ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

Annual Report
1 January – 31 December 2015

Prepared by the AMC Secretariat of Gavi, The Vaccine Alliance

Gavi
The Vaccine Alliance

AMC ADVANCE MARKET COMMITMENTS for vaccines

Contents

Abbreviations

AMC	Advance Market Commitment
AMP	Agence de Médicine Préventive
CDC	US Centers for Disease Control and Prevention
DTP	Diphtheria, Pertussis, Tetanus vaccine
EPI	Expanded Programme on Immunisation
FCE	Full Country Evaluations
FOC	Firm Order Commitment
Gavi	Gavi, the Vaccine Alliance
Gavi Secretariat	Secretariat of Gavi, the Vaccine Alliance
IAC	Independent Assessment Committee
IPD	Invasive Pneumococcal Disease
IRC	Independent Review Committee
M&E	Monitoring and Evaluation
NVS	New Vaccines Support
PEF	Partners' Engagement Framework
PCV	Pneumococcal Conjugate Vaccine
PROWG	Pneumo & Rota Operational Working Group
PSA	Provisional Supply Agreement
PSF	Product Summary File
RFP	Request for Proposals
SD	Supply Division (UNICEF)
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

Figures

Tables

Executive Summary

The purpose of this report is to provide an update on Advance Market Commitment (AMC) implementation activities, including supply and procurement, country demand, monitoring and evaluation, media and communications and financial reporting. This report is the seventh pneumococcal AMC Annual Report[i] and covers the period from **1 January to 31 December 2015**. This is the first AMC Annual Report where the reporting cycle is aligned with the calendar year; the aim of this change is to increase efficiencies and create alignment with other annual reporting requirements for the Gavi pneumococcal vaccine programme and the AMC Secretariat. With the transition to this reporting cycle, there is an overlap of three months (January - March 2015) with the 2015 AMC Annual Report, which covered the period 1 April 2014 – 31 March 2015.

Supply and Demand

The pilot AMC for pneumococcal vaccines is now in its sixth year of implementation and significant progress continues to be made.

A total of 133 million doses of pneumococcal conjugate vaccine (PCV) were procured through the AMC in 2015, a 33% increase from 2014 (100 million doses). With the current six supply agreements, the total contracted supply amount through 2024 amounts to 1.46 billion doses. Out of the US $1.5 billion AMC funds, the two suppliers that have pre-qualified PCV have been allocated US $1.095 billion of the funds. Twenty-seven percent of the AMC funds remain available.

In terms of country demand, 79% of AMC-eligible countries (58 out of 73) have been approved to introduce the AMC-eligible pneumococcal vaccines to date. As of 31 December 2015, 54 countries have introduced these life-saving vaccines, including eight during this reporting period (1 January to 31 December 2015)[ii]. The remaining four countries that have been approved for Gavi support are expected to introduce in the coming eighteen months. Despite the remarkable performance in terms of the number of introductions, there continued to be some challenges with introduction delays and vaccination coverage. Drawing from implementation lessons gathered to date, Gavi is strengthening the coordination mechanism among partners, identifying and addressing bottlenecks to assist countries in their pre- and post-introduction activities.

Based on Strategic Demand Forecast (SDF) v11.00 and v12.0, which were approved during the 2015 procurement cycle, the Gavi Secretariat, in consultation with UNICEF Supply Division (SD), decided to not issue a fourth Call for Supply Offers for the procurement of pneumococcal vaccines. The need for the next tender will be reassessed later in 2016 based on the AMC terms and conditions, the next version of the SDF and the outcomes of the next rounds of applications for New Vaccines Support (NVS).

[i] *Previous AMC Annual Reports can be found on the AMC website: http://www.gavi.org/library/gavi-documents/amc/*

[ii] *Four of these introductions took place in the January-March 2015 period and are therefore also covered in the previous AMC Annual Report (Cambodia, Nepal, Solomon Islands and Bangladesh).*

Monitoring and Evaluation

AMC progress continues against selected indicators as shown in Table 1. From programme start to 2014 (latest data available), it is estimated that more than 47 million children have been vaccinated with AMC-supported pneumococcal vaccines, with a projection of more than 80 million children vaccinated by 2015 (data to become available in July/August 2016). The continued scale up of PCV is forecasted to result in the prevention of 1 million deaths by 2020.

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

	2009	2010	2011	2012	2013	2014	2015
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	2
Cumulative number of AMC registered manufacturers who have made their registration public	0	4	4	4	4	4	4
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	100	133
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	59
Cumulative number of AMC-eligible/Gavi-supported countries that have been approved	3	17	37	46	51	55	58
Cumulative number of AMC-eligible/Gavi-supported countries introducing TPP vaccines	0[iii]	1[iv]	16	24	38	46	54
Coverage of PCV in AMC-eligible/Gavi-supported countries**	0%	1%	5%	9%	19%	28%	n/a**
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	47	n/a**

Source: Gavi Secretariat

** Indicator defined as the percentage of eligible population reached across Gavi 73 countries*

*** WUENIC coverage data and WHO-reported number of immunised for 2015 will be available in July 2016*

PCV coverage performance at the country level continues to be tracked, using WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) data, which are published annually in July. Information to date shows that countries continue to successfully introduce PCV into their routine systems, with PCV third dose (PCV3) coverage tracking well against the third dose coverage of Diphtheria-Pertussis-Tetanus vaccine (DTP3) by the second year of implementation, apart from a small subset of countries.

[iii] *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.*

[iv] *Same as above.*

As part of the AMC monitoring and evaluation framework, and as recommended by the Gavi Evaluation Advisory Committee and agreed by the AMC stakeholders, the first AMC Outcomes and Impact Evaluation took place in 2015 and the final report has been published in early 2016.

The Gavi Full Country Evaluations project, which will run from 2013 to 2016, continued to track PCV implementation in Mozambique, Uganda and Zambia, as well as the PCV introduction in Bangladesh in March 2015. This Gavi-funded project, which is separate from the AMC monitoring and evaluation framework, has provided important findings and recommendations for programme design and implementation.

Gavi also continues to fund a number of special studies demonstrating the effectiveness and impact of PCV to help facilitate evidence-based decision making in support of the introduction and continued implementation of pneumococcal vaccines in developing countries through the AMC.

Media and communication activities

Increasing AMC visibility through traditional, online and social media remains an important goal for Gavi's communications team. This multi-platform approach continues as 54 countries have now introduced pneumococcal vaccines in their national immunisation schedule.

Financial activities

From 1 January to 31 December 2015, US$ 514 million was disbursed to UNICEF for the purchase of pneumococcal vaccines[v]. Of this amount, US$ 150 million was from the AMC funds to pay for the AMC-funded portion of the vaccine purchase. The remaining US$ 364 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[vi].

Challenges and priorities ahead

With 58 AMC-eligible countries approved for PCV and 54 having already introduced since the first introduction in 2010, the priorities moving forward will be focused on supporting the four remaining future introductions of countries that have been approved, as well as supporting countries that have not yet applied to access pneumococcal vaccines through the AMC. For countries that have introduced, the priorities remain to sustain PCV implementation and improve coverage, as well as measuring impact of PCV, especially as countries start to transition from Gavi support. Reducing the price of pneumococcal vaccines and ensuring proper balance of supply and demand remain key priorities.

[v] *See Section 6.2 for further details*

[vi] *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.*

Background

Advance Market Commitments (AMC) 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 (TPP);

2. **to bring forward the availability of effective pneumococcal vaccines** for developing countries by guaranteeing the initial purchase price for a limited quantity of 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; and

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

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 79% of 73 AMC-eligible countries have submitted applications to Gavi for financial support and been approved for pneumococcal vaccine introduction.

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 seventh pneumococcal AMC Annual Report[vii] and covers the period from **1 January to 31 December 2015**. This is the first AMC Annual Report where the reporting cycle is aligned with the calendar year; the aim of this change is to increase efficiencies and create alignment with other annual reporting requirements for the Gavi pneumococcal vaccine programme and the AMC Secretariat. With the transition to this reporting cycle, there is an overlap of three months with the 2015 Annual Report (January-March 2015).

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 AMC Independent Assessment Committee (IAC) on 1 April 2016.[viii] For more information about the AMC Secretariat, please refer to Annex 1.

[vii] *Previous AMC Annual Reports can be found on the AMC website: http://www.gavi.org/library/gavi-documents/amc/*

[viii] *Note that as a public document, this report does not include any confidential information.*

1. Supply and Procurement update

1.1. WHO recommendation and AMC-eligible pneumococcal vaccines

WHO recommends the inclusion of pneumococcal vaccines be given priority in childhood immunisation programmes worldwide, especially in countries with under-five mortality of greater than 50 per 1,000 live births[1]. 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. Gavi currently supports PCV for administration in infant routine immunisation programmes.

WHO also states that catch-up vaccination can be conducted as part of pneumococcal vaccine introduction to accelerate herd protection and therefore the PCV impact on disease and carriage[2]. Following discussions in 2012, Gavi deemed it was not able to provide support for catch-up vaccination due to the PCV supply situation at the time. As the supply situation eases, Gavi may reconsider supporting a broader age group in the future, in line with WHO recommendation.

As of 31 December 2015, there are currently two pneumococcal conjugate vaccines (PCV) available for procurement under the AMC. These two vaccines meet the criteria for 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.

1.2. Pneumococcal conjugate vaccine, 10-valent

The 10-valent PCV (PCV10) is a liquid vaccine in a 2 dose vial without preservative, 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 IAC. Both doses in the vial 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 presentation lacking preservative, 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. After countries send a written confirmation to UNICEF, WHO is responsible for assessing that these conditions are met, after which UNICEF and the supplier are authorised to ship the first doses of the vaccine to countries. 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.

GSK is currently developing a multidose vial presentation of PCV10[3], which includes preservative and is expected to be pre-qualified by WHO in 2018.

1.3. 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.

Pfizer is currently developing a multidose vial presentation of PCV13, with a Phase 3 safety, tolerability and immunogenicity study completed in 2015[4]. The multidose vial presentation is expected to be pre-qualified by WHO at the end of 2016.

1.4. Supply Offers and Agreements

There have been three Calls for Supply Offers for supply of PCVs under the AMC to date. The third and last Call for Supply Offers was published in July 2012, followed by the signatures of two new supply agreements in July 2013. A summary of the First, Second and Third AMC Supply Agreements can be found in Annex 2. A summary of the current supply commitments is shown in Table 2 below.

Table 2. Status of overall supply commitments

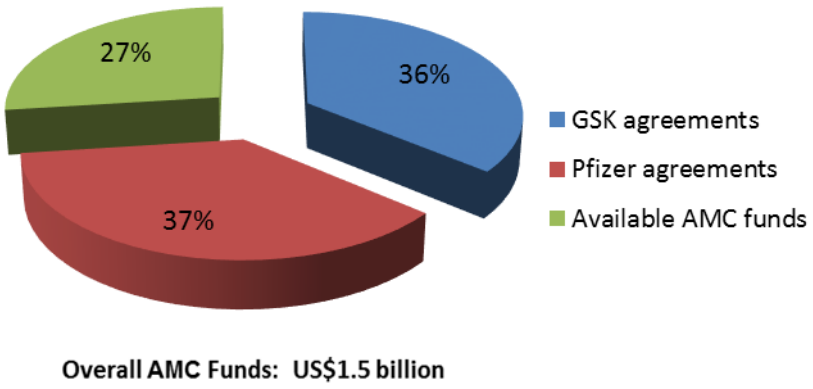
Manufacturer	Date of signature (week of)	Annual supply commitment (doses)	Tail price	Supply start date	AMC Funds allocated
GSK	23 March 2010	30 million	US $3.50	2010	US $225 million
Pfizer Inc.	23 March 2010	30 million	US$3.50; reduced to $3.40 mid 2013 and $3.30 from 2014*	2010	US $225 million
GSK	12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



Overall AMC Funds: US$1.5 billion

Based on Strategic Demand Forecast (SDF) v11.0 and v12.0 (see Section 1.2 below), which were approved during the 2015 procurement cycle, the Gavi Secretariat, in consultation with UNICEF SD, decided to not issue a fourth Call for Supply Offers for the procurement of pneumococcal vaccines. The need for the next tender will be re-assessed by partners later in 2016 based on the AMC Terms and Conditions, SDF v13.0 and the outcomes of the next rounds of applications for New Vaccines Support (NVS) to the Gavi Secretariat.

1.5. Doses contracted to date

The number of doses on contract has increased since the 2013 supply agreements have been signed, as additional doses were brought forward during the capacity development period in order to meet demand. Table 3 summarises the total contracted supply, as of July 2013.

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

Year	2010	2011	2012	2013	2014	2015	2016 - 2020[ix]	2021	2022	2023	2024	TOTAL
Doses procured/ contracted in 2010	5.5	28.9	54	60	60	39.2	300	47.4	5			**600**
Doses procured/ contracted in 2011			13	17	36	36	180	36	36	6		**360**
Doses contracted in 2013				3	19	64.8	250	50	50	49.2	14	**500**
TOTAL	**5.5**	**28.9**	**67**	**80**	**115**	**140**	**730**	**133.4**	**91**	**55.2**	**14**	**1460**

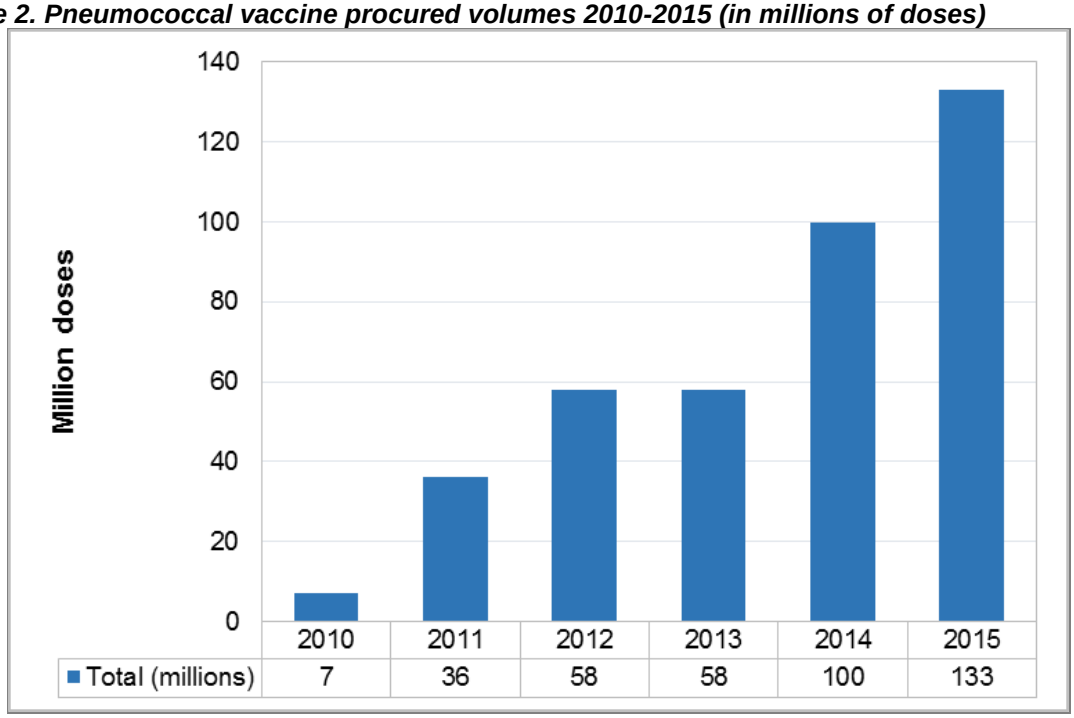
Source: UNICEF Supply Division
** Contracts are amended annually based on actual supply and demand to ensure that the total quantity on the supply agreements remain unchanged. Note: some numbers may appear not to add due to rounding.*

[ix] *In the period 2016-2020, annually contracted doses are 60 (first row, "Doses procured/ contracted in 2010"), 36 (second row, "Doses procured/ contracted in 2011") and 50 (third row, "Doses contracted in 2013").*

1.6. Doses procured between 2010 and 2015

A total of 133 million doses were procured in 2015. The total number of doses procured and delivered from 2010 to 31 December 2015 is summarised in Figure 2 below:

Figure 2. Pneumococcal vaccine procured volumes 2010-2015 (in millions of doses)



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 additional 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. Some supply constraints remained nonetheless.

1.7. Strategic Demand Forecasts (SDF)

The PCV SDF has evolved since the early versions, with important changes in the forecasted demand. A number of factors contributed to these changes, in particular revisions to assumptions about eligibility for Gavi support and country interest in the vaccine. However, by version 5.0 of the forecast, the long-term view of demand became relatively stable between forecasts. Routinely updated assumptions, for example of population and coverage estimates, had only moderate impacts to the longer-term aggregate forecast. On the other hand, the period between about 2015 and 2020 has experienced substantial revisions across many of the forecasts. The relative instability during this period reflects the uncertainty on the introduction plans for a few large countries, in particular India and Indonesia. Over the forecast versions, the expectation on when these countries would introduce has become later, as well as more gradual rollout assumptions, significantly decreasing demand estimates during this period over the forecasts.

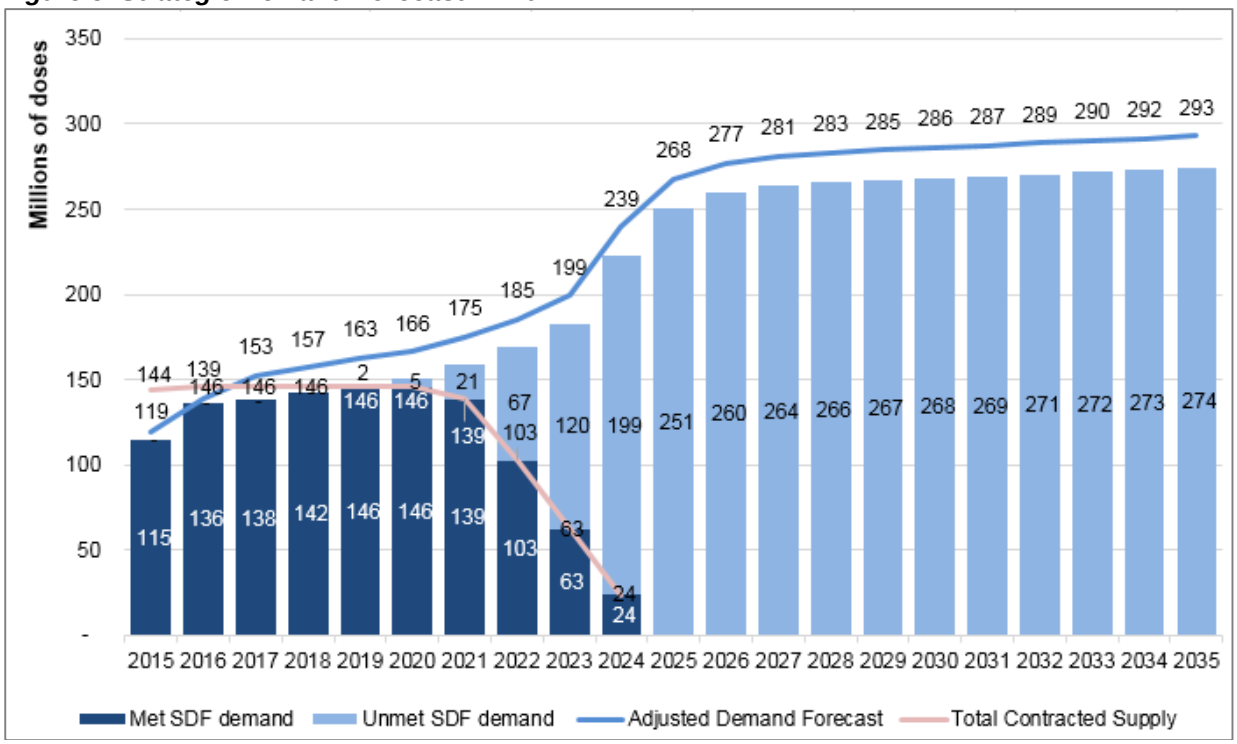
SDFs developed, published and/or analysed in the reporting period are as follows:

- SDF v10.0 was completed in October 2014 and included in the previous AMC Annual Report, and incorporated updated standard forecast inputs and assumptions. This included new information on introduction plans, as well as assuming across all scenarios that 4-dose vial presentations of PCV phase in when available. Based on this SDF v10.0, the Gavi Secretariat and UNICEF reassessed the need for the issuance of the next tender to meet the AMC objectives and concluded that there was no need to issue a Call for Supply Offer in 2015[5].
- SDF v11.0 was completed by the Gavi Secretariat in April 2015. This forecast incorporated small revisions, for example to introduction dates and production selection assumptions. Other assumptions were reviewed but was generally concluded that the assumptions should remain unchanged from the v10.0 forecast. Overall demand estimates remained similar to the v10.0 forecast.
- SDF v12.0 was completed in October 2015 and was published on the Gavi website in early 2016[6]. Updates in the forecast include refreshing key inputs to include the latest population and coverage estimates. The forecast also integrates new Gavi eligibility and co-financing policies, as well as some revisions to the projections for new introductions. The Gavi Secretariat and UNICEF completed an assessment of the need for the issuance of the next tender based on SDF v11.0 and v12.0 and concluded that a Call for Supply Offers was not needed[7]. The need for an issuance of the next tender will be reassessed by partners later in 2016 based on SDF v13.0.

The latest SDF, v12.0, is shown in Figure 3 below. Figure 3 shows two scenarios of the demand forecast, a SDF base case scenario using updated data for the surviving infant population and vaccine coverage estimates as previously used, and an "adjusted demand forecast" (ADF) using country estimates from Gavi applications, against total contracted supply. The ADF is produced to reflect the volume of PCV doses which have been financially committed by Gavi to countries that have been approved for Gavi support. For countries that have not yet applied or for the period beyond existing Gavi financial commitments, figures are based on the values and growth rates estimated in the SDF.

In comparison with the SDF v.10 included in the last Annual Report, there has been a slight decrease in the forecasted demand (ADF). A portion of the decrease is driven by later introductions, with a few moderate size countries (e.g. Vietnam, Sri Lanka) making a substantial difference during this period. The largest driver is the revision of targets in the short-term grant commitments, coupled with a more conservative extension of these commitments to the medium and long-term forecast. Some of the largest countries (e.g. Nigeria, Bangladesh, Pakistan, Ghana) had revisions to commitments between these forecasts; the extrapolation of this to the medium-term causes most of the decrease noted between v10 and v12.

Figure 3. Strategic Demand Forecast v12.0[x]



1.8. Availability of pneumococcal vaccines

The availability of supply continued to increase in 2015 and was able to meet the majority of the country demand. Nigeria was the only country where the phased PCV introduction continued to be planned around supply availability, similar to the previous year. In mid-2015, the manufacturer confirmed that it would be able to meet demand for the national roll-out in Nigeria from early 2016 onwards, one year ahead of schedule. The additional doses were made available due to introduction delays in large countries (e.g. Bangladesh, Phase 2 of Nigeria) as well as stock adjustments. From 2016 onwards, supply is expected to fully meet demand.

In 2014, Gavi finalised and published the Pneumococcal Vaccine Supply and Procurement Roadmap as part of its market shaping strategy. The Roadmap identified three main supply and procurement objectives:

- 1st Priority Objective: Cost of vaccines to Gavi and countries. The essential pneumococcal market-shaping objective is to significantly reduce the 'tail-price' weighted average price (WAP) short- to mid-term (2015–2020). So far, AMC procurement mechanisms achieved a 'tail-price' reduction of at most 6% from the initial 'tail-price' cap of US$ 3.50/dose. Thus, the price of the vaccine is currently challenging for sustainable pneumococcal vaccination in most Gavi-supported and Gavi-graduated countries.
- 2nd Priority Objective: Balance of supply and demand. In the short term (2014–2017), it is critical to achieve supply availability in line with existing production plans. It is also important to

[x] *Forecasted demand in Figure 3 is limited to the 73 AMC-eligible countries.*

access four-dose PCV presentations provided they can be used over multiple vaccination sessions. Mid- to long-term (2018 and beyond), it is desirable to have at least three suppliers of pneumococcal vaccines to ensure both supply security and competitiveness.

- 3rd Priority Objective: Appropriate and innovative vaccines. Overall, pneumococcal conjugate vaccines will always have limitations in terms of serotype coverage; there is a need for new technologies to emerge that will confer long-term serotype-independent protection. This is a long-term objective due to technological challenges. Also, some new technologies in development may lead to lower production costs.

An action plan was agreed upon by Gavi stakeholders, which optimises coordination and maximises achievement of the above supply and procurement objectives. Additional detail can be found in the Roadmap public summary, published on the Gavi website[8]. Gavi plans to commence an update to the Pneumococcal Vaccine Supply and Procurement Roadmap later in 2016.

1.9. 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 IAC in the determination of AMC eligibility. As described in the AMC Procedures Memorandum, 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 2015, no additional manufacturers registered with the AMC Secretariat. The list of AMC registered manufacturers who have made their registration public is as follows[9]:

- GlaxoSmithKline (GSK) Biologicals (Belgium)
- Panacea Biotec Ltd. (India)
- Pfizer Inc. (U.S.)
- Serum Institute of India (India)

To date, only two of these manufacturers are producing AMC-eligible pneumococcal vaccine. Gavi continues to actively monitor the pipeline development for other manufacturers.

2. Country demand and introductions overview

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

As of 31 December 2015, 58 of the 73 AMC-eligible countries (79%) have applied and been approved for support for pneumococcal vaccines.

Gavi opened two NVS application rounds in 2015, with a deadline for countries to submit applications by January and September 2015 for review by the Independent Review Committee in March and November 2015, respectively. However, no new countries applied for PCV support through the AMC during these two applications rounds. Further information on non-supported countries is provided in Section 2.5 below.

2.2. Introduction of PCV in countries in accelerated transition or transitioned from Gavi support

In June 2010, the Gavi Board approved that all Gavi-eligible countries as per the 2003 definition continue to have access to pneumococcal vaccines through Gavi under the terms and conditions of the AMC. As a result of this Board decision, countries in accelerated transitioned or transitioned from Gavi support[xi] that have not yet been approved for pneumococcal vaccine are able to apply and 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 AMC price from the outset. Also, all countries must have achieved DTP3 coverage at or above 70% according to WHO/UNICEF estimates. As of 31 December 2015, one graduating country – Mongolia – has been approved for support through the AMC and is planning to introduce in 2016. Other accelerated transition or transitioned countries that have not yet applied and are eligible to do so are as follows:

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

2.3. Pneumococcal vaccine introductions

As of 31 December 2015, 54 countries have introduced pneumococcal vaccines supported by the AMC. Eight of these introductions took place in the period between 1 January and 31 December 2015 (versus eight in 2014). One of these introductions, in Bangladesh, was a dual introduction with inactivated polio vaccine (IPV). All the introductions that have taken place to date are outlined in Table 4 below.

The Gavi Strategic Goal target of 45 PCV introductions in Gavi countries by the end of 2015 was therefore successfully reached, with the 45th introduction taking place in Georgia more than one year

[xi] *As per previous Gavi graduation terminology, graduating (accelerated transition) and graduated (transitioned) Gavi countries.*

ahead of schedule. This represents a rate of introduction in Gavi countries more than three times faster than Pentavalent (DTwP-HepB-*Hib*) vaccine introduction over an equivalent period[xii].

Of the 54 countries with Gavi-supported pneumococcal vaccine programmes, 13 countries were using PCV10, whereas the remaining 41 countries were using PCV13. In 2015, two countries requested a switch in PCV product, from PCV10 to PCV13 (Armenia and Azerbaijan), based on their original product choice at the time of application. These requests were reviewed and approved by the Alliance and both countries will be switching PCV product in 2016.

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 intro.)	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 intro.)	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 intro.)	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

[xii] *More than 54 PCV introductions in Gavi countries in the first five years of the programme (Dec 2010- Nov 2015), in comparison to 14 Pentavalent vaccine introductions in the equivalent period (2001-2005).*

	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
	Togo	PCV13	Introduced in June (joint intro. with rotavirus vaccine)	41
	Niger	PCV13	Introduced in August (joint intro. with rotavirus vaccine)	42
	Armenia	PCV10	Introduced in September	43
	Côte d'Ivoire	PCV13	Introduced in September	44
	Georgia	PCV10	Introduced in November	45
	Nigeria	PCV10	Introduced in December (phased intro.)	46
2015	Cambodia	PCV13	Introduced in January	47
	Nepal	PCV10	Introduced in January	48
	Solomon Islands	PCV13	Introduced in February	49
	Bangladesh	PCV10	Introduced in March (joint intro. with IPV)	50
	Guinea Bissau	PCV13	Introduced in June	51
	Lesotho	PCV13	Introduced in July	52
	Eritrea	PCV13	Introduced in August	53
	Uzbekistan	PCV13	Introduced in November	54

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

In order to continue to gather lessons learned on PCV programme implementation, the analysis carried out in 2014 to identify the common hurdles faced by countries at the time of introduction was updated at the end of 2015. The analysis was extended to 56 out of the 58 approved countries[xiii]; as highlighted previously, the global supply constraints in the earlier years of the programme created uncertainty for countries and impaired adequate planning, which led to further delays. Training and cold chain readiness remain the key bottlenecks, as well as the availability of funds (either due to delays in disbursement from Gavi to countries and/or to funding flow issues within the country as a result of decentralisation, for example) and competing priorities at country level, such as multiple concurrent vaccine introductions and campaigns. As highlighted in Section 2.6 below, Gavi continues to strengthen its resource allocation and coordination mechanisms to ensure that these key cross-cutting bottlenecks are addressed in future introductions.

2.4. Future pneumococcal vaccine introductions

Four Gavi countries already approved for pneumococcal vaccine support through the AMC are expected to introduce the vaccine in 2016-2017. These future pneumococcal vaccine introductions are outlined in Table 5 below. Three of the four countries have selected PCV13 as their preferred product presentation.

[xiii] *The two countries that originally introduced with donations were excluded from the analysis.*

Table 5. Future planned pneumococcal vaccine introductions

Year	Country	Product	Status	Cumulative No.
2016	Kyrgyzstan	PCV13	Planned for Q1	55
	Myanmar	PCV10	Planned for Q2	56
	Mongolia	PCV13	Planned for Q2	57
	Haiti	PCV13	Planned for Q4/2017	58

2.5. Future pneumococcal vaccine applications

From the 73 AMC-eligible countries, only 15 (21%) have not yet been approved to access pneumococcal vaccine through the AMC. Although a subset of these countries has expressed strong interest in introducing the vaccine in the near future, only four are eligible to apply to access Gavi support in 2016 based on Gavi eligibility and on DTP 3rd dose (DTP3) coverage, which must be higher than 70% (based on WHO/UNICEF Estimates of National Immunisation Coverage, WUENIC, 2014) as per Gavi application guidelines – Comoros, India, Korea DPR, and Tajikistan. India's introduction of pneumococcal vaccine through the AMC is being discussed as part of Gavi's Partnership with India for 2016-2021, approved by the Gavi Board in December 2015.

There are also seven countries in accelerated transition or transitioned from Gavi support that are eligible based on DTP3 coverage and can access PCV through the AMC, but these will need to fully fund the vaccine from the programme outset – Bhutan, Cuba, Indonesia, Sri Lanka, Timor Leste, Ukraine, and Vietnam. The remaining four countries are currently ineligible due to <70% DTP3 coverage – Chad, Guinea, Somalia, and South Sudan. Gavi will continue to support strengthening of health systems and routine immunisation in these countries to ensure adequate readiness to introduce PCV and other vaccines in the future.

There will be three rounds for NVS applications in 2016 during which countries can apply for PCV support. Table 6 shows the timeline for new application submission, review and decision. The existence of three separate rounds provides more flexibility and better alignment with countries' timelines and planning cycles.

Table 6. 2016 Gavi NVS application timelines

	Round 1	Round 2	Round 3
Deadline for application submission	15 January 2016	1 May 2016	9 September 2016
Application review dates	7-18 March 2016	17-24 June 2016	7-18 November 2016
Gavi Board decision	By June 2016	By November 2016	By March 2017

An update on the outcome of the 2016 applications rounds will be provided in the next AMC Annual Report.

2.6. Coordination and support for pneumococcal vaccine introductions and implementation

With the transition from the Business Plan to the Partners' Engagement Framework (PEF) for the 2016-2020 strategic period, Gavi continues to strengthen its coordination mechanisms with partners to ensure that technical assistance to countries can be delivered more efficiently and effectively. The new PEF structure, split between Foundational Support, Targeted Country Assistance and Strategic Focus Areas, ensures that Alliance resources, including technical assistance, are delivered more efficiently and effectively to address key bottlenecks at country-level.

At the global level, the Pneumo and Rota Operational Working Group (PROWG) was established in 2011 with the aim of facilitating effective partner coordination, including country communication and operational decision-making, in order to create favourable conditions for Gavi-supported countries to succeed with the application, introduction, and sustained use of pneumococcal and rotavirus vaccines as per Gavi's mission and AMC goals and objectives. It remains a critical forum to this day.

The PROWG members represent WHO, UNICEF SD, UNICEF Programme Division, PATH, Johns Hopkins University (JHU), and the Gavi Secretariat. The working group meets bi-weekly by teleconference to discuss the following key topics, among others:

- Monitor and support country application development, including development of introduction plans.
- Monitor preparedness issues and implementation milestones for successful launch and sustained use of the vaccines.
- Monitoring the progress of implementation, such as reports of faster (or slower) uptake of the vaccine post launch;
- In close collaboration with countries and regional offices, determine technical assistance needs and mobilise relevant resources to ensure successful application, programme planning and implementation.
- Gather lessons learned and analyse experiences to optimise and improve future introductions.

In the context of the new Gavi strategic cycle 2016-2020 and the evolving pneumococcal vaccine programme lifecycle, the PROWG objectives and terms of reference will be revisited later in 2016. A list of current PROWG members is provided in Annex 3.

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. PIEs are conducted as standalone assessments or as part of comprehensive Expanded Programme on Immunisation (EPI) reviews. During this period, nine countries[xiv] have conducted a PIE for PCV. 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. The PIEs carried out to date have identified that PCV introduction is generally successful and high coverage is reached within a short period, due to high demand. Some of the issues identified include

[xiv] *Armenia, Azerbaijan, Bangladesh, Georgia, Mauritania, Niger, Pakistan, Togo, and Uganda.*

cold chain and vaccine management, training and reporting & monitoring. Resolution of these aims to be addressed through PEF, and in particular through the Targeted Country Assistance.

2.7. Global Action Plan for the prevention and control of Pneumonia and Diarrhoea (GAPPD)

In 2013, WHO/UNICEF published the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD)[10]. GAPPD proposes a cohesive approach to ending preventable pneumonia and diarrhoea deaths and provides a roadmap for national governments and their partners to plan and implement integrated approaches for the prevention and control of pneumonia and diarrhoea. It brings together critical services and interventions, including immunisation, 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.

Gavi works within this broader context and supports the advancement of GAPPD. 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. Since 2014, Gavi also 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.

The WHO- and UNICEF-led pilot integration of services was still underway in 2015 in three countries (Zambia, Bangladesh, and India) in order to derive evidence-based lessons for use in national scale-up and application to other countries. Some GAPPD-related activities also took place in Uganda and Afghanistan.

- Zambia: the Mazabuka Action Plan for Pneumonia and Diarrhea (MAPPD) was launched in 2014. In November 2015, a team from WHO and CDC visited Zambia in order to develop a plan for the second year of life (2YL) platform. Mazabuka has been selected as a 2YL evaluation district given the synergies with the planned GAPPD interventions and related monitoring approaches. An update on GAPPD implementation and potential links with 2YL was provided, including the use of EPI sessions to provide comprehensive health education to caregivers, such as on the use of oral rehydration salts and zinc.
- Bangladesh: the implementation of the Moulvibazar action plan for pneumonia and diarrhoea (MAPPD) has continued in 2015, during which time a number of monitoring visits were undertaken at the district and national level in Bangladesh. The planned activities for 2016/17 will include a strong focus on coordination between relevant departments and stakeholders, on supply and logistics of GAPPD-relevant commodities, and on improving data quality and use as part of Health Management Information System strengthening.
- India: the Government of India prioritised the development of State and district level road maps for addressing pneumonia and diarrhoea in a coordinated manner and by end of 2015 an Integrated Action Plan for Pneumonia and Diarrhoea (IAPPD) was developed with WHO support and scaled-up in 62 High Priority Districts in four states (Uttar Pradesh, Bihar, Rajasthan and Madhya Pradesh).

- Uganda: the country developed a detailed comprehensive roadmap for ending preventable deaths from pneumonia and diarrhoea in 2014 and during 2015 intensified implementation of integrated approaches by introducing the Ethiopian model of integrated delivery of services using Health Extension Workers.
- Afghanistan: the country held a consultation for the development of a national plan of action for the diarrhoea and pneumonia control in December 2015. The plan, including its implementation framework, will be finalised in 2016. The consultation provided an opportunity for stakeholders from the donor community and child health related programmes to discuss and identify best approaches for addressing diarrhoea and pneumonia mortality and morbidity in a coordinated manner.

In 2015, a paper was published on the development of the integrated GAPPD[11]. This paper further describes the conduct of the series of workshops which were conducted as part of the GAPPD initiative by WHO and UNICEF, with support from other partners to facilitate the inclusion of coordinated actions for pneumonia and diarrhoea into the national health plans of 36 countries with high child mortality. The paper presents findings from these workshops and from post workshop follow-up activities.

3. AMC Independent Assessment Committee

The Independent Assessment Committee (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.[xv] In addition, the IAC establishes when and if an adjustment of the pre-set long-term price of vaccines is necessary. During the current 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 4.

[xv] *Also see section 3.2 of the 2010 AMC Annual Report, http://www.gavi.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 AMC 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 was completed in 2015 instead of in 2014 (see 4.2 below).

4.1. Programme Performance Reporting

Gavi has a comprehensive PCV results framework currently being used for regular monitoring of the Gavi pneumococcal vaccine programme and the AMC. At the end of 2015, some additional indicators were added to reflect the new Gavi strategy 2016-2020. Table 7 below highlights some of the key indicators being tracked, for which information can be made publicly available.

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

	2009	2010	2011	2012	2013	2014	2015
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	2
Cumulative number of AMC registered manufacturers who have made their registration public	0	4	4	4	4	4	4
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	100	133
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	59

	2009	2010	2011	2012	2013	2014	2015
Cumulative number of AMC-eligible/Gavi-supported countries that have been approved	3	17	37	46	51	55	58
Cumulative number of AMC-eligible/Gavi-supported countries introducing TPP vaccines	0[xvi]	1[xvii]	16	24	38	46	54
Coverage of PCV in AMC-eligible/Gavi-supported countries**	0%	1%	5%	9%	19%	28%	n/a**
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	47	n/a**

Source: Gavi Secretariat

** Indicator defined as the percentage of eligible population reached across Gavi 73 countries*

*** WUENIC coverage data and WHO-reported number of immunised for 2015 will be available in July 2016*

Pneumococcal vaccine coverage performance in Gavi countries continues to be closely monitored. In 2014, 3rd dose coverage amongst 73 Gavi-eligible countries was 28%, based on the WUENIC data published in July 2015[12], a 9% point increase in relation to 2013. For the subset of Gavi countries that introduced the vaccine prior to 2014 (n=38), 3rd dose coverage has reached 75%. The current projection for 3rd dose coverage in 2015 is 39%, just below the 2015 Gavi Strategic Goal target of 40%. These data will become available in July 2016 and reported in the next AMC Annual Report.

Figure 4 shows the PCV3 coverage in 2014 (WUENIC July 2015 data), as well as the weighted average coverage of 75% omitting 2014 (i.e. mid-year) introductions. For the same group of countries, DTP3 coverage was 82%, demonstrating that most countries continue to successfully introduce PCV into their routine systems. In 68% of countries, PCV3 coverage is within 5% points of DTP3 coverage by the second year of implementation. There is a subset of countries where 2014 PCV3 coverage was below average and lower than DTP3; this subset includes countries with phased introductions (e.g. Lao PDR), countries using modified schedules (e.g. Moldova, with PCV3 administered at 12 months), and countries where PCV is facing implementation issues (e.g. in Congo DR, where due to a faster than planned phased roll-out frequent stock-outs were faced in 2014, and in Uganda, where PCV roll-out stalled due to numerous challenges and was only fully introduced nationwide by mid-2014; more information in Section 4.3 below). The situation in these countries is being closely monitored and bottlenecks are being addressed through Alliance support.

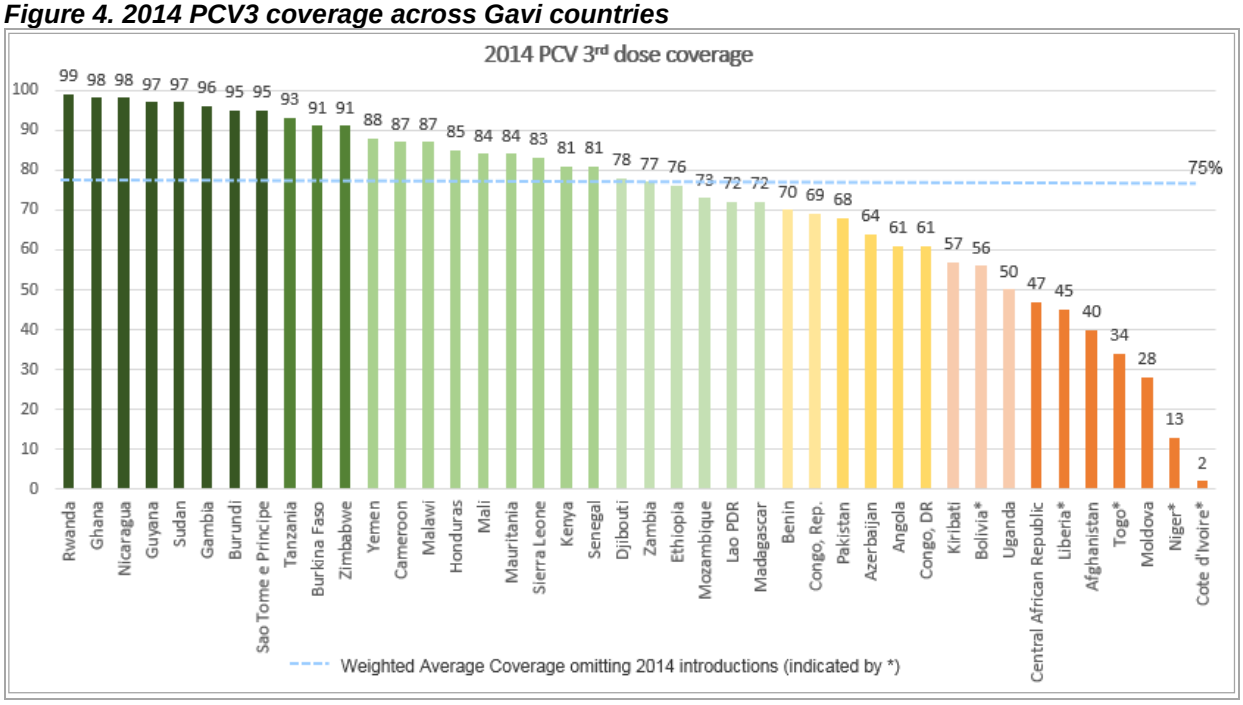
One area that continues to be monitored closely is the impact of the introduction of inactivated polio vaccine (IPV) in the immunisation schedule of PCV. Given that IPV is administered at the same time as the 3rd dose of DTP, a few countries have chosen to move the PCV 3rd dose administration to a later visit (e.g. Nepal, 9 months, with measles first dose; Bangladesh, 18 weeks, visit for PCV only; Moldova, 12 months), to avoid three injections at the 3rd DTP visit. Initial administrative data from Bangladesh indicate that this new schedule may have had a slight impact on coverage in the first months of implementation; the situation is being closely monitored to ensure that it is addressed with support from Alliance partners in case it persists. In the case of Nepal, the change is not in line with WHO

[xvi] 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.

[xvii] Same as above.

recommendation, which recommends at least 8 weeks between 1st and 2nd dose in the 2p+1 schedule. Immunogenicity studies are currently being carried out in Nepal to ensure that the change to a novel schedule does not affect the immunogenicity of PCV.

Figure 4. 2014 PCV3 coverage across Gavi countries



4.2. AMC Outcomes and Impact Evaluation

In 2015, and as per the AMC monitoring and evaluation framework, the Gavi Secretariat commissioned The Boston Consulting Group (BCG) for an Outcomes and Impact evaluation, in order to assess the extent to which the pilot AMC has achieved its stated objectives and the overarching goal of reducing morbidity and mortality from pneumococcal disease. The evaluation also captures lessons learned in the pilot and recommendations for future impact evaluations of the AMC.

The Request for Proposals (RFP) for the evaluation was published in March 2015. AMC stakeholders and partners were widely consulted on the evaluation questions, design options and other methodological matters. The RFP was also reviewed and approved by Gavi's EAC. Proposals were submitted through an open and competitive bidding process and then judged by an independent selection committee. The committee recommended the selection of BCG. After the review of the draft report by the AMC stakeholders, the final report was published on the Gavi website in early 2016[13]. The Gavi Secretariat has prepared a management response to the findings and recommendations, which is publicly available with the report on the Gavi website. The EAC is also preparing an independent assessment of the quality and usefulness of the report. Their assessment will be included as part of the EAC Chair's report at the Gavi Board meeting in June 2016.

The evaluation has validated that the pilot pneumococcal AMC contributed towards reducing morbidity and mortality from pneumococcal disease, accelerating vaccine supply availability (as per the second objective of the AMC) and uptake (as per the third objective of the AMC) in Gavi countries, as well as supporting reduction in morbidity and mortality from pneumococcal disease, with 3 million under-five

deaths estimated to be averted by 2030. Although the AMC has not succeeded in accelerating research and development (R&D) for additional manufacturers, as per the first objective of the AMC, it did have two positive R&D effects: first, it proved that there would be a large low-income country market after the conclusion of the AMC, which likely encouraged many manufacturers to continue to pursue development. Second, the creation of this market stimulated presentation innovation specifically for Gavi markets by existing suppliers.

4.3. Full Country Evaluations

In 2013, Gavi launched a set of evaluations to collect real-time data on immunisation programmes, vaccine-related issues and the contribution of Alliance support in four countries. There are four countries taking part in the Full Country Evaluations (FCE) project: Bangladesh, Mozambique, Uganda and Zambia. Local research institutions in all FCE countries are partnering with the Institute of Health Metrics and Evaluation (IHME) and PATH to collect information, data, and evidence to help improve immunisation programmes. The introduction and implementation of PCV in the routine immunisation programme (routinisation) in these four countries were evaluated as part of this project.

The first and second Annual Report (2013 and 2014) evaluated the introduction process of PCV in Mozambique, Uganda and Zambia (available on the Gavi website). The third FCE Annual Report (2015) includes the joint introduction with IPV in Bangladesh and the ongoing monitoring of PCV routinisation in Mozambique, Uganda, and Zambia. The report also presents preliminary findings of the impact of the PCV introduction on pneumococcal disease burden, based on studies in Mozambique. The 2015 report also includes a number of key recommendations for the Alliance and for the four FCE countries. The final report will become available on the Gavi website in the second quarter of 2016, along with an Alliance management response to the recommendations, as it has been done for the previous annual reports.

Evaluation findings indicated Gavi FCE countries have experienced variable success in introducing and routinising PCV. PCV has been fully routinised in Mozambique. In Uganda and Zambia, however, PCV3 delivery remains below that of pentavalent vaccine and suboptimal routinisation in both countries has been driven by vaccine stock-outs at multiple levels of the health system. In Uganda, the initial findings indicate that these stock-outs were a result of a number of factors, namely high demand caused by eligible unvaccinated children from the previous birth cohort and challenges in forecasting demand at health facility, district and national levels due to lack of standard method to estimate vaccine needs (e.g. lack of updated tools to estimate previous consumption). The full root causes for these stock-outs are still being investigated by the FCE team. The evaluation findings also indicate that in Uganda geographic inequities in PCV coverage remain, reflecting existing bottlenecks in the immunisation system.

The preliminary findings in Bangladesh show that PCV was rapidly scaled up following the joint launch with IPV but that there is substantial drop-out due to the schedule of the third visit at 18 weeks. This drop-out had decreased towards the end of 2015 and, as mentioned in 4.1 above, the situation is being closely monitored by the country and in-country Alliance partners and will be addressed if the high drop-out persists.

Preliminary findings from pneumococcal vaccine effectiveness studies, including nasopharyngeal carriage surveys pre- and post-PCV introduction and pre- and post-surveillance of invasive pneumococcal disease suggest that the scale-up of PCV is reducing pneumococcal disease burden in Mozambique. More results will be reported in the next AMC Annual Report, including those from the case-control study in Mozambique and a nasopharyngeal carriage study conducted in Bangladesh.

As per the previous years, the four countries and the Alliance partners will continue to implement the key evaluation recommendations in order to address PCV-related implementation bottlenecks and improve programme performance; the PEF and the Targeted Country Assistance will be the main mechanism used by the Alliance to provide support.

More details will be included in the 2015 report and the PCV implementation in all four FCE countries will continue to be evaluated in 2016 and reported in the next AMC Annual Report. Final annual reports (cross-cutting and country-specific) from these evaluation will be made available on the Gavi website throughout the evaluation period[14].

4.4. Estimates of the impact of pneumococcal vaccination

In 2011, a multidisciplinary group with expertise in mathematical modelling was established by Gavi and the Bill & Melinda Gates Foundation to estimate the impact of vaccination in the 73 Gavi countries. This group has continued to engage, reviewing their approaches and incorporating the latest data on diseases in scope as appropriate.

A description of the methods and results from this first round of modelling was published in the journal Vaccines in April 2013 and a publication with the latest approaches is currently under review with Lancet Global Health. Gavi impact estimates are updated biannually using similar methodology, with the most recent round completed in mid-2015. The latest update of these estimates included a broader range of benefits measured, such as future deaths, cases and disability adjusted life years (DALYs) averted, the economic benefits of vaccination (e.g. cost of illness averted).

Based on current projections (SDF v.11), PCV use will avert nearly 1 million future deaths among children vaccinated in Gavi countries by 2020.

4.5. Special studies on pneumococcal vaccines

In addition to support for surveillance, Gavi funds a number of special studies to help facilitate evidence-based decision making for vaccine introduction and impact monitoring to support sustained 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 the historical and ongoing studies and key findings are provided in Annex 5.

The earliest assessments in Gavi countries were supported under the PneumoADIP and VI-TAC grant, including pneumococcal vaccine effectiveness and impact studies in Kenya and South Africa, economic impact evaluations of pneumococcal vaccines in Ghana and The Gambia, concluded in 2015. PCV impact in Kenya will continue for two additional years to monitor potential changes in the epidemiology of disease including serotype epidemiology.

These Gavi-funded special studies yielded important findings that continue to evolve the PCV evidence landscape and to inform policies. 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 is also being collected on a variety of PCV dosing schedules to determine the most effective schedules to reduce pneumococcal disease. In addition to

the dosing landscape and Gambia economic peer-reviewed publications, in 2014 the Kenya and South Africa effectiveness studies produced several key publications highlighting their results including herd protection with reductions in transmission of the disease by reducing nasopharyngeal colonisation of vaccine-serotype strains in both vaccinated and unvaccinated individuals; reductions in antibiotic resistant strains of the disease in the very young; and overall substantial effectiveness of PCV against vaccine serotype and all serotype invasive pneumococcal disease (IPD) among children, as well as the broader scope of PCV impact on severe disease. Results from South Africa have shown that routine use of PCV is effective against presumed bacterial pneumonia at a magnitude similar to that measured in randomised controlled trials. More recently, results from The Gambia indicate that cases of childhood invasive forms of pneumococcal disease are reduced by more than one-half with introduction of PCV.

In June 2013, Gavi issued a RFP for the 'Evaluation of PCV Effectiveness in Asia' to assess the impact of PCV in early adopting Gavi countries in Asia, and upon recommendation of an Adjudication Committee, Gavi commissioned three 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. Data collection for these studies began in late 2013 and early 2014 and final results are anticipated in 2016-2017. A fourth study, to assess the impact of phased PCV introduction on the incidence of radiological pneumonia in Mongolia has been commissioned and began collecting pre-introduction data in 2015 with results anticipated in 2018 due to delayed timeline for vaccine use in the study setting.

Gavi 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 potential changes in circulating strains with anticipated results in 2017.

As mentioned previously, pneumococcal vaccine effectiveness and impact studies are also underway in Bangladesh and Mozambique as a component of the FCE work, including population-based assessment of changes in disease transmission and impact of PCV on invasive pneumococcal disease and x-ray confirmed pneumonia 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.

5. Media and Communications

Increasing AMC visibility through traditional, online and social media remains an important goal for Gavi's communications team. This multi-platform approach continues as 54 countries have now introduced pneumococcal vaccines in their national immunisation schedule.

5.1. Communications overview 2015

Gavi continues to highlight and explain the AMC in relevant communications materials, particularly around pneumococcal vaccine launches, ongoing special studies, and special events such as World Pneumonia Day. In addition to sharing the updated material, Gavi has also ensured that appropriate speaking points are incorporated into the speeches of Alliance spokespeople at launch ceremonies and other events.

On World Pneumonia Day 2015, Gavi highlighted the record number of children protected against the leading cause of pneumonia as countries strengthen their immunisation programmes. Since 2010, when Gavi first started supporting PCV vaccine through the AMC, 54 Gavi-supported countries have now introduced PCV as part of their routine immunisation programmes. In 2014, Gavi surpassed its 2015 target of 45 PCV introductions and is now on track to introduce the vaccine in 79% of the 73 Gavi-supported countries by the end of 2016. The latest figures released by Gavi on the 7th World Pneumonia Day showed that PCV coverage is increasing steadily. In all 73 Gavi-supported countries coverage increased from 1% in 2010 to 28% in 2014. It is forecasted that Gavi's pneumococcal vaccines should avert 1 million additional deaths by 2020, 600,000 of them in the 2016-2020 period. In 2014 alone, 21 million children were immunised with PCV, bringing to 47 million the total of children who have received PCV since the first Gavi-supported introduction in 2010. 2015 numbers will become available in Q3 2016.

A number of pneumococcal vaccine launches were marked with press releases or feature stories in 2015 on the Gavi website, including a particular focus on Bangladesh, with a specific infographic developed for the launch, and on Nepal, highlighting the 2015 introduction and the ongoing pneumococcal disease surveillance[15].

5.2. Communications outlook for 2016

Gavi will continue to integrate AMC messaging into all relevant materials and seek to profile the AMC mechanism during pneumococcal vaccine launches. Gavi will continue to brief journalists who are demonstrating an interest in the AMC, the Gavi model and in innovative finance mechanisms more generally, to ensure fair and accurate representations of the AMC.

The AMC impact evaluation will also be a key moment for communicating about the mechanism and what it has helped Gavi and developing countries to achieve.

5.3. Donor & stakeholder communication

Continuing in 2015, 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 obtain input on key issues. Topics included the SDF and implications, PCV roadmap development, revised disease burden and impact estimates progress on implementation, the progress on AMC targets and supply and implementation of vaccines. With regards to vaccine introductions, AMC donors were kept informed of progress and invited to participate in the vaccine launch events. Throughout 2015, donors and other stakeholders were also closely consulted and involved in the AMC Outcomes and Impact evaluation, completed by BCG in December 2015.

The pneumococcal AMC also continued to receive attention from broader audiences throughout the year. In November 2015, the Secretariat briefed the Advance Market Commitment Working Group at the White House (under Planning for Federal Sustainability in the Next Decade) on the pilot pneumococcal AMC. The purpose of this working group is to design and implement AMCs and other "demand pull" procurement mechanisms that can catalyse clean energy technology commercialisation. The group was keen to hear about the history, implementation and mechanics of the AMC for pneumococcal vaccine.

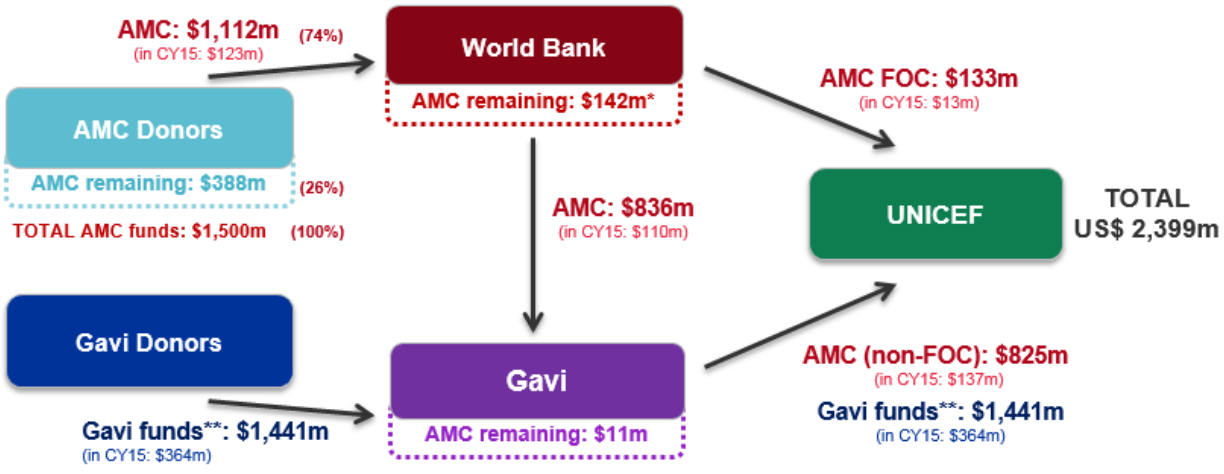
6. Financial Activities

The financial structure of the AMC remains unchanged from previous years. 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.[xviii]

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.

Figure 5. Summary of AMC Financial Process Flow and funds disbursed (inception to 31 December 2015)



'CY15': Calendar Year 2015

* *Includes $59.8m of Canadian Initial Funds, not yet available for disbursement*

** *Allocated from general funds to pay for tail price portion of vaccine & related fulfilment costs*

Source: Gavi Secretariat. Note: some numbers may appear not to add due to rounding.

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

Details are provided in sections 6.1 - 6.3 below.

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.

The three fixed-schedule donors have together pledged a total of US$ 765 million to the 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.

6.2. Donor contribution receipts

As of 31 December 2015, the World Bank had received a total of US$ 1,112 million from AMC donors (see Table 8 below). The Bill & Melinda Gates Foundation, the Government of Canada and the Norwegian Ministry of Foreign Affairs have all paid the total amounts that they had committed to pay under their respective grant agreements.

Table 8. Grant receipts from AMC donors, as of 31 December 2015 (in US$ millions)

(in US$ millions)	Grant Amount	Paid-in Amount	Remaining Balance
Fixed Schedule Donors			
Bill & Melinda Gates Foundation	50	50	-
Italy	635	424	211
Russian Federation	80	48	32
sub-total:	**765**	**522**	**243**
On Demand Donors			
Canada	200	200	-
Norway	50	50	-
United Kingdom	485	339	146
sub-total:	**735**	**589**	**146**
Total	**1,500**	**1,112**	**388**

Source: The World Bank

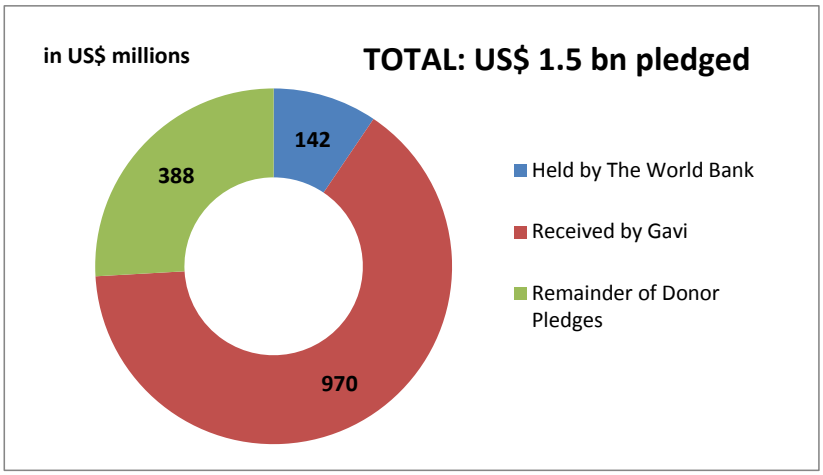
The World Bank has recorded the AMC donor funds in its financial statements as designated assets, with a corresponding liability to provide the funds to Gavi for the purchase of pneumococcal vaccines subject to the terms and conditions of the AMC. To enhance the predictability of AMC funding, the

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[xix].

AMC donor funds: inflow to Gavi

As of 31 December 2015, the World Bank had disbursed US$ 970 million (US$ 836 million to Gavi and US$ 133 million directly to the UNICEF procurement account relating to the Firm Order Commitments). Of the US$ 970 million, US$ 123 million was disbursed during 2015 (US$ 110 million to Gavi and US$ 13 million directly to the UNICEF procurement account relating to the Firm Order Commitments). This leaves a balance of US$ 142 million held by the World Bank, of which US$ 82 million is available for immediate disbursement to Gavi (see figures 6 and 7).

Figure 6. Status of AMC donor funds, as of 31 December 2015 (in US$ millions)

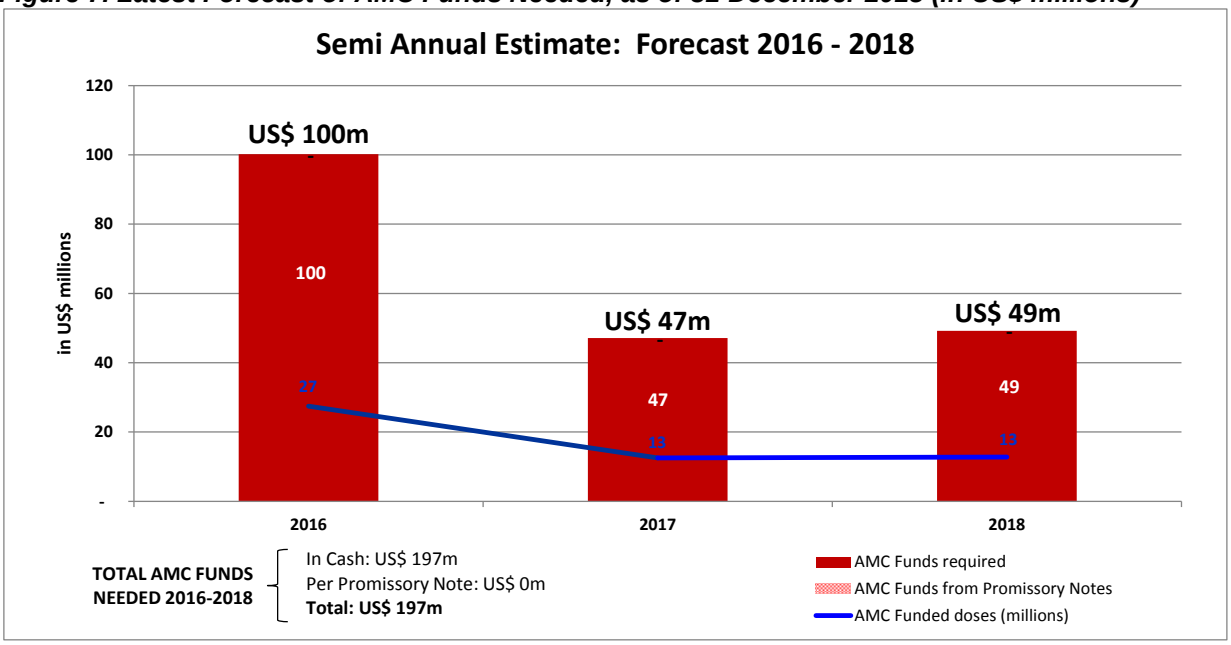


Source: Gavi Secretariat

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 two SAEs during 2015 (in June and in November), the latest of which forecasted a need for US$ 197 million of AMC funds to procure 53 million doses of the pneumococcal vaccine between 1 January 2016 and 31 December 2018.

[xix] *A provision was made in the AMC Stakeholders Agreement to finance the IBRD's financial management and administrative service fees primarily via investment income (with any shortfall thereafter paid by the United Kingdom, up to a certain limit). Given the market conditions over the past several years, the realised investment income has been far less than originally forecasted and, therefore, insufficient to cover these fees (in addition, the amount provided by the United Kingdom has also not been enough to cover the fees). As a result, it was subsequently agreed to use a burden sharing model between Gavi, the IBRD and AMC donors to fund the remainder.*

Figure 7. Latest Forecast of AMC Funds Needed, as of 31 December 2015 (in US$ millions)



Source: Gavi Secretariat. Note: some numbers may appear not to add due to rounding.

6.3. UNICEF procurement: outflow of AMC donor funds

During 2015, US$ 514 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US$ 150 million pertains to the AMC-funded portion of the vaccine purchase. The remaining US$ 364 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[xx]. 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 supply agreement amounting to US$ 13 million (see Figures 6 and 9). From inception of the programme through 31 December 2015, a total of US$ 2,399 million has been disbursed for the procurement of pneumococcal vaccines through the AMC (US$ 958 million was AMC-funded and US$ 1,441 was Gavi-funded).

Six supply agreements have been signed under the AMC programme, to date.[xxi] The AMC funds allocated under the first two Pfizer agreements and the first two GSK agreements have been fully disbursed and the remaining doses under those agreements are now being procured at those agreements' tail prices. It is anticipated that the remainder of AMC funds allocated to the third Pfizer agreement will be fully disbursed during 2016, while the third GSK agreement will continue to receive AMC funds through 2017.

In total, as at 31 December 2015 US$ 357 million has been transferred to Gavi's 'UNICEF procurement account' regarding the FOCs for the six existing signed supply agreements. Of this amount, US$ 223

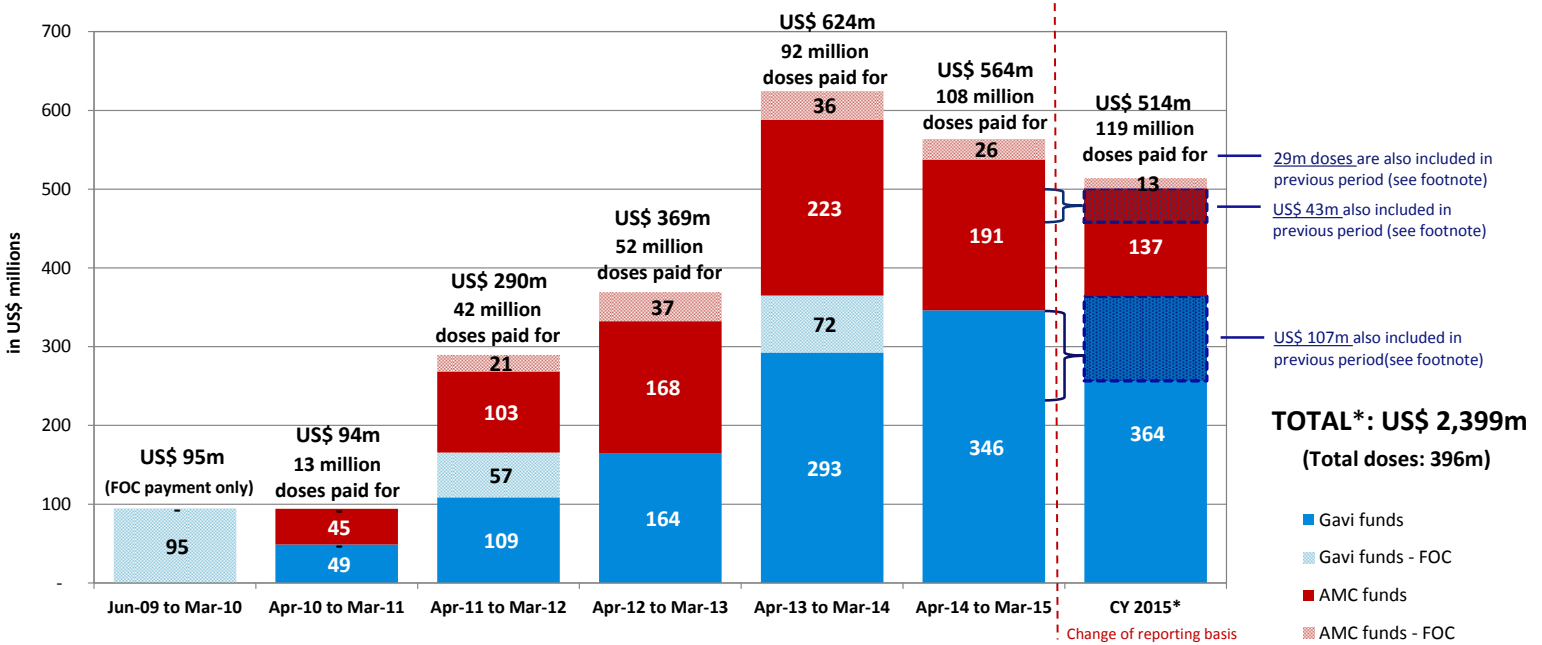
[xx] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US$ 0.16 per dose in 2015), in addition to the cost of the vaccine itself. These costs typically include the cost of syringes, safety boxes and freight.*
[xxi] *For details refer to Section 1.2 and Annex 1*

million represents the Gavi-funded portion of the FOCs and US$ 133 million represents the AMC-funded portion of the FOCs. Of the US$ 357 million transferred, US$ 327 million (approximately 92%) has been utilised and this represents the draw-down of already transferred FOC funds relating to all six supply agreements.

Figure 8. Total cash disbursements to Gavi's 'UNICEF procurement account' (inception to 31 December 2015, in US$ millions)

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	Apr-14 to Mar-15	CY 2015* Q1	CY 2015* Q2 - Q4	CY 2015* Total	TOTAL*	of which: AMC / Gavi	of which: FOC	of which: Non-FOC
AMC Funds - FOC	-	-	21	37	36	26		13	13	133	958	133	
AMC Funds	-	45	103	168	223	191	43	94	137	825			825
Gavi Funds - FOC	95	-	57	-	72	-	-	-	-	223	1,441	223	
Gavi Funds	-	49	109	164	293	346	107	257	364	1,218			1,218
TOTAL:	95	94	290	369	624	564	150	364	514	2,399		357	2,043



* Given the change of the reporting cycle to a calendar year basis, data for Q1 2015 have been included not only in CY 2015 (to show a complete calendar year), but also continue to be included in the period Apr-14 to Mar-15 for the sake of consistency with prior years' reports. However, Q1 2015 is included in the (overall) total only once.

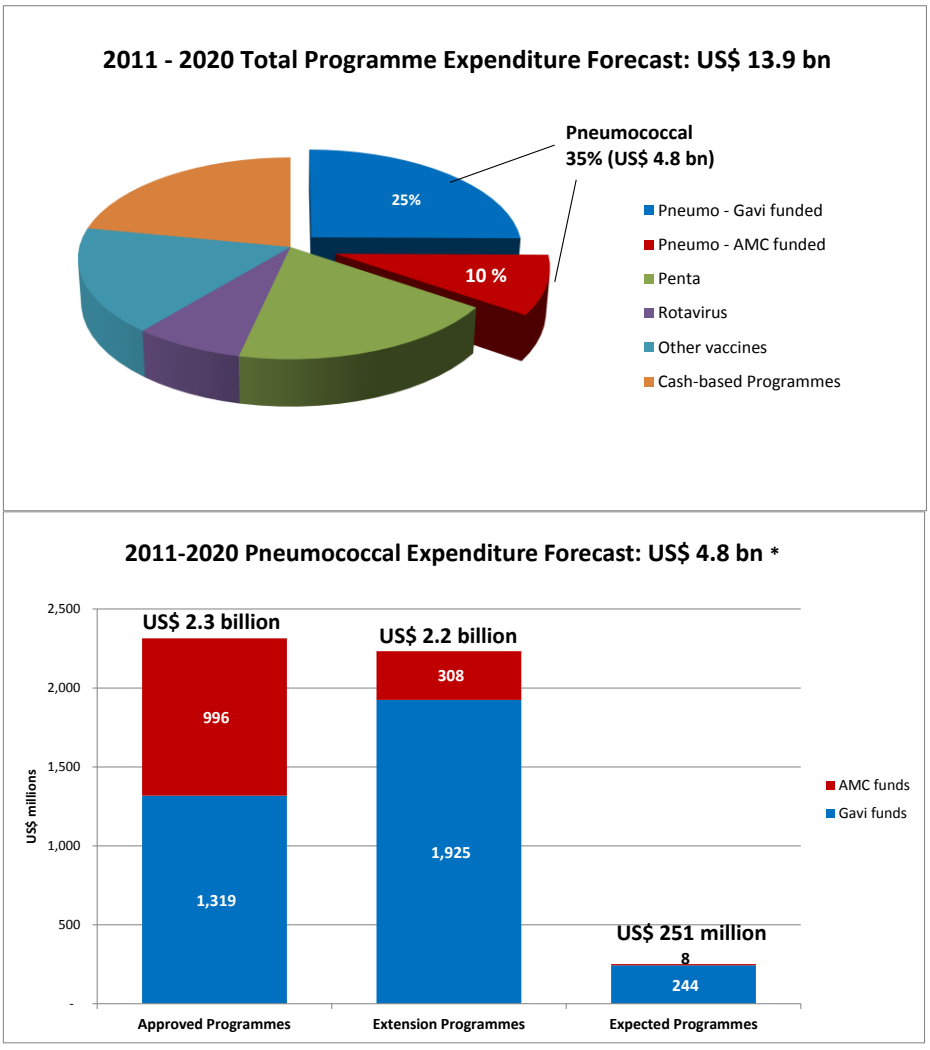
Source: Gavi Secretariat. Note: For the latest two reporting periods (April 14 – March 15 and CY 2015) the total numbers of doses have increased from the previous reporting periods while the overall amounts paid have decreased. This is due to a higher proportion of doses being procured under the Gavi-funded tail price only. Some numbers may appear not to add due to rounding.

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

At the December 2015 Gavi Board meeting, an update was presented of Gavi's Long Term Financial Forecast.[xxii] Total programme expenditures are projected to be US$ 13.9 billion for the 2011-2020 period, of which pneumococcal vaccine expenditures are anticipated to amount to US$ 4.8 billion, representing approximately 35% of total programmatic expenditures (see Figure 9).

For the 2016 and 2017 programmatic years, commitments had been made to 56 countries (or were forecasted as extensions to approved programmes) to receive financial support for the procurement of the pneumococcal vaccine. The approved funding for 2016 and 2017 amounts to US$ 189 million and US$ 43 million, respectively, and the funding for programme extensions for 2016 and 2017 amounts to US$ 364 million and US$ 436 million, respectively. These amounts are included as part of the total 2011-2020 "Approved Programmes" and "Extension Programmes", presented in Figure 9 below.

Figure 9. AMC Within Total Gavi Forecasted Expenditure 2011-2020



Source: Gavi Secretariat
** Approved Programmes are those approved by the Gavi Board. Extension Programmes are forecasted continuations of those programmes, subject to future approval. Expected Programmes are defined as those which have received conditional IRC recommendation or are forecasted based on Adjusted Demand Forecast v12.0 and the latest supplier assumptions.*

[xxii] *December 2015 Board Paper entitled "Board-2015-Mtg-3-Doc 06 Financial Forecast and Programme Funding Request"*

7. Challenges and Future Priorities

The implementation of the pilot pneumococcal AMC has been very successful to date, with high demand and uptake at country level. Some challenges remain nonetheless: there has been a decrease in new country demand in the past 24 months, with no new applications since the end of 2013; despite high vaccination coverage overall, a small subset of countries is facing PCV coverage challenges; and countries are starting to transition out of Gavi support and will start to fully self-finance the PCV programme. Moving forward, key priorities include supporting the remaining four countries that have not yet introduced pneumococcal vaccine and strengthening health systems and decision-making processes in those that have not yet applied to access PCV through the AMC. For countries that have introduced, the priorities remain to sustain PCV implementation and improve coverage. As countries start to transition out of Gavi support, measuring impact continues to be key, as is reducing the price of pneumococcal vaccines. Ensuring proper balance of supply and demand also remains a key priority.

7.1. Supporting country introductions

Efforts are focused to ensure that the remaining four approved countries are ready to introduce pneumococcal vaccines in the 2016-2017 period and that technical assistance is provided where appropriate to ensure high quality of implementation. Alliance partners continue to closely monitor country introduction status and coordinate technical assistance activities, with the aim of identifying and resolving issues with the support of the partners working at the country level. Lessons drawn from these contexts can inform future pneumococcal vaccine introductions, as well as the roll-out of other vaccines.

7.2. Strengthening health systems and routine immunisation

Supporting the application, introduction and implementation of pneumococcal vaccines in the AMC-eligible countries that have not yet applied for pneumococcal support also remains a key priority, particularly the eight that remain Gavi eligible. Four of the eight countries are not eligible to apply due to the >70% DTP3 coverage eligibility criterion, so the current focus of the Alliance is on strengthening the routine immunisation system in the short term to ensure that the pneumococcal vaccine can be introduced as soon as possible to address the high pneumococcal disease burden in these settings.

7.3. Sustaining implementation and ensuring high coverage

The Gavi-wide efforts on strengthening of health systems and routine immunisation are also key to address the challenges that some of the AMC-eligible countries are facing with PCV implementation. In addition, PCV implementation will continue to be closely monitored to identify issues in coverage performance in specific countries and/or settings. Efforts will also be made to better leverage PCV implementation towards improving coverage and equity of other vaccines, given the high demand for this vaccine at country level.

7.4. Ensuring sustainability for transitioning and transitioned countries

So far, AMC procurement mechanisms achieved a ‘tail-price’ reduction of at most 6% from the initial ‘tail-price’ cap of US$ 3.50/dose. This price of the vaccine may be challenging for sustainable pneumococcal vaccination as Gavi countries start to transitioning out of support. As outlined in the Pneumococcal Vaccine Supply and Procurement Roadmap, a key priority objective is also to significantly reduce the ‘tail-price’ WAP short- to mid-term (2015–2020). Sustainability is also being addressed through the new Gavi 2016-2020 strategy and Partners’ Engagement Framework, particularly through the SFAs for Sustainability and Political Will.

Demonstrating the impact of PCV is also key to ensure sustainability of the programme after transition. A focus on gathering evidence on vaccine effectiveness and impact will continue moving forward, through Gavi-supported special studies. The AMC Outcomes and Impact Evaluation to assess the achievements of the AMC pilot took place in 2015 and will be published in early 2016, so more details will be available in the next Annual Report.

7.5. 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 provided assurance that manufacturers would invest in scaling up production capacity and that supply would be available to meet long-term demand from countries. 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 production capacity in order to meet additional country demand and will demonstrate the ability of the limited supplier base to continue to meet the requirements. As the demand increases to more than 150 million doses annually, the limited supply base remains a risk to implementation. The Gavi Secretariat will continue to work closely with UNICEF SD to monitor the supply situation and manage the supply and demand balance.

8. Conclusion

Country demand for pneumococcal vaccines has been unprecedented, with close to 80% of the 73 AMC-eligible countries already approved for support and 54 introductions as of 31 December 2015. Ahead of the eight introductions in AMC-eligible countries during the reporting period, the 2015 target for number of pneumococcal introductions had been reached in November 2014, more than one year ahead of schedule. Third dose PCV coverage also increased 9% points from 2013 to 2014, reaching 28% in 2014, and is projected to reach 39% by the end of 2015. Based on current projections through year 2020, PCV use will avert an estimated 1 million future deaths among children vaccinated in Gavi countries.

Despite this unparalleled success, as countries enter the pathway to transition from Gavi support, programme sustainability becomes an area of increased focus for the Alliance. Gavi will continue to support this transition pathway in order to ensure that the PCV programme, as well as other vaccine programmes, are programmatically and financially sustained in future years.

Annex 1 – Membership of the AMC Secretariat

Team	Staff member
Vaccine Implementation	**Melissa Ko** (March 2015 – Present) Senior Programme Manager **Johanna Fihman** (January – February 2015) Senior Programme Manager **Sara Sá Silva** Vaccine Programme Manager
Resource Mobilisation	**Katja Rouru** (September 2015 – Present) Senior Manager **Ariane McCabe** (January – August 2015) Senior Manager
Finance	**Eric Godfrey** Senior Manager, Financial Planning, Analysis and AMC
Monitoring & Evaluation	**Hope Johnson** Head, Outcomes & Impact **Alba Vilajeliu** Programme Officer, Evaluations
Advocacy and Public Policy	**Lori Sloate** Deputy Director
Communications	**Frédérique Tissandier** Senior Manager
Market Shaping	**Wilson Mok** Senior Manager, Price Forecasting
Legal	**Alison Jensen** Associate Legal Counsel

Source: Gavi Secretariat, as of 31 December 2015

Annex 2 – 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 Period3F[xxiii] 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.

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.

[xxiii]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.

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 remained 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 3 – 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	**Melissa Ko** (March 2015 – present) Senior Programme Manager, Vaccine Implementation, Country Programmes **Johanna Fihman** (January – February 2015) Senior Programme Manager, Vaccine Implementation, Country Programmes **Sara Sá Silva** Vaccine Programme Manager, Vaccine Implementation, Country Programmes
PATH	**Candace Rosen** (January – August 2015) Senior Policy and Advocacy Officer **Jessica Fleming** (September – December 2015) Senior Research Scientist, Vaccine Access and Delivery
JHU	**Audrey Mitchell** (April – August 2015) Scientific Communications & Policy Officer (International Vaccine Access Center) **Julie Buss Younkin** (November 2015 – present) Scientific Communications & Policy Officer (International Vaccine Access Center)
UNICEF Programme Division	**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	**Jesus Barral-Guerin** Senior Contracts Manager **David K. Mutuerandu** Contracts Manager - PCV **Gideon Chelule** Contracts Manager – Rotavirus vaccine
WHO	**Carsten Mantel** Leader – Priority Area New Vaccines and Innovation **Hemanthi Dassanayake-Nicolas** Technical Officer – Strategic Information Group, EPI

	Alejandro Ramirez Gonzalez Technical Officer – Programme Operations, EPI **Isaac Gobina** Technical Officer – Programme Operations, EPI

Source: PROWG Terms of Reference, as of 31 December 2015

Annex 4 – 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

Halvor Sommerfelt
Professor of Epidemiology, Center for International Health, and Director, Centre for Intervention Science in Maternal and Child Health (CISMAC), 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 December 2015

Annex 5 – Summary of Gavi investments in surveillance PCV special studies

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. Surveillance		
WHO Coordinated global surveillance networks for Invasive Bacterial Vaccine Preventable Diseases (IB-VPD) **Hib Initiative supported IB-VPD surveillance in India and Pakistan**	Ongoing Completed	With guidance from an informal technical advisory group (ITAG), WHO continues to support countries in improved data quality, analysis and interpretation of the data and enhanced country ownership and transition of surveillance to support country monitoring of the impact of new vaccine introductions (Hib, PCV, Meningococcal A).
B. VI-TAC Special Studies		
1. Grant A-4: January 2009 - September 2013		
Landscape analysis of PCV dosing	Analysis of dosing studies published through 2014 is complete. 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)	Evaluation of impact of PCV7 is complete. Publication in Vaccine in 2012 discussed effects of study on changes to PCV dosing schedule made by South African NAGI. Presentations given at ISPPD 2012 and 2014. Publication in PIDJ on risk factors for IPD among children in South Africa. Publication in CID in 2014 on effectiveness of PCV in this case-control study. Publication in PIDJ in 2015 on risk factors for IPD.	Even in a setting of routine use and with high pneumococcal transmission, PCV delivered on a novel 2+1 schedule is highly effective for HIV-uninfected children (VE 74%), but insufficient among HIV-infected children (VE -12%). This may indicate the benefit of a booster dose for HIV+ children on this schedule. In addition, the study identified risk factors for IPD in HIV-uninfected children include underlying medical conditions, upper respiratory infections, daycare attendance, HIV exposure and siblings under 5 years of age.
Effectiveness of PCV7 against presumed bacterial pneumonia (PBP) **(South Africa)**	This case-control study measuring PCV effectiveness in HIV-infected and HIV-uninfected children is complete and published. This was the first published study on the impact of PCV on pneumonia in conditions of routine use in Africa. Poster displayed at ISPPD 2014. Publication in Thorax in 2015 showed effectiveness of PCV at	In the matched case-control study, PCV7 was 39.2% effective (95% CI: 8.46-59.6%) in preventing PBP (defined as consolidation on chest X-ray) in children 3 months to 2 years of age (those who had received two primary doses plus a booster), under conditions of routine use and using a hospital control group for comparison. There was vaccine efficacy of 20.1% when including children beginning after the first dose of PCV. Importantly, these effectiveness estimates were similar to those found in the more controlled environment of

Study	Status of Activities	Key findings
	preventing PBP in HIV-uninfected children.	randomized trials.
Pneumo/Rota 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 who are looking to adhere to the recent GAPPD recommendations.	Time series analysis of PCV impact manuscript has been drafted and will be submitted for publication in Q1 2016.
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 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 is complete. Poster displayed at ISPPD 2014. Manuscript describing the cost of pentavalent and pneumococcal conjugate vaccine delivery in the Gambia before and after introduction published in April 2014 in *Vaccine*. Manuscript for the Gambian pneumococcal economic impact study has been submitted and is expected to be published in 2016.	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, over 85% of which was the cost of vaccine. 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 in Kenya. Presentations at ISPPD-9 in March 2014. Manuscript on impact of PCV10 on NP-carriage of *S. pneumoniae* and non-typeable *H. influenzae* was published in *Lancet Global Health* in June 2014. Multiple additional publications expected, including analyses on PCV impact on pneumonia and IPD and indirect effects. Publication in *Lancet Global health* in 2016 shows results from 15 years of surveillance following Hib introduction; these data came from the surveillance system also tracking pneumococcal disease.	Substantial 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, 2014, and 2015 there have cumulatively been only 3 cases of vaccine-type IPD in children under 5 years in the Kilifi Health and Demographic Surveillance System. 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 prevalence of vaccine-serotype pneumococci carried in both children targeted for vaccination & in older people who were not vaccinated. Vaccine effectiveness of Hib vaccine during 15 years of use was 93% in children younger than 13 years of age (using a 3-dose schedule without a booster)
PCV13 Effectiveness (South Africa)	This study is a continuation of the VI-TAC Special Study in South Africa PCV7 evaluation (Grant A-4). The continuation extends the effectiveness analysis through the switch to PCV13, which has replaced PCV7. The data on the PCV13	Preliminary analysis indicates that vaccine effectiveness against PCV13 vaccine-type disease and PCV13 additional serotypes for HIV-uninfected children was 84% (95%CI: 55-94) and 95% (95% CI: 69-99), respectively. The vaccine effectiveness for PCV13 vaccine-type disease could not be estimated for HIV-infected children in this preliminary analysis.

Study	Status of Activities	Key findings
	effectiveness study have been compiled and a preliminary manuscript drafted; submission for publication is expected by Q2 of 2016.	
C. PneumoADIP Special Studies		
1. Grant: March 2004 - December 2013		
PCV Impact in Kenya	Rolled over to VI-TAC. (see above)	
PCV Impact in The Gambia	Rolled over to VI-TAC in part (for economic analyses); additional continuation funding provided by BMGF. This is a continuation of the Gambia PCV7 Impact study and is now evaluating the impact of PCV13.	Incidence of IPD decreased after vaccine introduction by 55% (95% CI 30%–71%) in the 2–23 month age group (253 vs 113 per 100 000 in 2013/14). This was due to an 82% (64%–91%) reduction of serotypes covered by PCV13.
Cost-effectiveness of PCV catch-up (Kenya)	Analysis of the impact and cost-effectiveness of PCV catch-up among under-one year olds, under-two year olds (current WHO recommendations), and under 5 year olds, in Gavi-eligible countries is ongoing. The disease transmission model is complete and preliminary cost-effectiveness results are available but have not been published. The Interactive Pneumococcal Vaccination Policy Model is designed to be an interactive web-based tool that models health benefits, costs, and cost-effectiveness of PCV; incorporation of the catch-up analyses is ongoing and thus the tool is still in development.	Preliminary results from the disease transmission model found that catch-up campaigns not only lead to more rapid reduction in the IPD burden but also increases efficiency of the vaccine schedule in the first years after vaccination through rapid establishment of herd protection. Any catch-up campaign in the first years after introduction, particularly among under two and five year olds, is likely to prevent a high number of IPD cases for comparatively fewer extra vaccine doses than routine immunization. Under 1 year old catch up campaigns achieve additional direct benefits but fewer indirect benefits. Preliminary cost-effectiveness results suggest catch up campaigns in the target age group may result in cost savings from the societal perspective.
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, and Tamil Nadu). The analysis generated new evidence in 3 categories: (i) death & cases averted; (ii) disease costs averted; and (iii) productivity loss averted. Presentation at ISPPD-9 in March 2014. All activities for this project have been completed; manuscript under development.	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%).
D. Other Gavi Targeted Assessments		
1. PCV Effectiveness in Asia		
Impact of PCV-10 on IPD in Lower Sindh,	Enrolment into a case-control study evaluating PCV impact on IPD,	Surveillance for IPD has detected 64 cases of IPD (24 cases of radiologically proven pneumonia & 40

Study	Status of Activities	Key findings
Pakistan (Aga Khan University)	meningitis and pneumonia and using surveillance data began in 2013 and will be ongoing until case count targets are met. A simultaneous cost-of-illness study using the same cases continues along a similar timeline. A nasopharyngeal carriage survey comparing pre-introduction (2013) to post-introduction carriage (2014-2016) will complete data collection in Q1 2016; while the final round of a vaccine coverage survey is also schedule to complete by Q1 2016. Vaccine promotion activities and assessment are underway.	of meningitis) within the study catchment area since 2013. Only 16 of these are vaccine serotype cases which will contribute to the case-control analysis; 28 cases are needed to complete this portion of the study. Study findings from the coverage estimates, NP carriage are anticipated beginning in 2016. Case-control and cost of illness study results are expected in 2018.
Impact of PCV on disease, nasopharyngeal carriage, and health economics in Nepal (Oxford University)	Enrolment continues in surveillance-based studies evaluating invasive bacterial disease and pneumonia, along with studies examining PCV impact on nasopharyngeal carriage in hospitalized pneumonia cases and healthy children. A head to head immunogenicity study comparing two dose schedules (at 6+10 weeks and 6+14 weeks, respectively) opened recruitment in August 2015. An analysis of impact on hospitalized pneumonia and meningitis using administrative data began in Q4 2015, while an economic impact study (cost of illness) was approved by the required review boards and is expected to begin data collection by mid-2016.	Preliminary analysis of pre-introduction data (i.e. pre-2015) indicate that pneumococcal carriage rates in hospitalized pneumonia cases were 42%. The community carriage study in children 24-59 month of age shows 82% carriage in rural children and 58% in urban children, respectively. Although serotyping is ongoing and data is only complete through 2014, it appears that despite variation in carriage of all strains of pneumococci, the vaccine-type strains are common in both settings: 29% in the urban arm and 34% in the rural arm. Complete study results, including post-introduction findings, analyses of surveillance data, head-to-head immunogenicity results, the review of administrative data on hospitalized pneumonia and meningitis, and the economic impact study are expected to begin rolling out in 2017.
Impact of PCV introduction on hospitalised pneumonia, IPD and nasopharyngeal carriage in Lao PDR (Murdoch Children's Institute)	Pre-PCV13 data collection was complete as of 2014. Post-introduction carriage survey began in 2015 and will continue through 2016. Surveillance for IPD continues, with the serotyping of current and archived collection of isolates dating to 2004 ongoing. The retrospective pneumonia review has commenced.	Preliminary pre-introduction results suggest approximately 35% of healthy children and infants carry pneumococci in the nasopharynx, while approximately 20% carry vaccine-type pneumococci. Over 80% of carriage samples with pneumococci contained antibiotic resistant genes as identified by microarray. Post-introduction findings, along with IPD surveillance and retrospective pneumonia review results anticipated in 2017.
Impact of PCV on hospitalized pneumonia and nasopharyngeal carriage in Mongolia (Murdoch Children's Institute)	Hospitalized pneumonia enrolment began in 2015, with chest x-ray capacity building activities ongoing such that 85% of cases enrolled between October and December had an x-ray image recorded. The first community carriage survey was successfully completed between May and August 2015. Vaccine introduction is expected to begin in August 2016 in two of four districts under surveillance.	Preliminary estimated carriage of pneumococcus among health children and infants is 54% prior to vaccine implementation. Preliminary analysis of pre-introduction hospitalized pneumonia data suggests approximately half of all pneumonia admissions have confirmed pneumococcal etiology. Post-introduction results expected beginning in 2018.
2. Centers for Disease Control and Prevention (2013-2016)		
Evaluating the impact of PCV in Burkina Faso	Evaluation of the impact of PCV on meningitis using data from national surveillance continues data collection.	Study findings anticipated in 2017.

Study	Status of Activities	Key findings
	Analysis of baseline (pre-introduction) meningitis surveillance is almost complete and will be presented at ISPPD 2016 in Glasgow, Scotland. Post-introduction data collection will continue through 2016, including for the proposed indirect cohort study. If the numbers of vaccinated and unvaccinated cases are sufficient, analysis will commence in Q2.	
3. Full Country Evaluations (2013-2016)		
3.1 Evaluating the impact of PCV on nasopharyngeal carriage, IPD and x-ray confirmed pneumonia in Mozambique	Data collection and analysis is ongoing. Preliminary results are part of the 2015 FCE report. Results of case-control study are expected in 2016.	Preliminary findings from vaccine effectiveness studies, including nasopharyngeal carriage surveys pre- and post-PCV introduction show a 41% (95% CI 16-59) reduction on PCV10 serotype-specific pneumococcal carriage among HIV-uninfected children receiving three doses of PCV; and 31% (95% CI 11-47) reduction on PCV10 serotype-specific pneumococcal carriage among HIV-infected children receiving three doses of PCV. The pre-and-post surveillance of invasive pneumococcal disease show an estimated significant 72.5% (95% CI 8 to 91.7) reduction in PCV10 serotype-specific invasive pneumococcal disease and suggest that the scale-up of PCV is reducing pneumococcal disease burden in Mozambique. These are preliminary results on pneumococcal vaccine effectiveness studies and represent changes on 18 months post-introduction and are based on observational studies. In 2016 FCE Annual Report, results for the case-control study in addition to updated preliminary results will be reported.
3.2 Impact of PCV on nasopharyngeal carriage in Bangladesh	Data collection and analysis is ongoing. Nasopharyngeal swabs were collected at baseline, before introduction of PCV-10 while post vaccination samples will be collected in Q2 2016.	Study findings anticipated in 2016.

Sources

[1] WHO position paper on pneumococcal vaccines: http://www.who.int/wer/2012/wer8714.pdf?ua=1

[2] WHO policy on Interrupted or Delayed Routine Immunisation: http://www.who.int/immunization/policy/Immunization_routine_table3.pdf?ua=1

[3] PCV10 multidose vial ongoing clinical trial: https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-000750-11/3rd and https://clinicaltrials.gov/ct2/show/NCT02447432?term=synflorix&rank=5

[4] PCV13 multidose vial clinical trial: https://www.clinicaltrials.gov/ct2/show/NCT01964716?term=prevenar13&spons=pfizer&rank=11

[5] UNICEF published statement on decision not to issue a Call for Supply Offers based on SDF v.10: http://www.unicef.org/supply/files/UNICEF_and_Gavi__Decision_on_Issuing_a_Call_for_Supply_Offer_based_on_Strategic_Demand_Forecast.pdf

[6] Gavi Strategic Demand Forecast v.12: http://www.gavi.org/library/gavi-documents/supply-procurement/gavi-strategic-demand-forecast/

[7] UNICEF published statement on decision not to issue a Call for Supply Offers based on SDF v.11 and v.12: http://www.unicef.org/supply/files/PCV_Tenders_Feb_2016_FINAL.pdf

[8] Pneumococcal vaccine roadmap: http://www.gavi.org/Library/GAVI-documents/Supply-procurement/Pneumococcal-vaccine-roadmap--public-summary/

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

[10]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

[11] Qazi et al., 2015. Ending preventable child deaths from pneumonia and diarrhoea by 2025. Development of the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea. Arch Dis Child 2015;100(Suppl 1):s23–8. http://adc.bmj.com/content/100/Suppl_1/S23.full

[12] 2014 WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC): http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/

[13] AMC Outcomes and Impact Evaluation: http://www.gavi.org/Results/Evaluations/Pneumococcal-AMC-outcomes-and-impact-evaluation/

[14] Full Country Evaluations reports on Gavi website: http://www.gavi.org/results/evaluations/full-country-evaluations/

[15] Gallery on Gavi website "Fighting pneumonia in Nepal - surveillance, strains and schedules": http://www.gavi.org/Library/Audio-visual/Galleries/Fighting-pneumonia-in-Nepal/