCV	21	21	49	52	59	59
Cumulative number of AMC-eligible/GAVI-supported countries that have been approved	3	17	37	46	51	55
Cumulative number of AMC-eligible/GAVI-supported countries introducing TPP vaccines	0[i]	1[ii]	16	24	38	40
Coverage of PCV in AMC-eligible/GAVI-supported countries***	0%	1%	4%	9%	n/a**	n/a
Cumulative number of children vaccinated with GAVI support (in millions)	-	0.5	4	10	n/a**	n/a

* Year-to-date through 31 March 2014

** WUENIC coverage data and WHO-reported number of immunised for 2013 will be available in late 2014

*** Indicator defined as the percentage of population reached across GAVI73 countries

Coverage performance at the country level is tracked, using WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) data which are published annually. Information to date showed that countries are able to successfully introduce PCV into their routine systems, with PCV 3rd dose coverage tracking well against the 3rd dose coverage of DTP vaccine by the second year of implementation.

The first AMC Impact Evaluation was originally planned for 2014, but as per recommendation from the GAVI Alliance Evaluation Advisory Committee and agreement with AMC stakeholders, the evaluation is postponed to 2015. Separately, in 2013, the GAVI Alliance launched a new set of evaluations to collect real-time data on immunisation programmes, vaccine-related issues and the contribution of GAVI Alliance support in five countries. Bangladesh, India, Mozambique, Uganda and Zambia are taking part in the Full Country Evaluation project, which will run from 2013 to 2016. GAVI's support for new and underused vaccines will be assessed, along with cash-based support to countries. The introductions of PCV in Mozambique, Uganda and Zambia in 2013, as well as upcoming introduction in Bangladesh in late 2014, are being evaluated as part of the Full Country Evaluations.

GAVI is currently funding a number of special studies to help facilitate evidence-based decision making in support of the introduction and continued implementation of pneumococcal vaccines in developing countries. The ongoing activities related to vaccine impact and surveillance will be key inputs to the planned AMC Impact Evaluation.

Financial activities

From 1 April 2013 to 31 March 2014, US $624 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US $259 million was from the AMC funds to pay for the AMC

[i] Two countries introduced PCV in 2009, but with a vaccine that was not TPP compliant. They have since switched to a TPP vaccine in 2011.

[ii] Same as above.

top-up portion of the vaccine purchase. The remaining US $365 million was allocated from general GAVI funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs.

Challenges and priorities ahead

With over half of the AMC-eligible countries having introduced PCV, the priorities moving forward will be focused on supporting country implementation, measuring impact, and ensuring proper balance of supply and demand. Lessons learned on challenges in PCV implementation will serve as guides to direct technical assistance for future introductions. Broader efforts at the GAVI Alliance to contribute to health systems strengthening especially with an increasing focus on supply chain are aimed at improving coverage of routine immunisation, including PCV. Focus on gathering evidence on vaccine effectiveness and impact will continue through GAVI-supported special studies, and the AMC Impact Evaluation will be initiated in the next reporting cycle. In the coming years, a significant scale up of production capacity will be required in order to meet the increasing demand. Therefore, close monitoring of the supply component especially in light of a limited supplier base is essential.

Background

Advance Market Commitments (AMCs) for vaccines aim to encourage the development and production of affordable vaccines tailored to the needs of developing countries. In June 2009, the Governments of Italy, the United Kingdom, Canada, the Russian Federation, Norway and the Bill & Melinda Gates Foundation, collectively pledged a total of US $1.5 billion to fund a pilot AMC against pneumococcal disease.

The overarching goal of the pilot AMC is to reduce morbidity and mortality from pneumococcal diseases, preventing an estimated seven million childhood deaths by 2030. The objectives of the pneumococcal AMC are:

1. **to accelerate the development of pneumococcal vaccines** that meet developing country needs (e.g. in terms of serotype composition and vaccine presentation) as specified in the Target Product Profile;

2. **to bring forward the availability of effective pneumococcal vaccines** for developing countries by guaranteeing the initial purchase price, for a limited quantity of the new vaccines, that represents value for money and incentivises manufacturers to invest in scaling-up production capacity to meet developing country vaccine demand;

3. **to accelerate vaccine uptake** by ensuring predictable vaccine pricing for countries and manufacturers, through binding commitments by participating companies to supply vaccines at low, long-term and sustainable prices after the AMC finances are depleted;

4. **to test the effectiveness of the AMC mechanism** as an incentive for supplying much needed vaccines and to learn lessons for developing possible future AMCs for other vaccines.

Following the initiation of the Pneumococcal AMC in 2009, the first vaccines became available for procurement under the AMC terms and conditions, and the first roll-out occurred in Nicaragua in December 2010. To date 75% of 73 AMC-eligible countries have submitted applications to GAVI for financial support and been approved for pneumococcal vaccine introduction.

On 30 October 2013, representatives from the GAVI Alliance partner organizations met at the Mid-Term Review (MTR) meeting to review progress made towards delivering on the goals set at the 2011 Pledging Conference. Following the MTR conference, GAVI is now entering the replenishment phase to resource the long-term country demand for vaccines. GAVI is also developing its 2016-2020 strategy, which will be approved in 2014. The next GAVI replenishment will be essential to ensure accelerated vaccine rollout and impact of core GAVI supported vaccines, including pneumococcal vaccine.

The purpose of this report is to provide an update on AMC implementation activities, including supply and procurement, country demand, monitoring and evaluation, media and communications and financial reporting. This report is the fifth pneumococcal AMC Annual Report[iii] and covers the period from 1 April 2013 to 31 March 2014. The report was developed by the AMC Secretariat at GAVI, in collaboration with the World Bank and UNICEF Supply Division (SD), and was approved by the Independent Assessment Committee on 1 May 2014.[iv]

[iii] Previous AMC Annual Reports can be found on the AMC website: http://www.gavialliance.org/library/gavi-documents/amc/
[iv] Note that as a public document, this report does not include any confidential information.

1. Supply and Procurement update

1.1. AMC eligible pneumococcal vaccines

WHO recommends the inclusion of pneumococcal vaccines be given priority in childhood immunisation programmes world-wide, especially in countries with under-five mortality of greater than 50 per 1000 live births. For administration to infants, three primary doses (3p+0 schedule) or, as an alternative, two primary doses plus a booster (2p+1 schedule) are recommended. Primary vaccination can be initiated as early as at 6 weeks of age.

As of 31 March 2014, there are currently two pneumococcal conjugate vaccines (PCV) available for procurement under the AMC. These two vaccines meet the criteria for the Target Product Profile (TPP), which describes the minimum characteristics required for a pneumococcal vaccine to be eligible for AMC financing. No additional manufacturers are expected to have WHO-prequalified vaccines before 2018.

1.1.1. Pneumococcal conjugate vaccine, 10-valent

The 10-valent PCV (PCV10) is a liquid vaccine in a 2 dose vial, produced by GlaxoSmithKline. It was launched in Europe in 2009, obtained WHO prequalification on 12 March 2010 and was deemed AMC-eligible on 16 April 2010 by the AMC Independent Assessment Committee (IAC). PCV10 is supplied as a two dose liquid vaccine without preservative which is considered novel by WHO. Therefore, both doses are required to be used within six hours of the vial being opened, otherwise, any remaining dose will need to be discarded.

Due to the novelty of the presentation, WHO requires that countries ensure programmatic readiness to introduce PCV10, with a pre-condition of special training requirements (i.e. specific training on the use of this presentation must have taken place at all levels before shipment and distribution of the vaccine), and the placement of stickers that state '*do not return an opened vial of PCV10 to the fridge*' on refrigerators at all levels. Upon written confirmation from the country to UNICEF, WHO is responsible for assessing that these conditions are met before UNICEF and supplier is authorised to ship first doses of the vaccine to any country. WHO will also assist the countries in performing post introduction evaluations six to 12 months after the introduction, with a specific focus on assessing health care worker knowledge and behaviour related to the safe use and handling of this vaccine presentation.

1.1.2. Pneumococcal conjugate vaccine, 13-valent

The 13-valent PCV (PCV13) is a liquid vaccine in a one dose vial, produced by Pfizer Inc. It obtained WHO prequalification on 22 August 2010 and was deemed AMC eligible by the AMC IAC on 23 August 2010. UNICEF Supply Division started the procurement of PCV13 to GAVI-supported countries in September 2010 upon IAC approval of the vaccine, with first delivery taking place in October 2010.

1.2. Supply Offers and Agreements

In July 2013, following the publication of the third Call for Supply Offers on 27 August 2012, UNICEF in its capacity as procurement agency for the GAVI Alliance entered into two new supply agreements for the supply of pneumococcal conjugate vaccines under the Advance Market Commitment (AMC). These new supply agreements include the first decrease to the AMC Tail Price as well as additional short term supply to support the accelerated introduction in a number of countries.

There have been three Calls for Supply Offers for pneumococcal vaccines under the AMC to date. A summary of the First, Second and Third AMC Supply Agreements can be found in Annex 1. A summary of the current supply commitments is shown in the table below.

Table 2. Status on overall supply commitments

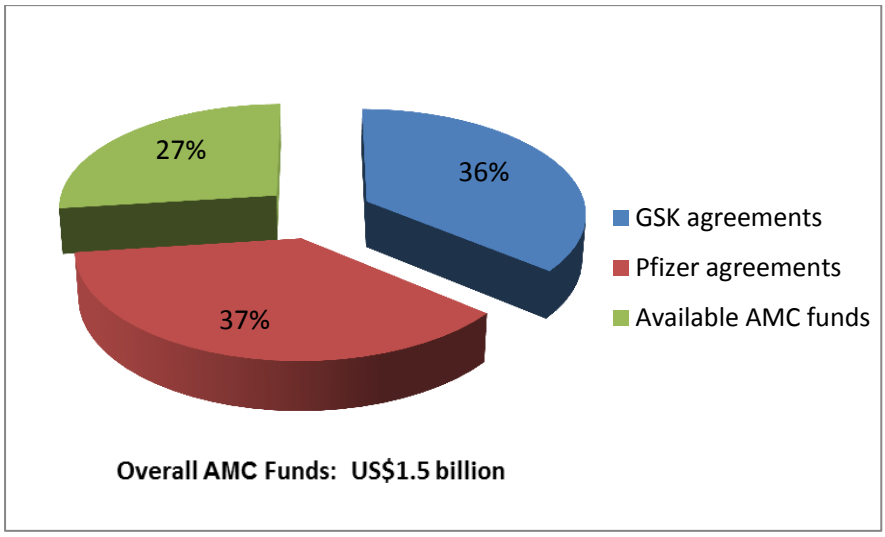
Manufacturer	Date of signature (week of)	Annual supply commitment (doses)	Tail price	Supply start date	AMC Funds allocated
GSK	23 March 2010	30 million	US $3.50	Jan 2012	US $225 million
Pfizer Inc.	23 March 2010	30 million	US$3.50; reduced to $3.40 mid 2013 and $3.30 from 2014*	Jan 2013	US $225 million
GSK	12 Dec 2011	18 million	US $3.50	Jan 2014	US $135 million
Pfizer Inc.	12 Dec 2011	18 million	US $3.50; reduced to $3.40 mid 2013 and $3.30 from 2014*	Jan 2014	US $135 million
GSK	22 July 2013	24 million	US $3.40	Jan 2015	US $180 million
Pfizer Inc.	22 July 2013	26 million	US $3.40 in 2013; US $3.30 from 2014 onwards	Jan 2016	US $195 million

* Reduced tail price applied as per Pfizer's third supply agreement

In addition to the annual supply commitment achieved under the third Supply Agreements and the first reduction in tail prices under the AMC, additional supply was also secured for delivery in the short term for 2013 to 2015. The reduction in the tail price will likely contribute to a total savings of US $157 million over the lifetime of the agreements.

The allocation of AMC funds is summarised in Figure 1.

Figure 1. Allocation of AMC funds



Based on SDF v8.0 forecasts (see Section 1.2 below), GAVI, in consultation with UNICEF SD, decided to not issue a fourth Call for Supply Offers for the procurement of pneumococcal vaccines in 2014 given sufficient supply on contract to meet the demand of already approved countries. The need for the next tender will be re-assessed later in 2014 based on SDF v9.0 and the outcomes of the next rounds of New Vaccines Support applications to the GAVI Secretariat expected in May and September.

1.3. Doses contracted to date

With the new supply agreements, the number of doses on contract has increased. Additional available doses have been brought forward during the capacity development period to meet demand. Table 3 summarises the total contracted supply, as of 31 March 2014.

Table 3. Total annual contracted supply as of July 2013, in millions

Year	2010	2011	2012	2013	2014	2015	2016 - 2020	2021	2022	2023	2024	TOTAL
Doses procured/ contracted in 2010	5.5	28.9	54	60	60	39.2	60	47.4	5			**600**
Doses procured/ contracted in 2011			13	17	36	36	36	36	36	6		**360**
Doses contracted in 2013				3	19	64.8	50	50	50	49.2	14	**500**
TOTAL	**5.5**	**28.9**	**67**	**80**	**115**	**140**	**146**	**133.4**	**91**	**55.2**	**14**	**1460**

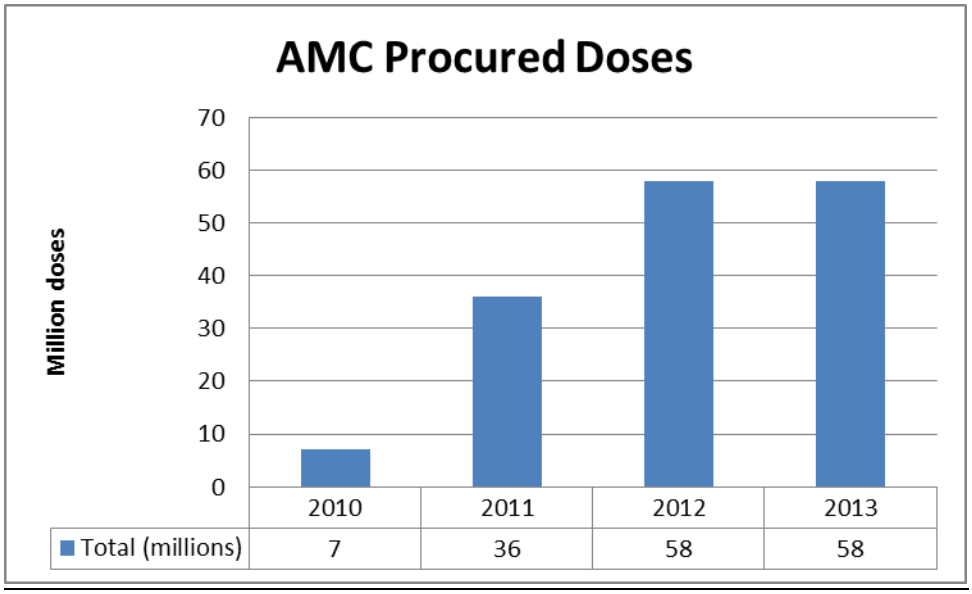
* Contracts are amended annually based on actual supply and demand to ensure that the total quantity on the supply agreements remain unchanged

Source: UNICEF Supply Division

1.4. Doses procured between 2010 and 2013

The total number of doses procured and delivered to date is summarised in Figure 2 below:

Figure 2. Pneumococcal vaccine procured volumes, in millions of doses, 2010-2013



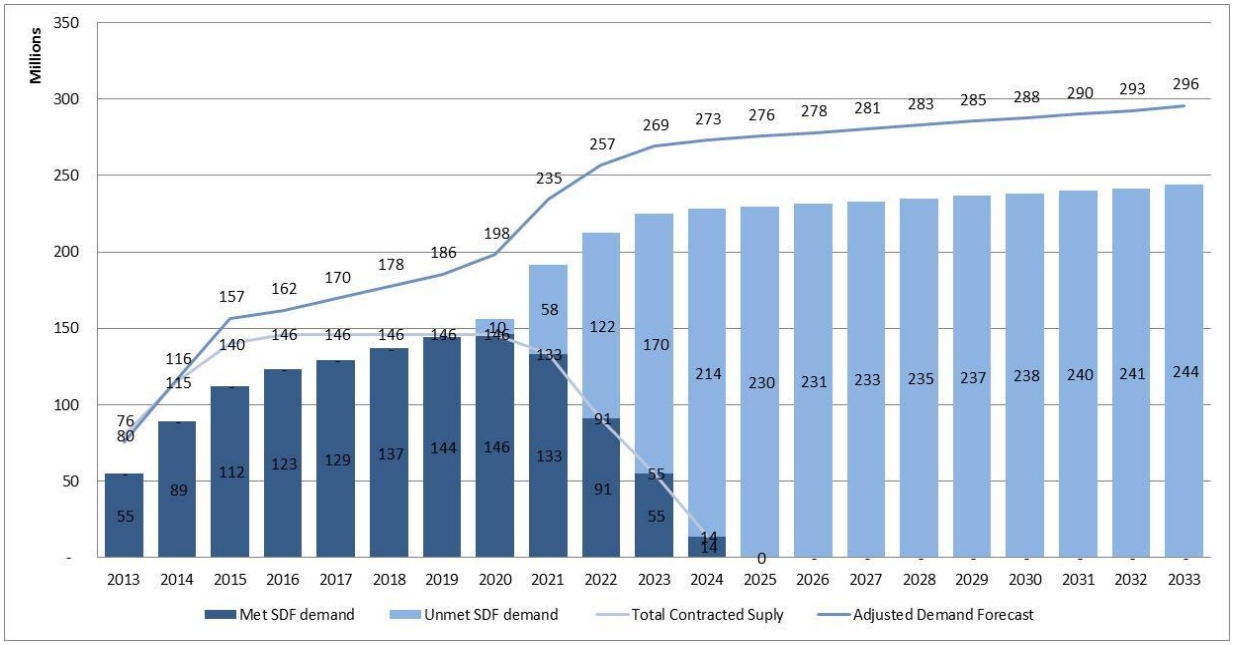
Source: UNICEF Supply Division (Please note that the figure above indicates the number of doses placed on purchase orders during the respective years, including for delivery in a subsequent year).

It should be noted that special measures were undertaken with both suppliers in 2012 to ensure production at maximum capacity level to ensure sufficient supply availability for 2013, when demand was projected to outpace supply. This resulted in early procurement of approximately 10 million additional doses in 2012 instead of in 2013. These doses were delivered during 1st half of 2013 to minimise delays in country introductions.

1.5. Strategic Demand Forecasts

Strategic Demand Forecast (SDF) v8.0 was finalised in September 2013 and published on the AMC website[1]. Figure 3 shows two scenarios of the demand forecast, an SDF base case using the same data sources for surviving infant population and vaccine coverage as previously used, and an "adjusted demand forecast" (ADF) using country estimates as data sources, against contracted supply. The ADF is produced to reflect the volume of PCV doses which have been financially committed by GAVI to countries that have already been approved for GAVI support, based on their applications to GAVI.

Figure 3. Strategic Demand Forecast v8.0



In 2013, GAVI undertook a review of the SDF accuracy based on experiences to date on several vaccine programmes, including the pneumococcal vaccine programme. The SDF methodology was first established in 2009. One of the findings is that the SDF under-estimates the projected demand for the GAVI market in the short term compared to actual doses shipped (determined based on GAVI-committed doses, actual country requests and available supply). Adjustments to SDF methodology resulted from this review, and will be reflected in the future versions of the SDF.

Previous versions of the SDF have been summarised in prior Annual Reports. SDFs published or developed in the reporting period are as follows:

- SDF v7.0 was approved in April 2013. This version was not published on the AMC website as a new procurement cycle was already in process.
- SDF v8.0 served as a basis for consultations between the GAVI Secretariat and UNICEF to determine if a new Call for Supply Offers should be issued. The publication of SDF v8.0 was delayed until early 2014 due to discussions required to inform this decision. These included the finalisation of SDF v8.0 which projected demand below actual contracted supply for the 5 year horizon, findings from the SDF accuracy work, considerations of the Adjusted Demand Forecast with committed doses, and the recently concluded supply agreements.
- SDF v9.0 was recently approved by the GAVI Secretariat, and together with outcome of the next rounds of New Vaccines Support applications to the GAVI Secretariat expected in May and September, the AMC Secretariat and UNICEF will consult and reassess the need for the issuance of the next tender to meet the AMC objectives. An update will be provided in the 2014 Pneumococcal AMC Annual Report.

1.6. Availability of pneumococcal vaccines

The third tender for PCV concluded in July 2013 and additional doses of the vaccine were made available in the second half of 2013 for countries that were approved for introduction in either late 2013 or early 2014.

While the availability of supply is increasing and reducing the gap between supply and demand, in April 2013, GAVI was informed of production issues for one of the products (PCV10), which resulted in a

reduction of total 2013 available supply by 14 million doses. This was reported to AMC stakeholders in June 2013. The root causes were identified by the manufacturer and production resumed; however, the capacity lost could not be recovered. With this unforeseen supply disruption, since mid-2013 UNICEF Supply Division continues to work closely with all affected countries to manage demand against the available supply, by allocating the quantities shipment by shipment to each country based on information of stock levels, increasing the frequency of deliveries and utilising buffer stocks to avoid stock outs while maximising the utilisation of globally available supply. Smaller countries which were planning to introduce with this product were able to continue with their implementation without interruptions. However, this production issue resulted in delays in introduction for over a year in two large countries – Bangladesh and Nigeria. In March 2014, the manufacturer provided a further update that the production capacity ramp-up is proceeding slower than expected, which would affect delivery of doses towards the end of 2014. This situation has been managed by UNICEF Supply Division through re-allocation of supply to countries, such that the upcoming introductions in the two large countries would not be further delayed.

Based on the current supply available, new applicants from the 2013 application round that were recently approved for GAVI support could receive PCV supply as early as the end of 2014. The need for a fourth Call for Supply Offers will be revisited in late 2014 after new PCV applications for GAVI support are received.

During this reporting period, GAVI Secretariat has initiated the development of a Pneumococcal Vaccine Supply and Procurement Roadmap as part of its market shaping strategy. More information is forthcoming in the next reporting cycle.

1.7. AMC registered manufacturers

Following the signature of AMC legal agreements on 12 June 2009, manufacturers can enter into an AMC Registered Manufacturers' Agreement with the GAVI Alliance and the World Bank. As part of the registration agreement, manufacturers formally agree to the AMC terms and conditions; accept to provide an annual update on expected timing for application for AMC Eligibility and for WHO prequalification; and recognise the role of the Independent Assessment Committee (IAC) in the determination of AMC eligibility. As described in the AMC Procedures Memorandum, AMC Registered Manufacturers' Registration Procedures, manufacturers interested in participating in the AMC must submit an AMC registered manufacturer application package to the AMC Secretariat. This registration does not imply any commitment from manufacturers to participate in the AMC. It is, however, a prerequisite to take part in UNICEF's calls for supply offers.

Details about the registered manufacturers are confidential unless a firm agrees to have its registration made public. In 2013, there was one additional manufacturer who has registered with the AMC and has chosen to make their registration public -- PnuVax SL Biopharmaceuticals, Inc. The list of AMC registered manufacturers who have made their registration public is as follows[2]:

- GlaxoSmithKline (GSK) Biologicals (Belgium)
- Panacea Biotec Ltd. (India)
- Pfizer Inc. (U.S.)
- PnuVax SL Biopharmaceuticals, Inc. (Canada)
- Serum Institute of India (India)

To date, only two of these manufacturers are producing AMC-eligible pneumococcal vaccine. GAVI is actively monitoring the pipeline development at other manufacturers.

2. Country demand and introductions overview

2.1. GAVI-supported countries approved for the introduction of PCV

GAVI opened a New Vaccine Support application round in 2013, with a deadline for countries to submit applications by 15 September 2013. Seven countries applied for GAVI support in this round to introduce pneumococcal vaccines, including the first graduating country who applied to access AMC price (see Section 2.2).

The seven countries were reviewed by the Independent Review Committee (IRC) in November 2013. Following this review, six countries were recommended for approval and one country was recommended for conditional approval. As of 31 March, in total, 55 of the 73 AMC-eligible countries (75%) have applied and been approved for support for pneumococcal vaccines.

2.2. Graduating and graduated countries introduction of PCV

In June 2010, the GAVI Board approved that all GAVI-eligible countries as per the 2003 definition continue to have access to pneumococcal vaccines (PCV) through GAVI under the terms and conditions of the AMC. As a result of this Board decision, countries graduating and graduated from GAVI support that have not yet been approved for pneumococcal vaccine are able to apply to introduce this vaccine under the terms and conditions of the AMC provided that they procure through UNICEF. However, these countries will need to self-finance the tail price component of the price from the outset. Also, all countries must have achieved DTP3 coverage at or above 70% according to WHO/UNICEF estimates. As of 31 March 2014, one graduating country – Mongolia – has been approved for support through the AMC. Other graduating and graduated countries that are eligible to apply are as follows:

- Bhutan
- Cuba
- Indonesia
- Sri Lanka
- Ukraine
- Timor Leste

2.3. Pneumococcal vaccine introductions

2013 marked an unprecedented year of PCV introductions. In the period between 1 April 2013 and 31 March 2014, sixteen countries introduced pneumococcal vaccines procured through the AMC (versus 8 in the prior reporting period). To date, there have been 40 pneumococcal vaccine introductions and these are outlined Table 4. Of the 40 pneumococcal vaccine introductions that have taken place, eight countries are using PCV10, whereas the remaining 32 countries are using PCV13.

Table 4. Pneumococcal vaccine introductions to date

Year	Country	Product	Status	Cumulative No.
2009	Gambia	PCV7 (donation)	Switched to PCV13 in 2011	1
	Rwanda	PCV7 (donation)	Switched to PCV13 in 2011	2
2010	Nicaragua	PCV13	Introduced in December	3
2011	Guyana	PCV13	Introduced in January	4
	Yemen	PCV13	Introduced in January	5

	Kenya	PCV10	Introduced in January	6
	Sierra Leone	PCV13	Introduced in January	7
	Mali	PCV13	Introduced in March	8
	Congo, DR	PCV13	Introduced in April (phased introduction)	9
	Honduras	PCV13	Introduced in April	10
	Central African Republic	PCV13	Introduced in July	11
	Benin	PCV13	Introduced in July	12
	Cameroon	PCV13	Introduced in July	13
	Burundi	PCV13	Introduced in September	14
	Ethiopia	PCV10	Introduced in October	15
	Malawi	PCV13	Introduced in November	16
2012	Ghana	PCV13	Introduced in April* (joint intro. with rotavirus vaccine)	17
	Zimbabwe	PCV13	Introduced in June*	18
	Pakistan	PCV10	Introduced in October (phased introduction)	19
	Congo Rep	PCV13	Introduced in October	20
	Madagascar	PCV10	Introduced in November	21
	Sao Tome & Principe	PCV13	Introduced in November	22
	Djibouti	PCV13	Introduced in December	23
	Tanzania	PCV13	Introduced in December* (joint intro. with rotavirus vaccine)	24
2013	Mozambique	PCV10	Introduced in April	25
	Uganda	PCV10	Introduced in April (phased introduction)	26
	Kiribati	PCV13	Introduced in May	27
	Angola	PCV13	Introduced in June	28
	Zambia	PCV10	Introduced in July joint intro. with measles second dose)	29
	Sudan North	PCV13	Introduced in August	30
	Moldova	PCV13	Introduced in October	31
	Lao PDR	PCV13	Introduced in October	32
	Burkina Faso	PCV13	Introduced in October (joint intro. with rotavirus vaccine)	33
	Senegal	PCV13	Introduced in November	34
	Mauritania	PCV13	Introduced in November	35
	Papua New Guinea	PCV13	Introduced in November	36
	Afghanistan	PCV13	Introduced in December	37
	Azerbaijan	PCV10	Introduced in December	38
2014	Liberia	PCV13	Introduced in January	39
	Bolivia	PCV13	Introduced in January	40

** Ceremonial launch; National introduction in the month following*

Out of the sixteen countries that introduced during this reporting period (1 April 2013 and 31 March 2014), twelve had to delay their introductions due to supply constraints, eight of which had originally intended to launch in the previous calendar year, 2012. Countries were promptly updated on the supply situation, to inform their planning for PCV introduction. The conclusion of the third supply agreements in July 2013 allowed new supply to be made available to countries in the second half of the year, resulting in many introductions in late 2013 and early 2014.

Out of these sixteen countries, five countries experienced other hurdles which resulted in further postponement of their introductions of over three months after supply was confirmed. Seven other countries had supplies available for them in 2013 but have delayed their introductions to after Q2 2014,

beyond the current reporting period. To capture lessons learned, an analysis was conducted to identify common issues faced by the countries. These include insufficient human resources capacity at the country level to manage competing priorities, delayed expansion of cold chain capacity, political issues and organisational changes in countries, and delays in making funding available at national and/or sub-national levels for pre-introduction activities, among other factors. To address these issues, GAVI Alliance is strengthening its coordination mechanism to ensure that technical assistance to countries can be delivered more efficiently and effectively. A new WHO data repository tool which was rolled out in 2013 is being refined, to enable partners to better track the status of pre-introduction activities and provide support where needed. Bottlenecks in GAVI Secretariat's cash disbursement process are also being identified, so that disbursements for vaccine introduction grants can be made available earlier for future vaccine introductions.

At the country level, programmatic challenges post-introduction are being gathered through Post Introduction Evaluations (PIEs), which are evaluations of the overall impact of the introduction of a new vaccine(s) on a country's national immunisation programme. During this period, seven countries have conducted a PIE. A PIE focuses on a range of programmatic aspects, such as pre-introduction planning, vaccine storage and wastage, logistics of administering the vaccine, and community receptiveness to the vaccine. It is used to rapidly identify problem areas needing correction within the immunisation programme, either pre-existing or resulting from the introduction of a new vaccine, and provide valuable lessons for future vaccine introductions.

2.4. Future pneumococcal vaccine introductions

Fifteen other GAVI-approved countries are expected to introduce the pneumococcal vaccines in 2014-2016. This includes two large countries – Bangladesh and Nigeria – which were affected by the PCV10 production issue and therefore had to postpone their introductions from 2013.

These future pneumococcal vaccine introductions are outlined in the table below:

Table 5. Future planned pneumococcal vaccine introductions

Year	Country	Product	Status	Cumulative No.
2014	Togo	PCV13	Planned for May	41
	Cote d'Ivoire	PCV13	Planned for June	42
	Georgia	PCV10	Planned for 3Q	43
	Lesotho	PCV13	Planned for 3Q	44
	Niger	PCV13	Planned for 3Q	45
	Nepal	PCV13	Planned for 3Q	46
	Guinea Bissau	PCV13	Planned for 3Q	47
	Armenia	PCV10	Planned for 3Q	48
	Bangladesh	PCV10	Planned for 4Q	49
2015	Nigeria	PCV10	Planned for 1Q (phased introduction)	50
	Haiti	PCV13	Planned for 1Q	51
	Cambodia	PCV13	Planned for 1Q	52
	Eritrea	PCV13	Planned for 1Q	53
	Uzbekistan	PCV13	Planned for 1Q	54
2016	Mongolia	PCV13	Planned for 1Q	55

In February 2014, GAVI announced two new rounds of New Vaccine Support applications for 2014. Table 6 shows the timeline for new application submission, review and approval. This year, there will

be two windows of opportunities for countries to apply for GAVI support, as part of an effort to provide more flexibilities for countries and better align GAVI application cycles with the timelines in countries.

Table 6. 2014 GAVI New Vaccine Support (NVS) timelines

2014	Application submission cut-off dates	Independent Review Committee dates	GAVI CEO or Executive Committee Decision
For all types of GAVI support	1 May	23 June – 4 July	September 2014
	15 September	10 – 21 November	February 2015

The Strategic Demand Forecast v8.0 estimates that a total of 55 countries will have introduced pneumococcal vaccines by 2015, compared to the GAVI Alliance Business Plan target of 45 for the same period. PCV coverage as a percentage of population reached across all 73 GAVI-supported countries is projected to reach ~37% (versus target of 40%) by 2015. The targets were set based on SDF v2.0.

2.5. Coordination and support for pneumococcal vaccine introductions

Given the increased number of introducing countries and the links between pneumococcal and rotavirus introductions, the Pneumo/Rota Operational Working Group (PROWG) was established in 2011 (built on the previous the Pneumo Ad-hoc Introduction Group) to ensure close coordination and improved information flow around pre- and post-launch activities, and report programme performance for both pneumococcal and rotavirus vaccines. This continues today as a critical forum for GAVI Alliance partners coordination to support introduction and sustained use of pneumococcal and rotavirus vaccines in countries.

The Pneumo/Rota Operational Working Group (PROWG) members represent WHO, UNICEF SD, UNICEF Programme Division, VITAC[v] and the GAVI Secretariat. The working group meets weekly by teleconference and the focus of the calls is on the following areas:

- Monitoring of country readiness to introduce, including expected introduction date, cold chain capacity, and training;
- Monitoring the progress of implementation, such as reports of faster (or slower) uptake of the vaccine post launch;
- Country ranking and allocation of limited available supply, as required;
- Supporting communication on supply availability and supply options to countries.

A list of current PROWG members is provided in Annex 2.

To support countries in introducing pneumococcal vaccines, in October 2013, WHO published new guidance documents to guide district and health facility staff on how to introduce the pneumococcal vaccine. In addition, new interactive resources were developed and distributed to countries to strengthen training for healthcare workers. Technical assistance to countries in areas of application development support, vaccine introduction planning, cold chain and logistics, communication and social

[v] Vaccine Implementation Technical Advisory Consortium (VITAC) - A technical assistance consortium of PATH, Johns Hopkins University (JHU), US Centers for Disease Control and Prevention (CDC) and others PATH member represents VITAC at the PROWG.

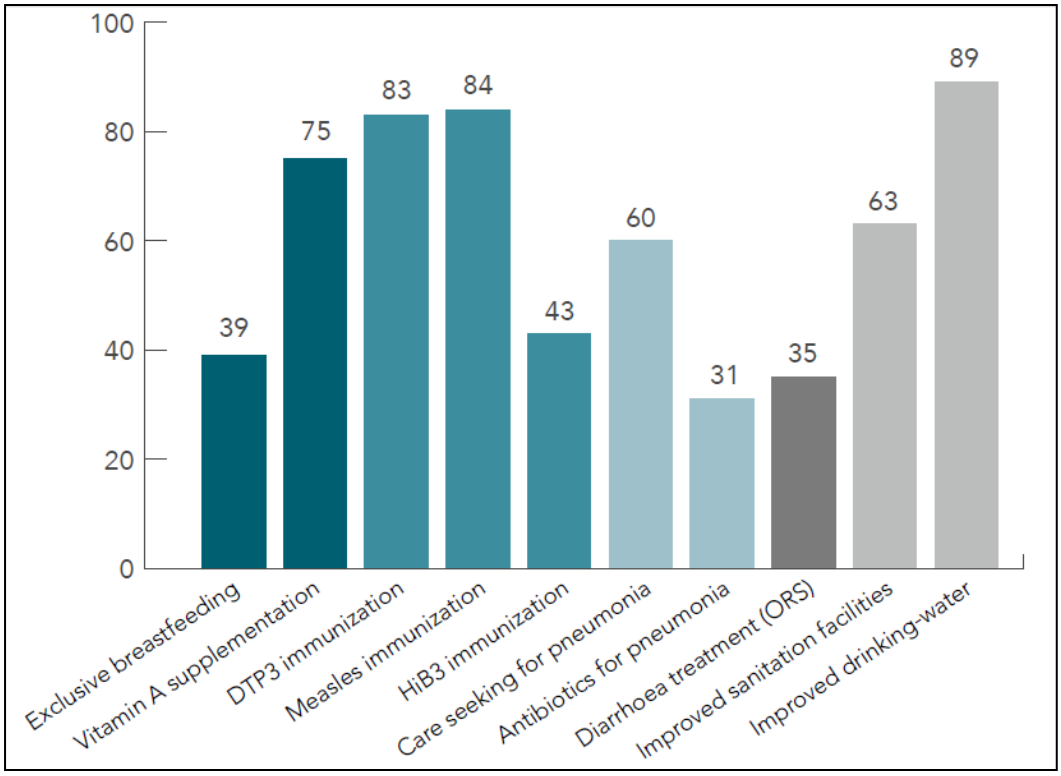
mobilisation, and monitoring and surveillance continues to be provided by WHO, UNICEF Programme Division, PATH and other partners.

2.6. Global Action Plan for the prevention and control of Pneumonia and Diarrhoea (GAPPD), published April 2013

In April 2013, WHO/UNICEF published the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD)[3], which are two major vaccine preventable killers of young children. Together, these diseases account for 29% of all deaths of children less than 5 years of age and result in the loss of 2 million young lives each year. GAPPD proposes a cohesive approach to ending preventable pneumonia and diarrhoea deaths. It brings together critical services and interventions to create healthy environments, promotes practices known to protect children from disease and ensures that every child has access to proven and appropriate preventive and treatment measures.

Many interventions have been shown to be effective. However, services are provided piece-meal and those most at risk are not being reached. Figure 4 shows the complementary interventions for prevention and treatment of these two diseases, including the use of vaccines which has higher coverage than that of other core interventions. As pneumococcal vaccines are introduced, and their coverage approaches that of DTP3 immunisation, this presents a unique opportunity to strengthen the integration of service deliveries and help improve the coverage of other important interventions.

Figure 4. Coverage of interventions for the prevention and treatment of pneumonia and diarrhoea (% of children)



Source: UNICEF's State of the World's children 2013

The GAPPD provides a roadmap for national governments and their partners to plan and implement integrated approaches for the prevention and control of pneumonia and diarrhoea. GAVI works within this broader context and supports the advancement of GAPPD. Starting in 2014, GAVI requires countries to describe in their PCV applications the status of implementation of other complementary

interventions for disease prevention and control, and how they could leverage the opportunity of new vaccine introduction to strengthen an integrated approach. This was not designed to raise the requirements for proposal approval, but rather, as an opportunity to prompt countries' consideration and planning on comprehensive disease prevention and control at the time of proposal development. Further efforts are underway, led by WHO and UNICEF, to pilot integration of services at the district level in selected countries.

3. AMC Independent Assessment Committee

The IAC serves a number of key functions. Most importantly, it has the mandate to review and approve the Target Product Profile (TPP) and thereby the minimum technical requirements that candidate products must meet to be eligible for AMC funding.[vi] In addition, the IAC establishes when and if an adjustment of the pre-set long-term price of vaccines is necessary. During the reporting period, the IAC has only been called upon to approve the AMC Annual Report.

The IAC currently comprises nine members representing expertise in: public health, health economics, vaccine business development, vaccine industry economics, contract law, public-private finance and clinical performance and delivery systems. A list of IAC members can be found in Annex 3.

[vi] Also see section 3.2 of the 2010 AMC Annual Report, http://www.gavialliance.org/funding/pneumococcal-amc/

4. Monitoring and Evaluation

In 2007 the United Kingdom's Department for International Development in conjunction with the Canadian International Development Agency commissioned a monitoring and evaluability assessment study on behalf of the AMC for Pneumococcal Vaccines Donor Committee. The study proposed a monitoring and evaluation framework including four key components:

- Annual monitoring to be implemented by the GAVI Secretariat;
- A Baseline Study to establish the context (industry and country situation) at the beginning of the intervention and to develop proposed counterfactuals (two counterfactuals were proposed to estimate what would happen if no AMC were to be implemented and to measure incremental impact of the AMC initiative on the vaccine market and pneumococcal disease and mortality);
- An independent Process and Design Evaluation to assess the AMC implementation process and the efficiency and effectiveness of the AMC design;
- Impact Evaluations every four years from the entry into the first AMC supply agreement to assess the achievements of the AMC and association (and to the extent possible, causality) between the AMC intervention and observed outcomes.

Annual monitoring is carried out by the AMC Secretariat and an Annual Report has been published on the AMC website each year from 2010. The Baseline Study was completed in 2010 and is available on the AMC website. The AMC Process and Design Evaluation was carried out in 2012. Upon recommendation of the GAVI Evaluation Advisory Committee and following consultations with AMC stakeholders in 2013, the first Impact Evaluation of the AMC will be commissioned in 2015 instead of in 2014 (see 4.2 below).

4.1. Programme Performance Reporting

In view of the recommendations made in the 2012 AMC Process and Design Evaluation, the Secretariat reviewed the existing set of indicators used for regular monitoring purposes. Some additional health metrics have now been added to ensure more thorough and comprehensive monitoring and tracking of progress in the AMC. Table 7 below highlights some of the key indicators being tracked, for which information can be made publicly available. The Secretariat will also implement the recommendation of the evaluators to regularly review and update performance indicators and will aim to set new targets as milestones are reached and more information becomes available.

Table 7. Selected non-confidential indicators for AMC progress tracking (based on calendar year view)

	2009	2010	2011	2012	2013	2014*
Objective 1: To accelerate the development of pneumococcal vaccines that meet developing country needs.						
Cumulative number of AMC eligible TPP vaccines	0	2	2	2	2	2
Cumulative number of AMC registered manufacturers who have made their registration public	0	4	4	4	5	5
Objective 2: To bring forward the availability of effective pneumococcal vaccines for developing countries.						
Annual number of doses of TPP vaccine procured under AMC by year (in millions)	0	7	36	58	58	-
Objective 3: To accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers.						
Cumulative number of countries that have applied for GAVI support for PCV	21	21	49	52	59	59

	2009	2010	2011	2012	2013	2014*
Cumulative number of AMC-eligible/GAVI-supported countries that have been approved	3	17	37	46	51	55
Cumulative number of AMC-eligible/GAVI-supported countries introducing TPP vaccines	0[vii]	1[viii]	16	24	38	40
Coverage of PCV in AMC-eligible/GAVI-supported countries***	0%	1%	4%	9%	n/a**	n/a
Cumulative number of children vaccinated with GAVI support (in millions)	-	0.5	4	10	n/a**	n/a

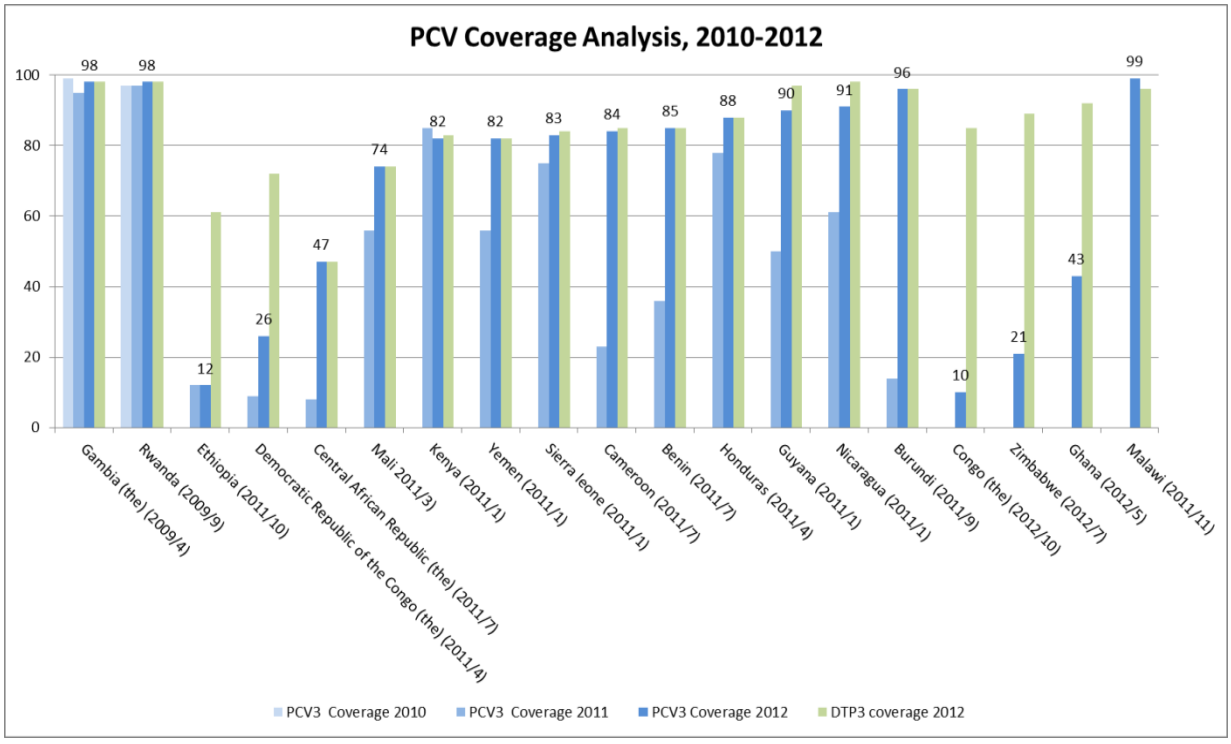
* Year-to-date through 31 March 2014

** WUENIC coverage data and WHO-reported number of immunised for 2013 will be available in late 2014

** Indicator defined as the percentage of population reached across GAVI73 countries

Pneumococcal vaccine coverage performance in countries is closely monitored. Figure 5 shows the PCV 3rd dose coverage versus DTP vaccine 3rd dose coverage, in countries that have introduced the pneumococcal vaccine (WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) data, published in July 2013[4]). The coverage data demonstrated that countries are able to successfully introduce PCV into their routine systems, with PCV 3rd dose coverage generally in line with DTP[ix] 3rd dose coverage by the second year of implementation.

Figure 5. PCV 3rd dose coverage performance[x]



[vii] Two countries introduced PCV in 2009, but with a vaccine that was not TPP compliant. They have since switched to a TPP vaccine in 2011.

[viii] Same as above.

[ix] DTP - Diphtheria, Pertussis, Tetanus vaccine; same vaccination schedule as PCV

[x] Note data issue in Ethiopia resulted in low figure reported. Phased introduction in DRC resulted in lower coverage.

4.2. AMC Impact Evaluation

The first AMC Impact Evaluation was originally planned for 2014. However, at its July 2013 meeting, the GAVI Alliance Evaluation Advisory Committee recommended that the evaluation be postponed from 2014 to 2015. This recommendation was made primarily due to recent PCV supply challenges which resulted in several delayed introductions. Following careful consideration of the overarching goal of the pilot AMC and the potential to demonstrate impact, the committee concluded that it was premature to conduct an impact evaluation of the AMC in 2014. The AMC stakeholders were consulted and agreed to the postponement of the impact evaluation until 2015.

It is hoped that as a result of the additional time, the impact evaluation will have more relevant evidence available on the outcomes and impact of pneumococcal vaccination and country experiences (e.g. more country years of PCV3 coverage estimates, more data from impact assessments, targeted studies, post-introduction evaluations and the full country evaluations). Work will begin on drafting the Request for Proposals (RFP) for this evaluation in late 2014. AMC stakeholders and partners will be widely consulted on the evaluation questions, design options and other methodological issues. The independent evaluation will be commissioned in 2015 and a bidder selected following a competitive selection process. A final report is expected in late 2015.

4.3. Full Country Evaluations

In 2013, the GAVI Alliance launched a new set of evaluations to collect real-time data on immunisation programmes, vaccine-related issues and the contribution of Alliance support in five countries. Bangladesh, India, Mozambique, Uganda and Zambia are taking part in the Full Country Evaluation project, which will run from 2013 to 2016. Local research institutions are partnering with the Institute of Health Metrics and Evaluation and PATH to collect information, data and evidence to help improve immunisation programmes.

The introductions of PCV in 2013 in Mozambique, Uganda and Zambia were evaluated as part of the full country evaluations and implementation of PCV will continue to be evaluated. The work in 2013 relied mainly on process evaluation methods (including document reviews, participant observation, key informant interviews and after-action reviews), and this will be complemented with data from other evaluation components including, but not limited to, health facility surveys, household surveys and administrative data in 2014 onwards. Initial evaluation findings reported in Q1 2014 indicate that Mozambique, Uganda and Zambia faced a number of common challenges with their introductions. These are being reviewed to inform development of corrective actions. The introduction and implementation of PCV in Bangladesh will also be evaluated through this project.

Results and findings from these evaluations will be made available on the GAVI website throughout the evaluation period[5].

4.4. Estimates of the impact of pneumococcal vaccination

In 2011, a multidisciplinary group with expertise in mathematical modelling was convened by the GAVI Alliance and the Bill & Melinda Gates Foundation to estimate the impact of vaccination in the 73 GAVI countries. A description of the methods and results from this first round of modelling was published in the journal *Vaccines* in April 2013[6]. In late 2013 a decision was made, in consultation with WHO and other technical partners, to shift the standard reference source for reporting on GAVI impact from an unpublished and unofficial WHO report to these peer-reviewed estimates. GAVI impact estimates are updated annually using similar methodology with the most recent round completed in early 2014. The latest update of these estimates will go beyond a narrow focus on future deaths averted to include a

broader range of benefits: cases and Disability Adjusted Life Years (DALYs) averted, and the economic benefits of vaccination (e.g. cost of illness averted). Based on current projections through year 2020 (SDF v.8), PCV use will avert an estimated 1.5 million future deaths among children vaccinated in GAVI countries. A peer-review publication with the latest impact modelling methods and estimates is anticipated in late 2014.

4.5. Special studies on pneumococcal vaccines

GAVI is currently funding a number of special studies to help facilitate evidence-based decision making in support of the introduction and continued implementation of pneumococcal vaccines in developing countries. Studies will assess the impact of PCV on health and economic outcomes and monitor potential changes in pneumococcal serotype epidemiology. The status of these studies and key findings are provided in Annex 4.

Assessments under the PneumoADIP and the initial VI-TAC grants, which included pneumococcal vaccine effectiveness and impact studies in Kenya and South Africa, economic impact evaluations of pneumococcal vaccines in Ghana and The Gambia, and an evaluation of different PCV dosing schedules, concluded in 2013. The assessment of PCV impact on disease in the Gambia, funded initially by the PneumoADIP and subsequently by other partners is ongoing. Preliminary findings from these studies indicate substantial effectiveness of PCV against vaccine serotype and all serotype invasive pneumococcal disease (IPD) among children in Kenya, South Africa and Gambia, as well as impact on nasopharyngeal colonisation across both vaccine targeted and broader age groups. Likewise preliminary analyses data from South Africa and Gambia show impact on presumed bacterial pneumonia and all-cause pneumonia hospitalisations. Health economic analyses from the Gambia have demonstrated that PCV is likely to be both cost-effective and cost-saving, reducing the substantial economic burden borne by families of children with disease. Evidence also shows that a variety of flexible PCV dosing schedules effectively reduce pneumococcal disease, consistent with results from the randomised controlled trials of these vaccines. PCV effectiveness studies in Kenya and South Africa will be continued through December 2015 under the current VI-TAC grant. Several peer-review publications have already been published (dosing landscape, Gambia economic); publications in disease impact and vaccine effectiveness are anticipated in 2014.

The technical evidence landscape on PCV is evolving quickly with the above-mentioned studies supported by GAVI contributing substantially to that evidence base from low-income countries. Many of these findings were presented at the 9th International Symposium on Pneumococci and Pneumococcal diseases (ISPPD-9) held in India, March 2014 (http://www2.kenes.com/isppd2014/Pages/Home.aspx). This meeting, with over 970 participants from 74 countries marked an important milestone in the pneumococcal vaccine community as impact studies from around the world involving second generation PCVs (PCV10 and PCV13) were a central topic of discussion. In addition to specific evidence of vaccine effectiveness and impact from the above-mentioned GAVI supported studies in early adopting African countries, the general themes of evolving evidence from around the world are that PCV have a substantial impact on pneumococcal disease burden and on pneumonia across a wide range of epidemiologic settings, that the disease reduction effects extend to age groups that are not targeted for vaccination and that the pneumococcal strains circulating in the community continue to evolve in response to vaccine induced pressure, but that the remaining strains remain substantially less likely to cause to disease than the strains targeted by the vaccine. Clinical development progress was also reported on novel pneumococcal vaccines that are not based on serotypes of pneumococcus.

In June 2013, GAVI issued a Request for Proposal (RFP) for the 'Evaluation of Pneumococcal Conjugate Vaccine (PCV) Effectiveness in Asia' to assess the impact of PCV in early adopting GAVI countries in Asia. Following a peer-review process and recommendations from an Adjudication Committee composed of experts in the field, GAVI has commissioned 3 Service Providers (Aga Khan

University, Murdoch Childrens' Research Institute, and Oxford University) to conduct PCV impact studies in Pakistan, Nepal, and Lao PDR. These studies will assess a range of outcomes, including disease effects (e.g. invasive pneumococcal disease and hospitalised pneumonia), effects on disease transmission (nasopharyngeal carriage), economic benefits and long-term sequelae. A fourth study, to assess the impact of phased PCV introduction on the incidence of radiological pneumonia in Mongolia is under consideration pending the receipt of vaccine doses for these purposes. Data collection for these studies began in late 2013 and early 2014, with results anticipated in 2016-2017.

GAVI recently contracted the US Centers for Disease Control and Prevention (CDC) and Agence de Médecine Préventive (AMP) to assist Burkina Faso in assessing the impact of PCV introduction on pneumococcal meningitis and changes in serotype distribution. Pneumococcal vaccine effectiveness studies will also be conducted in Bangladesh and Mozambique as a component of the Full Country Evaluations (FCE) work, including assessment of changes in community carriage of vaccine-type pneumococci and impact of PCV on invasive pneumococcal disease and x-ray confirmed pneumonia using a case-control methodology within an established Demographic Surveillance Site in Mozambique. These assessments of pneumococcal vaccines in selected epidemiologic settings will help to further assess the impact of vaccination on the burden of disease and serotype epidemiology. The findings of these studies will be key inputs to the planned AMC Impact Evaluation.

5. Media and Communications

GAVI aims to increase visibility of the AMC through traditional, online and social media. This multi-platform approach continues as pneumococcal vaccines are being rolled out in countries.

5.1 Communications overview 2013-14

GAVI continues to highlight and explain the AMC in relevant communications materials, particularly around pneumococcal vaccine launches. In addition to sharing the updated AMC factsheet with interested journalists and partners, GAVI has also ensured that appropriate speaking points are incorporated into the speeches of Alliance spokespeople at launch ceremonies and other events.

In July 2013, GAVI and UNICEF published the outcomes of the third tender on their respective websites. In addition, GAVI worked closely with vaccine industry partners to amplify messaging around the new pneumococcal vaccine supply agreements. This resulted in widespread, informed media coverage, particularly amongst industry-focused publications. This provided an opportunity to brief more journalists about the AMC.

On World Pneumonia Day 2013, GAVI, UNICEF, and WHO jointly published a press release highlighting essential interventions that will help reduce burden of pneumonia[7]. The theme of World Pneumonia Day 2013 was “Innovate to End Child Pneumonia”. To mark this milestone, Mauritania and Papua New Guinea introduced the pneumococcal vaccine in November last year. Other pneumococcal vaccine launches for which a press release or featured story was written included that of Angola (June 2013), Zambia (July 2013), Sudan (August 2013), Lao People’s Democratic Republic (October 2013), Senegal (November 2013), and Liberia (January 2014).

5.2 Communications outlook for 2014-2015

Looking forward, GAVI will continue to integrate AMC messaging into all relevant materials and seek to profile the AMC mechanism during pneumococcal vaccine launches.

GAVI will again look to brief journalists who are demonstrating an interest in the AMC, the GAVI Alliance model, and in innovative finance mechanisms more generally, to ensure fair and accurate representations of the AMC.

5.3 Donor & stakeholder communication

In 2013, additional efforts were made to provide updates to AMC stakeholders, through regular AMC stakeholder calls and an annual AMC stakeholder meeting. These provide opportunities to exchange information and input on key issues. These included updates on the publication of the process and design evaluation, 2013 pneumococcal vaccine tender, revised disease burden and impact estimates progress on implementation, the progress on AMC targets and supply and rollout of vaccines. With regards to vaccine introductions, AMC donors were kept informed of progress and invited to participate in the vaccine launch events.

6. Financial Activities

The financial structure of the AMC remains unchanged from the previous year. It is composed of the six AMC donors (the Bill & Melinda Gates Foundation, Canada, Italy, Norway, Russia and the United Kingdom), the World Bank, GAVI, UNICEF, GAVI-supported countries and eligible vaccine manufacturers.[xi]

In summary the process works as follows: the AMC donors, who have entered into grant agreements totalling US $1.5 billion with the World Bank, make annual payments to the World Bank. In turn, the World Bank holds the funds in trust for GAVI on behalf of the donors and confirms quarterly to GAVI the amounts being held for the AMC. To access these funds, GAVI submits a Quarterly Funding Request to the World Bank for vaccine purchase payments in the upcoming quarter. The request is based on the most recent demand forecast and on the quarterly Cash Management Plan submitted by UNICEF to GAVI.

Prior to procuring vaccines from AMC-eligible vaccine manufacturers, UNICEF sends a cash disbursement request for the necessary AMC and GAVI funds, upon receipt of which GAVI transfers the requested funds into a GAVI-held procurement bank account. These funds can only be withdrawn from the account by UNICEF. GAVI-supported countries are obliged to co-finance the pneumococcal vaccine, in accordance with GAVI's standard co-financing policy. Countries make their co-finance payments directly to UNICEF.

6.1. Donor Funds – inflow to the World Bank

The six donors are categorised into two groups. The first group, known as "fixed-schedule donors" (the Bill and Melinda Gates Foundation, Italy and the Russian Federation) make annual payments to the World Bank in accordance with predetermined payment schedules set out in the individual grant agreements. The second group of donors, known as "on-demand donors" (Canada, Norway and the United Kingdom), make payments in response to requests from the World Bank based on forecasts received from GAVI to meet specific funding needs.[a]

The three fixed-schedule donors have together pledged a total of US $765 million to the pneumococcal AMC. The three on-demand donors have pledged US $735 million (see Table 8). These pledges combined bring the total available AMC funds to US $1,500 million, funds that are dedicated solely to the procurement of the pneumococcal vaccine.

6.1.1. Donor contribution receipts

As of 31 March 2014, the World Bank had received a total of US $805 million from AMC donors (see Table 8 below). The Bill & Melinda Gates Foundation and the Norwegian Ministry of Foreign Affairs have paid the total amounts that they had committed to pay under their respective grant agreements.

[xi] Refer to AMC Annual Report 12 June 2009-31 March 2010 page 28-29 for the detailed description of the financial structure.

Table 8. Grant receipts from AMC donors, as of 31 March 2014 (in US $millions)

(in US$ millions)	Grant Amount	Cumulative Receipts	Remaining Balance
Fixed Schedule Donors			
Italy	635	317	318
Russia	80	40	40
Bill & Melinda Gates Foundation	50	50	-
On Demand Donors			
Norway	50	50	-
Canada	200	190	10
UK	485	159	326
Total	**1,500**	**805**	**695**

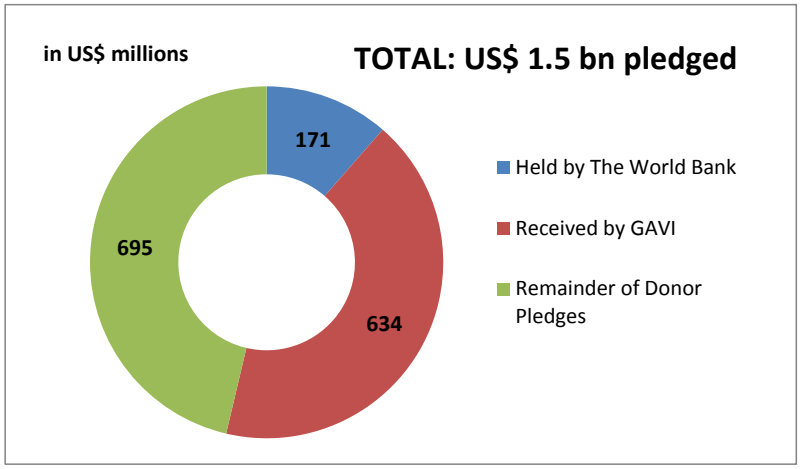
Source: The World Bank

The World Bank has recorded the AMC donor funds in its financial statements as designated assets, with a corresponding liability to provide the funds to GAVI for the purchase of pneumococcal vaccines subject to the terms and conditions of the AMC. To enhance the predictability of AMC funding, the World Bank committed to transfer funds to meet the AMC-funded portion of the vaccine price, upon request from GAVI in accordance with the AMC terms and conditions and with the schedule of donor payments, whether or not donors actually pay on schedule or default. The World Bank also provides financial management and administrative services with respect to donor contributions and AMC disbursements.

6.2. AMC donor funds: inflow to GAVI

As of 31 March 2014, the World Bank had disbursed US $634 million (US $540 million to GAVI and US $94 million directly to the UNICEF procurement account relating to the Firm Order Commitments). Of the US $634 million, US $149 million was disbursed from 1 April 2013 – 31 March 2014 (US $113 million to GAVI and US $36 million directly to the UNICEF procurement account relating to the Firm Order Commitments). This leaves a balance of US $171 million held by the World Bank, of which US $93 million is available for immediate disbursement to GAVI (see figures 6 and 9).

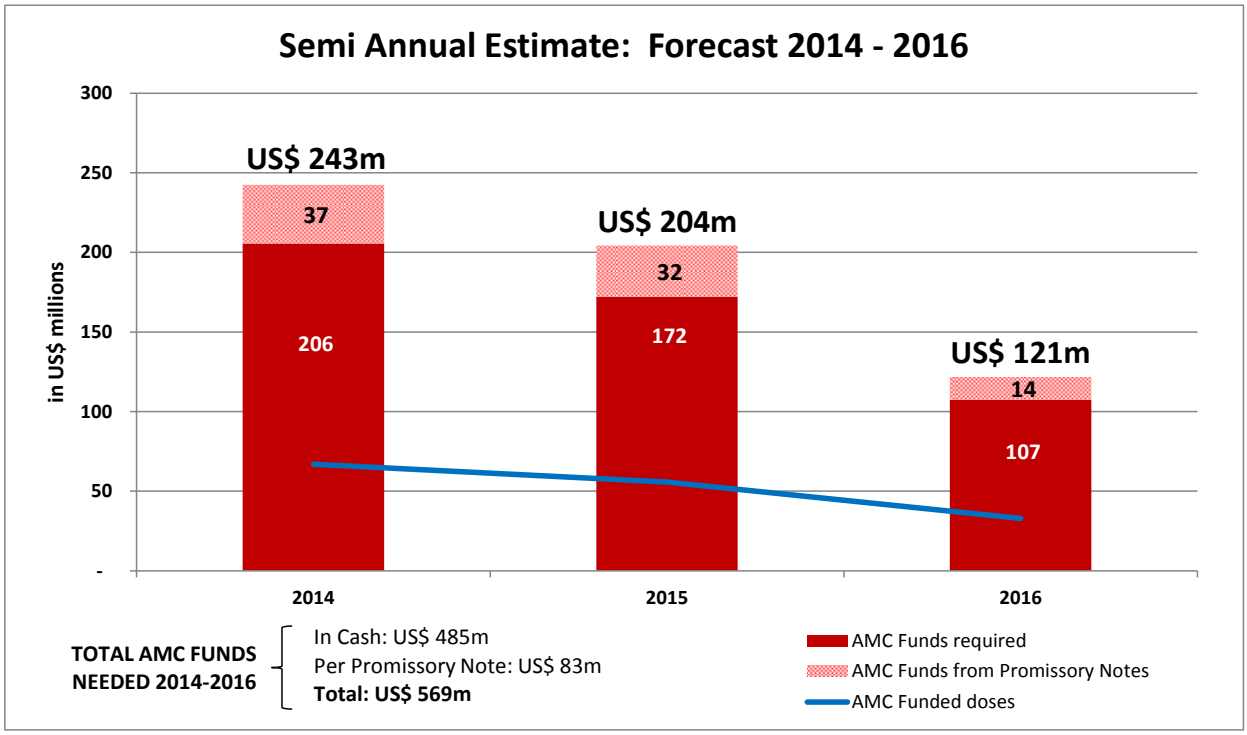
Figure 6. Status of AMC donor funds, as of 31 March 2014 (in US $ millions)



Source: GAVI Alliance Secretariat

As part of the reporting process, GAVI regularly submits a Semi-Annual Estimate (SAE) to the World Bank which provides forecasted demand for pneumococcal vaccine doses and corresponding AMC funding on a rolling three-year basis. GAVI submitted one SAE during the reporting period (in October 2013) which forecasted a need for US $569 million of AMC funds, including US $83 million from Promissory Notes, to procure 156 million doses of the pneumococcal vaccine between 1 January 2014 and 31 December 2016.

Figure 7. Latest Forecast of AMC Funds Needed, as of 31 March 2014



Source: GAVI Alliance Secretariat (note: some numbers may appear not to add due to rounding)

6.3. UNICEF procurement: outflow of AMC donor funds

From 1 April 2013 to 31 March 2014, US $624 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US $259 million was from the AMC funds to pay for the AMC top-up portion of the vaccine purchase. The remaining US $365 million was allocated from general GAVI funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[xii]. Total funds include the transfers relating to the AMC-funded portion of the minimum purchase obligation, also known as the Firm Order Commitment (FOC), on the GSK & Pfizer supply agreements amounting to US $36 million (see Figures 8 and 9).

As noted in Section 1.2, two new supply agreements were signed during the reporting period, bringing the total number of supply agreements under the AMC program to six.[xiii] To date, the AMC funding allocated under the first Pfizer agreement signed in 2010 has been fully disbursed and the remaining doses under this agreement are now being procured at the tail price. It is anticipated that the remainder

[xii] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US $0.19 per dose), in addition to the cost of the vaccine itself. These costs typically include the cost of syringes, safety boxes and freight.*
[xiii] *For details refer to Section 1.2 and Annex 1*

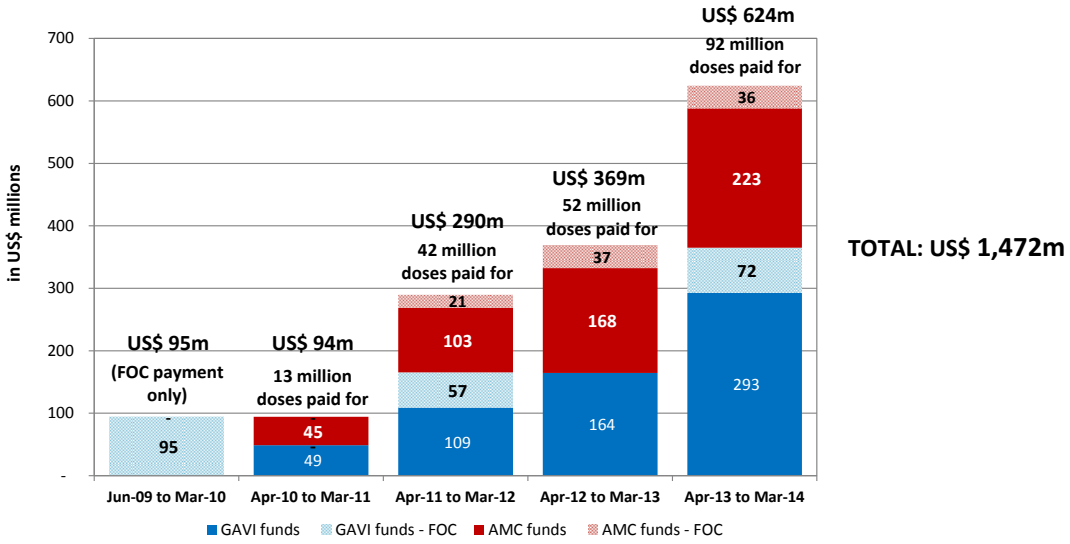
of AMC funding allocated to the first GSK supply agreement signed in 2010 will be disbursed during 2014. The remaining four supply agreements will continue to receive AMC top-up during 2014.

In total, as at 31 March 2014 US $318 million has been transferred to GAVI's 'UNICEF procurement account' regarding the FOCs for the six existing signed supply agreements and related Promissory Notes. Of this amount, US $223 million represents the GAVI-funded portion of the FOCs and US $94 million represents the AMC-funded portion of the FOCs. Of the US $318 million transferred, US $191 million (approximately 60%) has been utilised and this represents the draw-down of already transferred FOC funds relating to the first four supply agreements.

Figure 8. Total cash disbursements to GAVI's 'UNICEF procurement account', (inception to 31 March 2014)

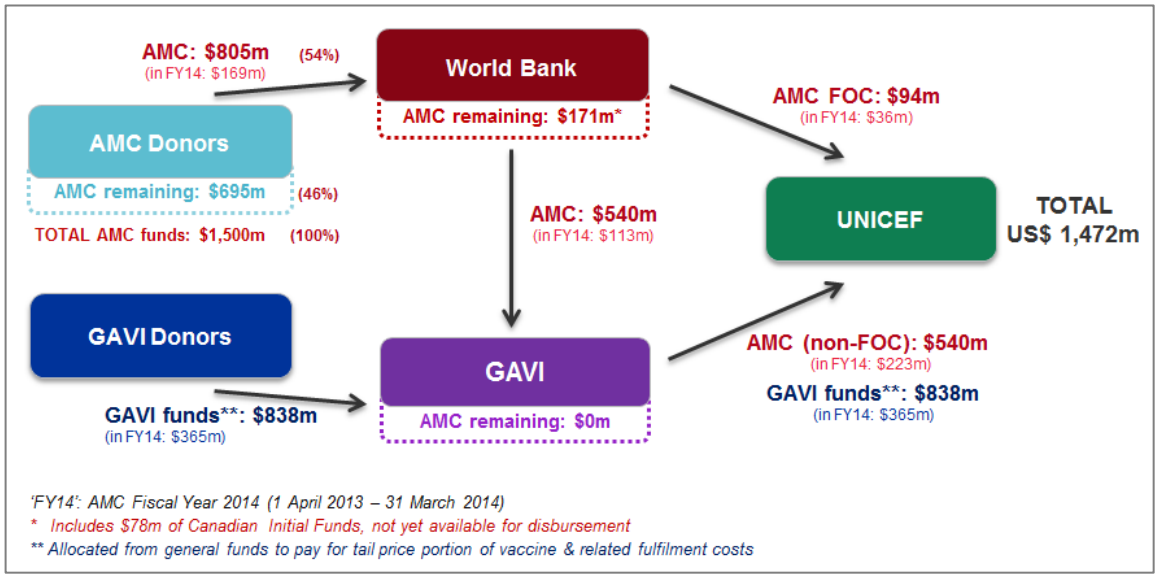
in US$ millions

Funding Source	Jun-09 to Mar-10	Apr-10 to Mar-11	Apr-11 to Mar-12	Apr-12 to Mar-13	Apr-13 to Mar-14	TOTAL	of which: AMC / GAVI	of which: FOC	of which: Non-FOC
AMC Funds - FOC	-	-	21	37	36	94	634	94	
AMC Funds	-	45	103	168	223	540			540
GAVI Funds - FOC	95	-	57	-	72	223	838	223	
GAVI Funds	-	49	109	164	293	615			615
TOTAL:	95	94	290	369	624	1,472		318	1,154



Source: GAVI Alliance Secretariat (note: some numbers may appear not to add due to rounding)

Figure 9. Overview of AMC Financial Process Flow and funds disbursed, (inception to 31 March 2014)



Source: GAVI Alliance Secretariat

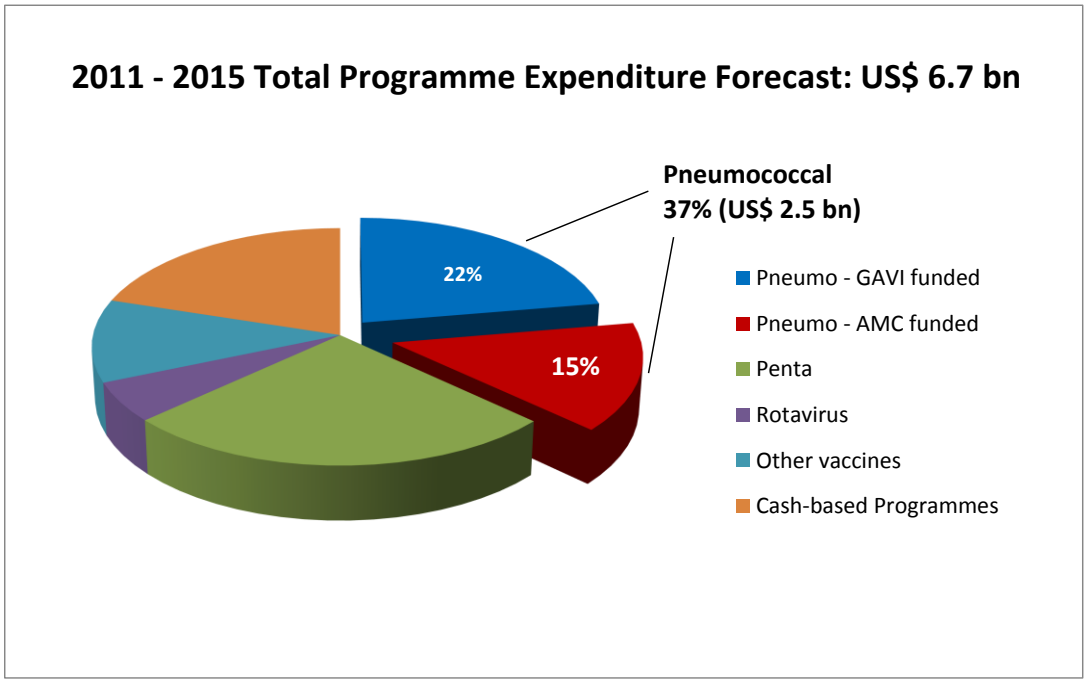
6.4. The AMC and GAVI's Long Term Financial Forecast

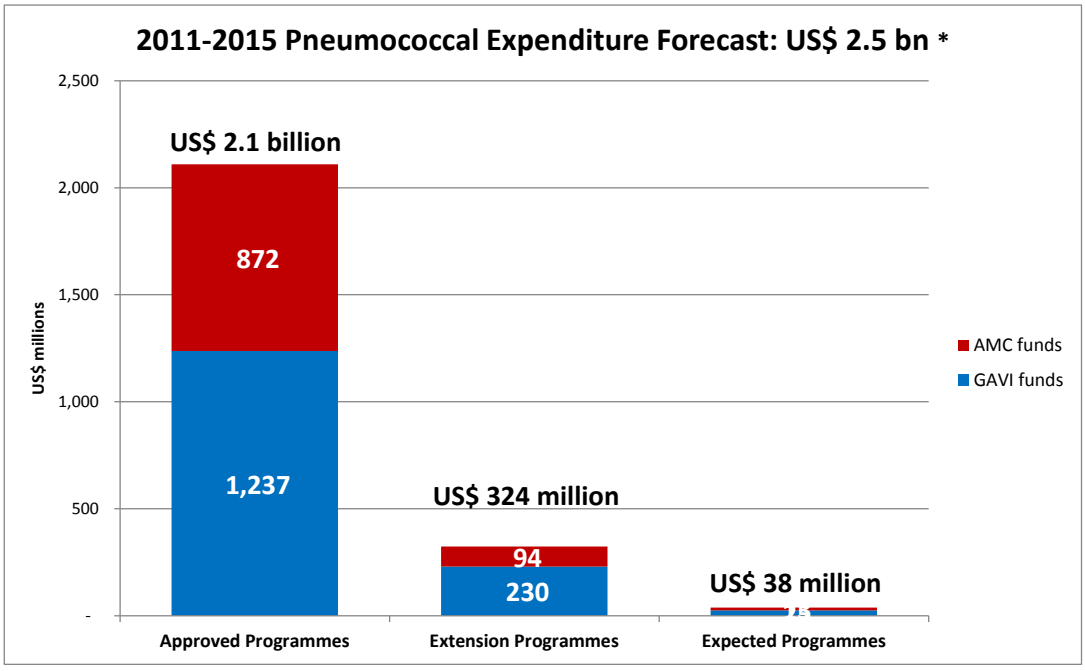
At the November 2013 Board meeting, an update was presented of GAVI's Long Term Financial Forecast.[xiv] For the period of 2011-2015, total programme expenditures are projected to be US $6.7 billion. Of this US $6.7 billion, pneumococcal vaccine expenditures are anticipated to amount to US $2.5 billion, representing 37% of total programmatic expenditures (see Figure 10).

For the 2014 and 2015 programmatic year, 51 countries had been approved to receive financial support for the procurement of pneumococcal vaccine. The 2014 commitments amount to US $572 million and 2015 commitments amount to US $596 million. The commitments are included as part of the total 2011-2015 "Approved Programmes" amounts presented in Figure 10 below.

[xiv] November 2013 Board Paper entitled "Board-2013-Mtg-3-Doc 06 Financial Forecast and Programme Funding approvals "

Figure 10. AMC Within Total GAVI Forecasted Expenditure 2011-2015





* Approved Programmes are those approved by the GAVI Board. Extension Programmes are forecasted continuations of those programmes, subject to future Board approval. Expected Programmes are defined as those which have received conditional IRC approval or are forecasted based on Adjusted Demand Forecast v8.0 and the latest supplier assumptions

Source: GAVI Alliance Secretariat

7. Challenges and Future Priorities

Country demand for the pneumococcal vaccines has been high, with 55 (75%) of the 73 GAVI-supported countries already approved for introduction. With 40 countries having introduced PCV since programme start in 2009, the priorities moving forward will be focused on supporting future introductions, sustaining PCV implementation and improving coverage, and measuring impact. Ensuring proper balance of supply and demand also remains a key priority.

7.1 Supporting country implementation and measuring impact

With all approved countries now allocated supplies and future introduction dates made more predictable, efforts are focused to ensure that countries are ready to introduce pneumococcal vaccines and that technical assistance is provided where appropriate to ensure high quality and continued acceleration of implementation. Alliance partners are reviewing country introduction status and coordinating technical assistance activities, with the aim of identifying and resolving issues with the support of the partners working at the country level.

Vaccine programme implementation in countries that have already introduced PCV will be closely monitored to identify issues in coverage performance. Lessons drawn from these countries can inform future pneumococcal vaccine, but also other vaccine introductions. Broader efforts are on-going at GAVI to support health systems strengthening, with an increasing focus on supply chain management, to improve coverage performance of routine immunisation programmes and ensuring programmatic and financial sustainability in countries.

Focus on gathering evidence on vaccine effectiveness and impact will continue, through GAVI-supported special studies. The AMC Impact Evaluation will be initiated in the next reporting cycle, to assess the achievements of the AMC.

7.2 Managing supply and demand

Thanks to the AMC, manufacturers have entered into 10+ year supply agreements, which is unique for a GAVI-supported vaccine. This provides assurance that manufacturers would invest in scaling up production capacity and that supply would be available to meet long-term demand from countries. With the third supply agreements increasing contracted supply for both PCV13 and PCV10 and rectified production problem with PCV10, the supply constraint situation will ease from 2015 onwards. While the scaling up of supply has so far been managed with limited interruptions by suppliers and flexibility to supply quantities across years, the coming years will require scaling up of 30-44% in production capacity in order to meet contracted quantities. The coming years will demonstrate the ability of the limited supplier base to continue to meet the requirements. As the demand increases to around 140 million doses annually, the limited supply base remains a risk to implementation. GAVI Secretariat will continue to work closely with UNICEF SD to monitor the supply situation and manage the supply and demand balance.

8. Conclusion

Several major milestones were achieved during the 2013-2014 reporting period. An unprecedented 16 AMC-eligible countries introduced pneumococcal vaccines in this reporting period, making the number of introductions to date 40 in total. Two new supply agreements were reached, marking the first decrease to the AMC tail price. The reduction in the tail price will likely contribute to a total savings of US $157 million over the lifetime of the agreements. The pneumococcal vaccines procured through the AMC are expected to have a significant reach and impact. Based on current projections through year 2020, PCV use will avert an estimated 1.5 million future deaths among children vaccinated in GAVI countries by 2020.

As the level of immunisation activities increases in countries, technical assistance needs to be deployed effectively and efficiently to support countries to introduce and sustain implementation of pneumococcal vaccines. GAVI-supported special studies will be advanced to continue to demonstrate the impact of pneumococcal vaccines. The supply constraint situation starts to ease with the addition of contracted doses but the limited supply base remains a concern; therefore, the balance of supply and demand needs to be carefully managed.

Annex 1 – Summary of Previous Call for Offers

First AMC Supply Agreements

The first procurement cycle for the supply of pneumococcal vaccines under the AMC was initiated with the issuance of a Call for Supply Offers on 4 September 2009. UNICEF SD received four offers in response to this first call. In March 2010, UNICEF SD entered into Provisional Supply Agreements (PSA) with two manufacturers – GlaxoSmithKline Biologicals (GSK) and Pfizer Inc. – the only companies whose Product Summary File (PSF) had been accepted by WHO for prequalification review. Each manufacturer committed to supply 30 million doses annually, with GSK starting in January 2012 and Pfizer Inc. in January 2013, and continuing for 10 years. Consequently, 15% of AMC funds were allocated to each manufacturer under this procurement round.

In addition to the above-mentioned PSAs, GSK and Pfizer agreed to provide in total 7.2 million, 24.2 million and 20 million doses in 2010, 2011 and 2012, as part of the AMC Capacity Development Period.[xv] Both suppliers have subsequently communicated the ability to increase such early supplies, should there be demand and based on demand, quantities on contracts have been increased by 7.8 million doses in 2011 and 4 million doses in 2012. The total quantities on these contracts with each supplier remain 300 million doses each, only the distribution over the years has changed.

Both GSK and Pfizer's products received WHO prequalification in 2010 and were deemed AMC Eligible by the AMC Independent Assessment Committee (IAC) respectively on 16 April 2010 and 23 August 2010. This was communicated to suppliers with a copy to UNICEF on 6 May 2010 and on 23 August 2010. As a result the PSAs automatically turned into effective Supply Agreements, allowing the procurement of those two vaccines.

Second AMC Supply Agreements

Following the publication of SDF v3.0 in March 2011, GAVI, in consultation with UNICEF, decided to issue a new Call for Supply Offers for the procurement of pneumococcal vaccines that was published on 8 April 2011 with a maximum target of 74 million doses by 2016. UNICEF SD received four offers by 6 May 2011.

In the week starting 12 December 2011, UNICEF as procurement agency on behalf of GAVI confirmed the entry into new supply agreements with GSK and Pfizer Inc. Per the timeline set out in the AMC legal agreements, the supply agreements should have been finalised by 9 September 2011. However, UNICEF SD and GAVI agreed to delay the procurement timeline in order to be able to take into account any new demand recommended for approval by the IRC following the May 2011 round in the award recommendations.

Both GSK and Pfizer Inc. will start supplying 18 million doses annually (Annual Supply Commitment) from 2014 for a period of 10 years, up to a maximum of 180 million doses. The tail price for this agreement is US $3.50. Consequently 9% of the AMC funds are allocated to each of the two manufacturers under this agreement according to the AMC terms and conditions. The total doses awarded to GSK and Pfizer Inc. under both supply agreements amounts to 48 million annually.

[xv] The capacity development period is defined as the period during which suppliers develop dedicated manufacturing capacity to serve GAVI-eligible countries under their respective Supply Agreements.

As part of the supply agreements, manufacturers have agreed to provide in total 30 million doses in 2012 and 2013 as part of the AMC Capacity Development Period.

UNICEF opted not to award the full quantities of the GAVI Strategic Demand Forecast for 2016 in response to this second tender. In order to incentivise manufacturers to accelerate the development of new vaccines, to contribute to the creation of a healthy market with multiple suppliers, and to enhance the possibility to access lower tail prices through future offers, quantities have been reserved for award at a later point in time. It should be noted, however, that 100% of the quantities offered for supply in 2012-2013 in response to tenders have been contracted. Furthermore, UNICEF considered that the unexpected ramp up of demand led to a faster than expected commitment of the AMC funding and that it would be prudent to pause to allow for a discussion with AMC stakeholders before proceeding to commit more than 50% of AMC funding at this early stage.

Fifty-two percent of the AMC funds corresponding to US $780 million remain unallocated following the completion of the second Call for Offers and will be available for successive rounds of calls for offers.

Third AMC Supply Agreements

Following the publication of the third Call for Supply Offers on 27 August 2012, GAVI announced two new supply agreements for the supply of pneumococcal conjugate vaccines under the Advance Market Commitment (AMC). These new supply agreements include the first decrease to the AMC Tail Price as well as additional short term supply to support the accelerated introduction in a number of countries.

On 24 July 2013, UNICEF, in its capacity as GAVI's procurement agency, confirmed its entry into new supply agreements with GlaxoSmithKline Biologicals (GSK) and Pfizer Inc.

GSK will start supplying 24 million doses annually (Annual Supply Commitment) from 2015 for a period of 10 years. Consequently 12% of the AMC funds are allocated to this manufacturer under this agreement according to the AMC terms and conditions. The tail price for this agreement is US $3.40. The total doses awarded to GSK under its three supply agreements amounts to 720 million.

Pfizer will start supplying 26 million doses annually (Annual Supply Commitment) from 2016 for a period of 10 years. Consequently 13% of the AMC funds are allocated to this manufacturer under this agreement according to the AMC terms and conditions. The Tail Price for this agreement is US $3.40 in 2013 and US $3.30 from 2014 onwards. The total doses awarded to Pfizer under its three supply agreements amounts to 740 million.

In addition, Pfizer has agreed that the reduced Tail Prices outlined above can be applied to all doses remaining to be procured under its first and second supply agreements. To access Pfizer's reduced Tail Price, GAVI has provided a financial guarantee for the Tail Price component, equivalent to 80% of the total contracted quantities in the period between 2013 and 2015. The standard AMC commitments of 20%, 15% and 10% in the first three years of each supply agreement will be counted towards the financial guarantee. It has also been agreed to accelerate the procurement of doses at US $7.00 under the new supply agreement to ensure that all doses at that price will have been procured before 2016.

As part of these supply agreements, GSK and Pfizer Inc. have agreed to provide a total of 42 million doses during the AMC capacity development period.

UNICEF has opted not to award the full quantities of the GAVI Strategic Demand Forecast for 2017 in response to this third tender and has only awarded quantities to meet the approved demand. Quantities have been reserved for award at a later point in time in order to incentivise manufacturers to accelerate the development of new vaccines, to contribute to the creation of a healthy market with multiple suppliers, and to enhance the possibility of accessing lower tail prices through future offers.

27% of the AMC funds corresponding to US $405 million remain unallocated and will be available for later calls for offers.

Annex 2 - Membership of the PROWG

The Pneumo Rota Operational Working Group (PROWG) is a sub-team of the Vaccine Implementation Management Team. Members are as follows:

Organisation	Members
GAVI Secretariat	**Carol Szeto** Senior Programme Manager, Vaccine Implementation, Country Programmes **Emily Wootton** (until November 2013) Programme Manager, Vaccine Implementation, Country Programmes
PATH	**Candace Rosen** Senior Policy and Advocacy Officer (representing VI TAC)[xvi]
UNICEF Programme Division	**Osman Mansour** (until October 2013) Senior Health Adviser, Health Section **Ben Hickler** Communication for Development (C4D) Specialist, Routine Immunization and New Vaccines, Health Section **Benjamin Schreiber** Senior Immunization Specialist, Health Section (alternate member)
UNICEF Supply Division	**Ann Ottosen** (until January 2014) Senior Contracts Manager **Jesus Barral-Guerin** Senior Contracts Manager **Gideon Chelule** Contracts Manager (alternate member) **Sonia Freitas** Contracts Specialist (alternate member)
WHO	**Hemanthi Dassanayake-Nicolas** Technical Officer – Strategic Information Group EPI **Carsten Mantel** Leader – Priority Area New Vaccines and Innovation

Source: GAVI Secretariat, as of 31 March 2014

[xvi] A technical assistance consortium of PATH, Johns Hopkins University (JHU), US Centers for Disease Control and Prevention (CDC) and others. - See more at: http://www.gavialliance.org/about/gavis-business-model/avi/#sthash.jUgDPQpx.dpuf

Annex 3 – Membership of the Independent Assessment Committee

George Amofah
Part-time Lecturer, School of Public Health, University of Ghana, Legon; Retired Deputy Director General, Ghana Health Service

Claire Broome (Chairperson)
Adjunct Professor Division of Global Health Rollins, School of Public Health Emory University Atlanta, Georgia, USA

Arthur Elliott
Senior Program Manager, Vaccines and Anti Viral Agents, US Department of Health and Human Services, USA

Bernard Fanget
CEO, Bernard Fanget Consulting; and VP R&D and Pharmaceutical Development, Neovacs, France

Shahnaaz Kassam Sharif
Chief Medical Specialist, Senior Deputy Director Medical Services, Head of Preventive and Promotive Health Services, Ministry of Health, Kenya

Mary Kitambi
Public Health Specialist, Ministry of Health and Social Welfare Tanzania

Soonman Kwon (Vice Chairperson)
Director, Brain Korea Centre for Aging and Health Policy, South Korea

Tracy Lieu[xvii]
Director, Division of Research, Kaiser Permanente Northern California

Halvor Sommerfelt
Professor of Epidemiology, Center for International Health, University of Bergen, and Senior Consultant, Norwegian Institute of Public Health, Norway

Vitaly Zverev
Director, I.I. Mechnikov Institute of Vaccine Sera under the RAMS, Russia

Source: GAVI Secretariat, as of 31 March 2014

[xvii] Membership term ended in 2013

Annex 4 – Summary of GAVI investments in PCV impact assessments

GAVI invests annually approximately US $15-22 million in surveillance and targeted assessments across the vaccine portfolio to inform evidence-based decision making, document programme outcomes and impact and generate learning to inform programme improvements from a subset of settings predominantly through primary data collection. The table below summarises recent GAVI commissioned investments in surveillance and targeted assessments for PCV.

Study	Status of Activities	Key findings
A. WHO Surveillance		
Coordinated global surveillance networks for Invasive Bacterial Vaccine Preventable Diseases (IB-VPD)	Ongoing	The RV and IB-VPD surveillance networks represent the largest GAVI surveillance investment. In 2013, the WHO initiated a number of activities to strengthen the quality and use of the data generated through the global RV and IB-VPD surveillance networks with guidance from an informal technical advisory group (ITAG). The ITAG assisted WHO in a Strategic Review of the RV and IB-VPD surveillance networks in September 2013 to critically assess the networks and provide recommendations for the future vision for the networks, with a focus on improved data quality, enhanced country ownership and transition of the network to support country monitoring of the impact of new vaccine introductions (Hib, PCV, Meningococcal A, RV).
B. VI-TAC Special Studies		
1. Grant A-4: January 2009 - September 2013		
Landscape analysis of PCV dosing	Nine-paper supplement published in the January 2014 issue of *Pediatric Infectious Diseases Journal*. Presentations given at ISPPD 2012.	The available literature shows that each of three schedules (3+1, 3+0 and 2+1) all showed significant reductions in pneumococcal disease (IPD and/or pneumonia), and many programs also used catch-up campaigns. Choice of schedule should balance practical considerations and epidemiology, but achieving high coverage should be a primary goal to ensure herd protection. Varying study designs and epidemiologic settings made direct comparison of impact between schedules difficult.
Effectiveness of PCV7 against IPD (South Africa)	Preliminary findings reveal that even in a routine use setting and with high pneumococcal transmission and a novel vaccine schedule PCV is highly effective for HIV-uninfected children but insufficiently so for HIV-infected children. Publication in *Vaccine* discussed effects of study on	An alternative dosing schedule (2+1) was found to be highly effective and provides another option for countries to use. There may be potential for a fourth primary dose given at 10 weeks of age for HIV-infected children.

Study	Status of Activities	Key findings
	changes to PCV dosing schedule made by South African NAGI. Presentations given at ISPPD 2012 and 2014. Manuscript submitted to *PIDJ* in Q2 2014 on risk factors for IPD among children in South Africa. Manuscript under review at *CID* on effectiveness of PCV in this case-control study.	
Effectiveness of PCV against presumed bacterial pneumonia (PBP) (South Africa)	Measuring effectiveness in HIV-infected and HIV-uninfected children. Publication in *Vaccine* 2012 highlighting study contribution to S. African policy-making. Implications: This study can inform the evidence gap on the impact of PCV on x-ray confirmed childhood pneumonia in developing-country settings. Interim results were presented at ISPPD 2012. Enrolment extended due to low numbers of HIV+ patients. Poster displayed at ISPPD 2014. Manuscript in development and submission to *Lancet Infectious Disease* planned for Q2 2014.	Complete results expected Q2 2014. Preliminary results indicate PCV effectiveness against PBP which was statistically significant and was similar in magnitude to vaccine efficacy measured by randomised controlled trials using difference vaccination schedules.
Pneumococcal time series (South Africa)	Data collection is complete. Implications: The impact of simultaneous introduction of PCV and rotavirus vaccine can inform other countries with high burden of pneumonia and diarrhea, and are looking to adhere to the recent GAPPD recommendations. Manuscript under development for both PCV (planned for submission in Q3 2014) and RV (first draft planned for completion by end of Q2 2014) study arms. Additional analyses being conducted to stratify results by HIV infection status.	Preliminary results show a significant decrease in all-cause hospitalisations during a period post-vaccine (PCV and rotavirus) introduction compared to a period pre-vaccine introduction; this was most marked in children under the age of 2 years. Additionally significant declines in all-cause pneumonia hospitalisations and all-cause diarrheal hospitalisations were found. The study sample size did not provide enough statistical power to complete an analysis of in-hospital mortality as an outcome.
PCV/Hib conjugate vaccine impact manual	The PCV/Hib impact manual has been completed and published on the WHO website for download. A presentation on the manual was made at NUVI meeting in May 2012.	The manual organises information on designing and conducting impact studies in one place for vaccine decision-makers and implementers in countries considering adoption or having recently adopted either Hib of PCVs. The manual includes guidance

Study	Status of Activities	Key findings
		for study design and tools to assist with study protocols.
Economic impact of PCV (The Gambia)	Assessment of the economic impact of The Gambia's introduction of PCV was completed and one manuscript has been published in the April 2014 issue of *Vaccine*. Gambian pneumococcal economic impact study was delayed because of low case enrollment and is still in process; a manuscript is expected to be completed in Q2 2014. Poster displayed at ISPPD 2014.	Economic impact of PCV introduction in The Gambia: The total incremental cost for transition to pentavalent and introduction of PCV together in The Gambia in 2009 amounted to $1,616,943 or $24.22 per fully-immunised child. Savings from the switch from tetravalent to pentavalent vaccine slightly offset the large additional cost of introducing PCV. The Gambian gov't assumed 16% of the added systems costs of the two vaccine schedule changes, while donor agencies contributed the remainder – GAVI (52%), UNICEF (31%), WHO (1%, plus significant staff time contributed for training).
2. Grant A-11: September 2012 – December 2015		
PCV10 Impact (Kenya)	This is a continuation from the PneumoADIP PCV impact evaluation. Implications: The inclusion of follow-on surveillance under VITAC provides the opportunity to establish a causal link between PCV10 and IPD incidence and generate additional data that will illustrate the effects of PCV introduction. Manuscript on impact of PCV10 on NP-carriage of *S. pneumoniae* and non-typeable *H. influenzae* was accepted by *Lancet Global Health* at the end of March 2014, now awaiting update on publication timeline. Presentations given at ISPPD 2014.	Dramatic reductions in the incidence of vaccine-type invasive pneumococcal diseases (IPD) among children less than five years of age have been shown since PCV10 was introduced in 2011. In 2013, the third year after vaccine introduction, there were no cases of VT-IPD among Kilifi Health and Demographic Surveillance System residents under than 5 years of age. The nasopharyngeal carriage study has shown that introduction of PCV10 in a developing country setting, with a catch-up campaign, has led to a two-thirds reduction in carriage prevalence of vaccine-serotype pneumococci both in children targeted for vaccination & in older people who were not vaccinated.
PCV13 Effectiveness (South Africa)	This study is a continuation of B.1 and evaluates the impact of PCV13 in South Africa, which substituted PCV7 with PCV13 partway through the original study period.	Preliminary findings from B.1 reveal that even in a routine use setting, with high pneumococcal transmission, PCV used on a novel schedule is highly effective for HIV-uninfected children but insufficiently so for HIV-infected children. This may indicate the benefit of a booster dose for HIV+ children on this schedule.
C. Hib Initiative Special Studies		
1. Grant: July 2005 – March 2014		
Invasive Bacterial	Bacterial meningitis	Number of confirmed Hib meningitis cases

Study	Status of Activities	Key findings
Disease surveillance in India	surveillance is ongoing at 3 sites. In addition to 1 paper in JID (above) 2 standalone papers have been published. 3 sub-studies are ongoing: retrospective analysis of stored CSF samples with real-time PCR assay, chart review at Chennai of all-cause pneumonia admissions to investigate potential decrease following Hib vaccine introduction, and NP carriage survey of Hib and *S. pneumoniae* at ICH.	at ICH, Chennai surveillance site has decreased by 82% since the vaccine was introduced in Tamil Nadu in Dec. 2011.
Hib and PCV impact in Pakistan	Bacterial meningitis surveillance is ongoing in 4 sites originally to measure the impact of Hib vaccine and has been extended to assess the early impact of PCV introduction on bacterial meningitis and nasopharyngeal carriage.	Cases of Hib meningitis have almost disappeared since pre-Hib introduction time period and studies illustrate the long-term community impact of bacterial meningitis overall, including neurologic sequelae.
D. PneumoADIP Special Studies		
1. Grant: March 2004 - December 2013		
PCV Impact in Kenya	Rolled over to VI-TAC.	
PCV Impact in The Gambia	Rolled over to VI-TAC in part (for economic analyses); additional continuation funding provided by GATES. This is a continuation of the Gambia PCV7 Impact study and is now evaluating the impact of PCV13.	
Cost-effectiveness of PCV catch-up	Analysis of the impact and cost-effectiveness of PCV catch-up among under-two year olds (current WHO recommendations) in GAVI-eligible countries. In this analysis, two models developed: a disease transmission model and an economic benefits model. Full integration of Kenya SIT model insights have been completed. Outputs of the cost-effectiveness model are pending. Preliminary results for the economic benefits model anticipated in Q2 2014. Full	Preliminary results from disease transmission model found that rapidly increasing the protection in the community via catch-up campaigns not only leads to more rapid reduction in the IPD burden but also increases efficiently of the vaccine schedule in the first years after vaccination through rapid establishment of herd protection in the unvaccinated population. However, once routine vaccination has established herd protection, it is similarly efficient as catch-up campaigns. Any catch-up campaign, particularly among under two and five year olds, is likely to additionally prevent a high number of IPD for comparatively few extra vaccine doses in the first years after vaccination.

Study	Status of Activities	Key findings
	redesign process continues.	
Economic value of vaccination in India	*The overarching goal of this analysis was to look at the potential health impact and costs averted through immunization with three vaccines—Hib, PCV, RV* vaccines. The project aimed to generate new evidence on the health and economic benefits of these vaccines *at the national level & in four states in India (Bihar, Delhi, Maharashtra, Tamil Nadu).* The analysis generated new evidence in 3 categories: (i) death & cases averted; (ii) disease costs averted; and (iii) productivity loss averted. All activities for this project have been completed; abstract submissions and manuscript development remain.	Introduction or scale-up Hib, PCV, and RV in India can result in immediate benefits to the gov't and households in terms of saving deaths and averting cases. Cost savings varied by vaccine and coverage scenarios. Across the 3 vaccination programs and coverage scenarios, the majority of the cost savings was attributable to averted lost productivity due to premature death. At the state level, the greatest savings to the public sector were realised in Bihar, where the burden of disease was high. Bihar also maintained the highest economic benefit from improved vaccination rates. Overall, the expanded use of PCV in India could result in US$2 billion of costs averted in a single year. Most of the total costs averted were due to lost productivity due to premature pneumococcal death. Across the 3 vaccines, majority of deaths averted were attributed to PCV (37%), followed by Hib (34%) and RV (29%).
E. Other GAVI Targeted Assessments		
1. PCV Effectiveness in Asia		
Impact of PCV-10 on IPD in Lower Sindh, Pakistan (Aga Khan University)	*Data collection began in Q4 2013.*	*Study findings anticipated in 2016.*
Impact of PCV on nasopharyngeal carriage in Nepal (Oxford University)	*Data collection to begin in 2014.*	*Study findings anticipated in 2018.*
Impact of PCV introduction on hospitalised pneumonia cases and nasopharyngeal carriage rates in Lao PDR (Murdoch Chldren's Institute)	*Data collection started Q4 2013.*	*Study findings anticipated in 2017.*
2. Centers for Disease Control and Prevention (2013-2014)		
Evaluating the impact of PCV in Burkina Faso	*Data collection is ongoing.*	*Analysis of pre-vaccine introduction data anticipated in 2014.*
3. Full Country Evaluation (2013-2016)		
3.1 Evaluating the impact of PCV on nasopharyngeal carriage, IPD and x-	*Data collection is ongoing.*	Study findings anticipated in 2016.

Study	Status of Activities	Key findings
ray confirmed pneumonia in Mozambique		
3.2 Impact of PCV on nasopharyngeal carriage in Bangladesh	*Nasopharyngeal carriage study to begin in 2014.*	Study findings anticipated in 2016.

Sources

[1] AMC website: http://www.gavialliance.org/library/gavi-documents/amc/

[2] Manufacturers' registration on AMC website: http://www.gavialliance.org/funding/pneumococcal-amc/manufacturers/registration/

[3]Global Action Plan for Prevention and Control of Pneumonia and Diarrhoea (GAPPD): http://apps.who.int/iris/bitstream/10665/79207/1/WHO_FWC_MCA_13_01_eng.pdf

[4] 2012 WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC): http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/

[5] Full Country Evaluation reports on GAVI website: http://www.gavialliance.org/results/evaluations/full-country-evaluations/

[6] Lee et al. *The estimated mortality impact of vaccinations forecast to be administered during 2011-2020 in 73 countries supported by the GAVI Alliance*. Vaccine, Volume 31, Supplement 2, Pages B61-B72, 18 April 2013. *http://dx.doi.org/10.1016/j.vaccine.2012.11.035*

[7] World Pneumonia Day 2013 GAVI press release: http://www.gavialliance.org/library/news/press-releases/2013/pneumonia-still-responsible-for-one-fifth-of-child-deaths/