ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

Annual Report
1 April 2014 – 31 March 2015

Prepared by the Secretariat of Gavi, The Vaccine Alliance

Gavi
The Vaccine Alliance

AMC ADVANCE MARKET COMMITMENTS for vaccines

Contents

Abbreviations

AMC	Advance Market Commitment
DTP	Diphtheria, Pertussis, Tetanus vaccine
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
PATH	Program for Appropriate Technologies for Health
PCV	Pneumococcal Conjugate Vaccine
PROWG	Pneumo & Rota Operational Working Group
PSA	Provisional Supply Agreement
PSF	Product Summary File
PQT	WHO Prequalification Team
NVS	New Vaccines Support
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

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Executive Summary

Supply and Demand

The pilot Advance Market Commitment (AMC) for pneumococcal vaccines is now in its fifth year of implementation and significant progress continues to be made.

The number of doses on contract has increased since the 2013 supply agreements were signed, as additional doses were brought forward during the capacity development period in order to meet demand. A total of 100 million doses of pneumococcal conjugate vaccine (PCV) was procured through the AMC in 2014 alone, a 40% increase from 2013 (58 million doses). With the current six supply agreements, the total contracted supply amount through 2024 now amounts to 1.46 billion doses. Out of the US $1.5 billion AMC funds, the two suppliers that have pre-qualified 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 Gavi-supported pneumococcal vaccines to date. A total of 50 countries have already introduced these life-saving vaccines, including ten during this reporting period (1 April 2014 to 31 March 2015). With the 45th PCV introduction in Georgia in November 2014, Gavi reached its Strategic Goal 2011-2015 target for “Number of PCV introductions in Gavi countries” more than one year ahead of schedule. Eight other countries that have been approved for Gavi support are expected to introduce in the coming two years. Despite the remarkable performance in terms of the number of introductions, there continued to be some delays in vaccine introductions. The factors contributing to this include insufficient human resource capacity at the country level to manage competing priorities in immunisation and health, delays in expanding cold chain capacity, political and organisational changes in countries, delays in making funding available at national and/or sub-national levels for pre-introduction activities, and delays in product registration at country level. Drawing from lessons gathered from introductions to date, Gavi is strengthening the coordination mechanism among partners, identifying and addressing bottlenecks in funding disbursements, and deploying refined tools to assist countries in their pre-introduction activities.

Based on Strategic Demand Forecast (SDF) v10.0, which was approved during the 2014 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 in 2015. The need for the next tender will be reassessed later in 2015 based on the AMC terms and conditions, SDF v11.0 and the outcomes of the next rounds of applications for New Vaccines Support (NVS).

Monitoring and Evaluation

AMC progress continues against selected indicators as shown in Table 1. From programme start to 2013 (latest data available), it is estimated that more than 25 million children have been vaccinated with AMC-supported pneumococcal vaccines, with a projection of more than 80 million children vaccinated by 2015. 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 (based on 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 Target Product Profile (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	-
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[i]	1[ii]	16	24	38	40	50
Coverage of PCV in AMC-eligible/Gavi-supported countries***	0%	1%	5%	10%	19%	n/a**	n/a
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	n/a**	n/a

Source: Gavi Secretariat

** Year-to-date through 31 March 2015*

*** WUENIC coverage data and WHO-reported number of immunised for 2014 will be available in July 2015*

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

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 3rd dose coverage tracking well against the 3rd dose coverage of DTP vaccine by the second year of implementation.

As recommended by the Gavi Evaluation Advisory Committee and agreed by the AMC stakeholders, the first AMC Impact Evaluation is taking place in 2015. The Request for Proposals (RFP) for this independent evaluation will be commissioned in Q2 2015 and a final report is expected in late 2015.

The Gavi Full Country Evaluation project, which will run from 2013 to 2016, continues to track PCV implementation in Mozambique, Uganda and Zambia in 2014, as well as the preparations for the PCV

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

[ii] *ibid.*

introduction in Bangladesh in March 2015. The project has provided important findings and recommendations for programme design and implementation.

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

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 close to 50 countries have now introduced pneumococcal vaccines in their national immunisation schedule.

Financial activities

From 1 April 2014 to 31 March 2015, US $564 million was disbursed to UNICEF for the purchase of pneumococcal vaccines[iii]. Of this amount, US $223 million was from the AMC funds to pay for the AMC top-up portion of the vaccine purchase. The remaining US $346 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[iv].

Challenges and priorities ahead

With 50 AMC-eligible countries having introduced PCV and 58 already approved for introduction since programme start in 2009, the priorities moving forward will be focused on supporting the 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, especially as countries start to graduate from Gavi support. Reducing the price of pneumococcal vaccines and ensuring proper balance of supply and demand remain key priorities.

[iii] *See Section 6.2 for further details*

[iv] *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 sixth pneumococcal AMC Annual Report[v] and covers the period from 1 April 2014 to 31 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 21 April 2015.[vi] For more information about the AMC Secretariat, please refer to Annex 1.

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

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

1. Supply and Procurement update

1.1. AMC eligible pneumococcal vaccines

WHO recommends the inclusion of pneumococcal vaccines be given priority in childhood immunisation programmes worldwide, especially in countries with under-five mortality of greater than 50 per 1000 live births. For administration to infants, three primary doses (3p+0 schedule) or, as an alternative, two primary doses plus a booster (2p+1 schedule) are recommended. Primary vaccination can be initiated as early as at 6 weeks of age. WHO also recommends[vii] that catch-up vaccination be conducted as part of pneumococcal vaccine introduction to accelerate herd protection and therefore the PCV impact on disease and carriage. However, to date, Gavi has not been able to provide support for catch-up vaccination due to the PCV supply situation.

As of 31 March 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.

1.1.1. 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 novelty of the presentation, WHO requires that countries ensure programmatic readiness to introduce PCV10, with a pre-condition of special training requirements (i.e. specific training on the use of this presentation must have taken place at all levels before shipment and distribution of the vaccine), and the placement of stickers that state ‘do not return an opened vial of PCV10 to the fridge’ on refrigerators at all levels. 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.

1.1.2. Pneumococcal conjugate vaccine, 13-valent

The 13-valent PCV (PCV13) is a liquid vaccine in a one dose vial, produced by Pfizer Inc. It obtained WHO prequalification on 22 August 2010 and was deemed AMC eligible by the AMC IAC on 23 August

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

2010. UNICEF SD started the procurement of PCV13 to Gavi-supported countries in September 2010, with first delivery taking place in October 2010. Pfizer is currently developing a multidose vial presentation of PCV13, with a Phase 3 safety, tolerability and immunogenicity study recently completed[1]. The multidose vial presentation is expected to be available for Gavi countries in 2017.

1.2. 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

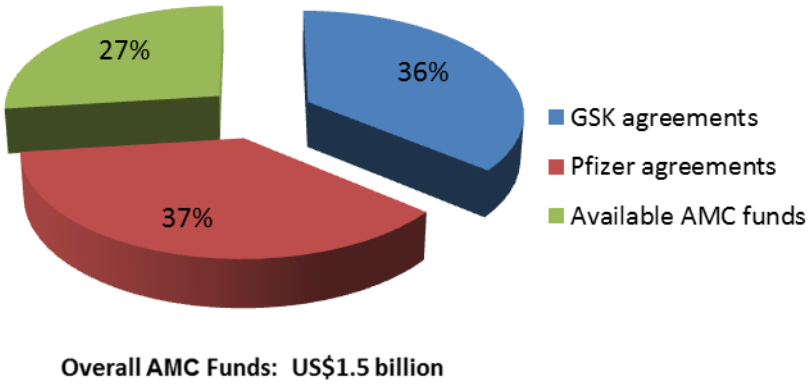
Manufacturer	Date of signature (week of)	Annual supply commitment (doses)	Tail price	Supply start date	AMC Funds allocated
GSK	23 March 2010	30 million	US $3.50	2010	US $225 million
Pfizer Inc.	23 March 2010	30 million	US$3.50; reduced to $3.40 mid 2013 and $3.30 from 2014*	2010	US $225 million
GSK	12 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) v10.0 (see Section 1.2 below), which was approved during the 2014 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 in 2015. The need for the next tender will be re-assessed by partners later in 2015 based on the AMC regulations, SDF v11.0 and the outcomes of the next rounds of applications for New Vaccines Support (NVS) to the Gavi Secretariat.

1.3. 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[viii]	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**

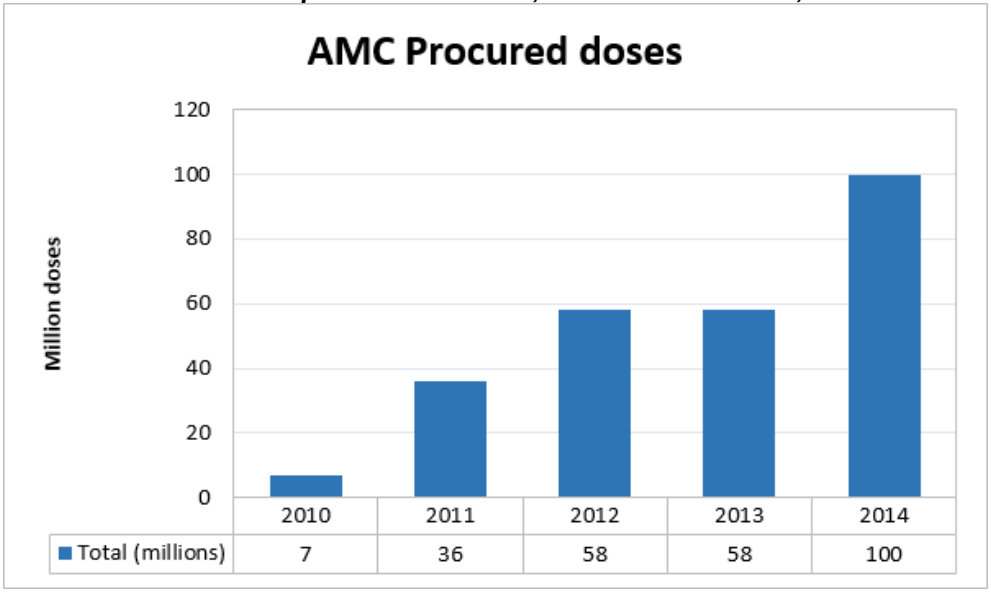
Source: UNICEF Supply Division
** Contracts are amended annually based on actual supply and demand to ensure that the total quantity on the supply agreements remain unchanged. Note: some numbers may appear not to add due to rounding.*

[viii] *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").*

1.4. Doses procured between 2010 and 2014

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

Figure 2. Pneumococcal vaccine procured volumes, in millions of doses, 2010-2014



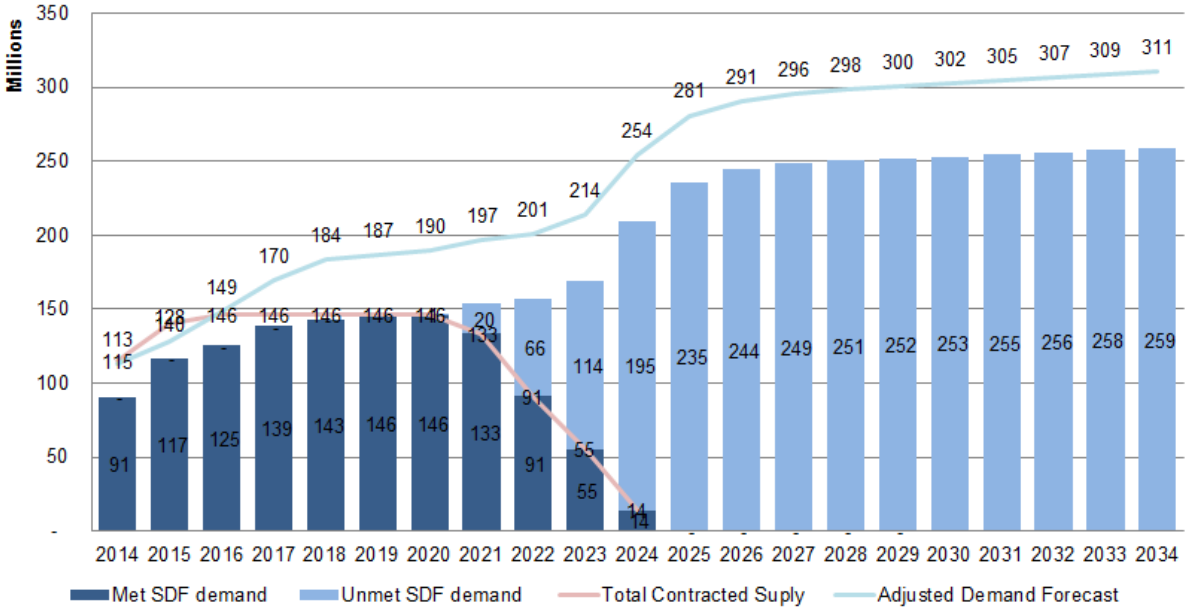
Source: UNICEF Supply Division. Please note that the figure above indicates the number of doses placed on purchase orders during the respective years, including for delivery in a subsequent year.

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

1.5. Strategic Demand Forecasts

The Strategic Demand Forecast (SDF) v10.0 was finalised in October 2014. Figure 3 shows two scenarios of the demand forecast, an SDF base case using the same data sources for surviving infant population and vaccine coverage as previously used, and an "adjusted demand forecast" (ADF) using country estimates as data sources, against contracted supply. The ADF is produced to reflect the volume of PCV doses which have been financially committed by Gavi to countries that have already been approved for Gavi support, based on their applications to Gavi. For countries that have not yet applied or for the period beyond existing Gavi financial commitments, figures are based on values and growth rates estimated in the SDF.

Figure 3. Strategic Demand Forecast v10.0[ix]



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

- SDF v8.0 served as a basis for consultations between the Gavi Secretariat and UNICEF to determine if a new Call for Supply Offers should be issued. The publication of SDF v8.0 was delayed until early 2014 due to discussions required to inform this decision. These included the finalisation of SDF v8.0 which projected demand below actual contracted supply for the 5 year horizon, findings from the SDF accuracy work, considerations of the Adjusted Demand Forecast with committed doses, and the recently concluded supply agreements.
- SDF v9.0 was approved by the Gavi Secretariat in April 2014 and published on the Gavi website in September 2014.[2]
- SDF v10.0 was completed in October 2014 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 will consult and reassess the need for the issuance of the next tender to meet the AMC objectives. An update of this assessment will be provided in the 2016 Pneumococcal AMC Annual Report.
- SDF v11.0 is currently being developed and will be completed in the second quarter of 2015. Further information on v11.0 will be provided in the 2016 Pneumococcal AMC Annual Report.

1.6. Availability of pneumococcal vaccines

Following the conclusion of the third tender and the signature of the third Supply Agreements in July 2013, the availability of supply continues to increase, closing the gap between supply and demand. Production capacity ramp-up proceeded slower than expected for one of the products (PCV10) in 2014 due to problems in manufacturer staff recruitment, but UNICEF SD was able to re-allocate supply to

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

countries, such that the three introductions planned for the second half of 2014, including those of two large countries, would not be further delayed due to supply. Nigeria is currently the only country where the phased PCV introduction is being planned around supply availability. The need for a fourth Call for Supply Offers will be revisited in 2015.

During this reporting period, 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 USD 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 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 3 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[3].

1.7. AMC registered manufacturers

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

Details about the registered manufacturers are confidential unless a firm agrees to have its registration made public. In 2014, there was one additional manufacturer who registered with the AMC but chose to make their registration confidential. The list of AMC registered manufacturers who have made their registration public is as follows[4]:

- 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 is actively monitoring 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 March 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 2014, with a deadline for countries to submit applications by 1 May 2014 and 15 September 2014, and one round in 2015, with a deadline of 25 January 2015. However, no new countries applied for Gavi PCV support during these three applications rounds.

2.2. Graduating and graduated countries introduction of PCV

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

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

2.3. Pneumococcal vaccine introductions

In the period between 1 April 2014 and 31 March 2015, ten countries introduced pneumococcal vaccines procured through the AMC (versus 16 in the prior reporting period). Two of these introductions were dual introductions with rotavirus vaccine (Togo and Niger).

To date, there have been 50 pneumococcal vaccine introductions and these are outlined Table 4. This represents a rate of introduction in Gavi countries more than three times faster than Pentavalent[x] vaccine introduction[xi]. With the 45th PCV introduction in Georgia in November, Gavi also reached its Strategic Goal 2011-2015 target for "Number of PCV introductions in Gavi countries" more than one year ahead of schedule. These are substantial achievements, especially considering the PCV supply constraints observed in the earlier years of the programme.

[x] *DTwP-HepB-Hib*

[xi] *More than 50 PCV introductions in Gavi countries in the first five years of the programme (2010-2015), in comparison to 14 Pentavalent vaccine introductions in the equivalent period (2001-2005).*

Of the 50 pneumococcal vaccine introductions that have taken place, 13 countries are using PCV10, whereas the remaining 37 countries are using PCV13.

Table 4. Pneumococcal vaccine introductions to date

Year	Country	Product	Status	Cumulative No.
2009	Gambia	PCV7 (donation)	Switched to PCV13 in 2011	1
	Rwanda	PCV7 (donation)	Switched to PCV13 in 2011	2
2010	Nicaragua	PCV13	Introduced in December	3
2011	Guyana	PCV13	Introduced in January	4
	Yemen	PCV13	Introduced in January	5
	Kenya	PCV10	Introduced in January	6
	Sierra Leone	PCV13	Introduced in January	7
	Mali	PCV13	Introduced in March	8
	Congo, DR	PCV13	Introduced in April (phased 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 introduction)	26
	Kiribati	PCV13	Introduced in May	27
	Angola	PCV13	Introduced in June	28
	Zambia	PCV10	Introduced in July joint intro. with measles second dose)	29
	Sudan North	PCV13	Introduced in August	30
	Moldova	PCV13	Introduced in October	31
	Lao PDR	PCV13	Introduced in October	32
	Burkina Faso	PCV13	Introduced in October (joint intro. with rotavirus vaccine)	33
	Senegal	PCV13	Introduced in November	34
	Mauritania	PCV13	Introduced in November	35
	Papua New Guinea	PCV13	Introduced in November	36
	Afghanistan	PCV13	Introduced in December	37
	Azerbaijan	PCV10	Introduced in December	38
2014	Liberia	PCV13	Introduced in January	39
	Bolivia	PCV13	Introduced in January	40
	Togo	PCV13	Introduced in June (joint intro.	41

			with rotavirus vaccine)	
	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	50

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

WHO currently recommends[xii] that catch-up vaccination be conducted as part of PCV introduction to accelerate herd protection and therefore the PCV impact on disease and carriage. However, this was not initially forecasted in the AMC and was due to the severe PCV supply constraints, so to date Gavi has not been able to provide support for catch-up vaccination.

Following the analysis carried out during the previous reporting period to identify the common hurdles faced by countries leading to introduction delays (competing priorities in the EPI, limited human resources, funding availability and product registration delays), Gavi continues to strengthen its coordination mechanism to ensure that technical assistance to countries can be delivered more efficiently and effectively. The WHO data repository, which was rolled out in 2013, has now been refined to include a specific PCV (and rotavirus vaccine) report that enables partners to better track the status of pre-introduction activities and provide support where needed. In addition, some language on product registration was added to the application guidelines and form to ensure that the registration process is started as early as possible. Bottlenecks in Gavi Secretariat's cash disbursement process have also been identified, so that disbursements for vaccine introduction grants can be made available earlier for future vaccine introductions.

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

2.4. Future pneumococcal vaccine introductions

Eight other Gavi-approved countries are expected to introduce the pneumococcal vaccines in 2015-2016. These future pneumococcal vaccine introductions are outlined in Table 5 below:

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

[xiii] *Azerbaijan, Burkina Faso, DR Congo, Mauritania, Pakistan, Moldova, Senegal, Uganda and Zambia.*

Table 5. Future planned pneumococcal vaccine introductions

Year	Country	Product	Status	Cumulative No.
2015	Lesotho	PCV13	Planned for Q2	51
	Guinea Bissau	PCV13	Planned for Q2	52
	Uzbekistan	PCV13	Planned for Q3	53
	Eritrea	PCV13	Planned for Q3	54
2016	Myanmar	PCV10	Planned for Q1	55
	Kyrgyzstan	PCV13	Planned for Q1	56
	Mongolia	PCV13	Planned for 2016	57
	Haiti	PCV13	Planned for 2016	58

In November 2014, Gavi announced three new rounds of applications for 2015, two of which for NVS applications. Table 6 shows the timeline for new application submission, review and approval. By having two NVS application rounds, there will be two windows of opportunity for countries to apply for Gavi NVS support. This is part of a Gavi-wide effort to provide more flexibility for countries and better align the application rounds with countries' timelines and planning cycles.

Table 6. 2015 Gavi NVS application timelines

	Type of support	Application submission cut-off dates	Independent Review Committee Dates	Gavi CEO or Executive Committee Decision
For all types of Gavi support	Any type of support (inc. NVS)	25 January	16 – 27 March	June 2015
	IPV and HSS	1 May	22 – 26 June	September 2015
	Any type of support (inc. NVS)	8 September	6 – 20 November	March 2016

As mentioned in 2.1 above, no countries applied for pneumococcal vaccine support in the round of January 2015.

From the 73 AMC-eligible countries, only 15 (21%) have yet to apply to access pneumococcal vaccine through the AMC. Of these, five are not eligible to apply in 2015 due to their DTP 3rd dose coverage being lower than 70% (Gavi application eligibility threshold). From the remaining ten, six are Gavi graduating and graduated countries that would need to fully finance the vaccine through the AMC, and four remain Gavi eligible and would be entitled to Gavi support. Gavi will support these countries if they wish to introduce PCV in their routine immunisation system in the near future.

2.5. Coordination and support for pneumococcal vaccine introductions

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

The PROWG members represent WHO, UNICEF SD, UNICEF Programme Division, VITACxiv and the Gavi Secretariat. The working group meets weekly by teleconference and the focus of the calls is on the following areas:

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

A list of current PROWG members is provided in Annex 3.

Given the lifecycle of the PCV programme and the evolving programme priorities, especially in the context of the new Gavi strategic cycle 2016-2020, the PROWG objectives and terms of reference will be revisited in 2015 to bring greater focus to the coverage and equity areas, as well as integrated approaches to disease prevention and control (section 2.6 below).

Technical assistance to countries in areas of application development support, vaccine introduction planning, cold chain and logistics, communication and social mobilisation, and monitoring and surveillance continues to be provided by WHO, UNICEF Programme Division, PATH and other partners.

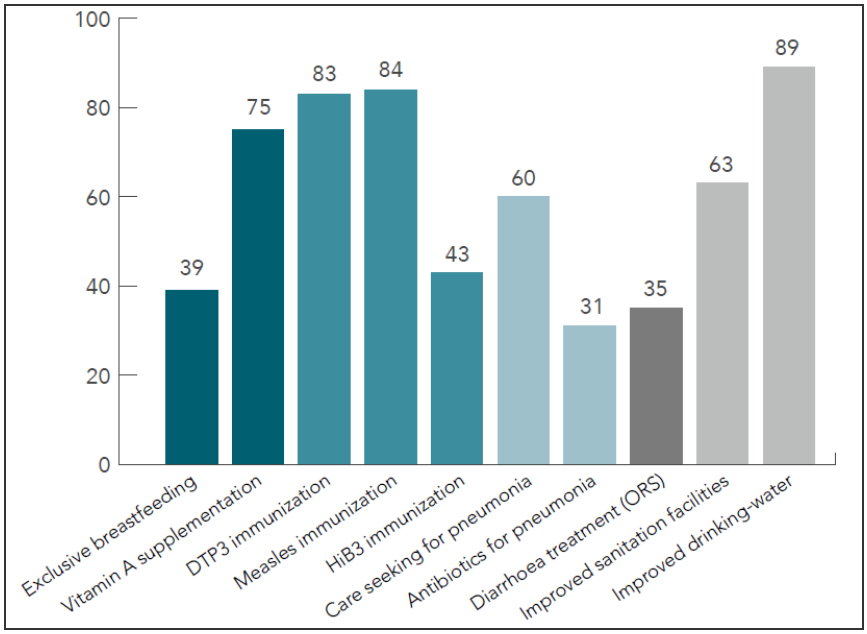
2.6. Global Action Plan for the prevention and control of Pneumonia and Diarrhoea (GAPPD)

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

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

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

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



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

The GAPPD provides a roadmap for national governments and their partners to plan and implement integrated approaches for the prevention and control of pneumonia and diarrhoea. Gavi works within this broader context and supports the advancement of GAPPD. A 2014 assessment by UNICEF indicated that 12[xv] out of the 22 Gavi countries analysed explicitly discussed integrated activities and messages about pneumonia and diarrhoea as part of their communication plan implementation. The actions focused on integrated messaging at vaccine promotion events, training sessions with community-level health workers and community members, discussions with suppliers (of ORT and zinc), and through posters and other communication media.

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.

Further efforts are underway, led by WHO and UNICEF, to pilot integration of services at the district level in selected countries (Zambia, Bangladesh, and India) in order to derive evidence-based lessons for use in national scale-up and application to other countries. An update in the progress of these pilots will be available in late 2015 and will be reported on in the 2016 AMC Annual Report.

[xv] *Afghanistan, Burundi, Ethiopia, Kenya, Mali, Mauritania, Mozambique, Niger, Sierra Leone, Tanzania, Togo and Zambia*

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.[xvi] 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.

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

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

4.1. Programme Performance Reporting

In view of the recommendations made in the 2012 AMC Process and Design Evaluation, Gavi has reviewed the existing set of indicators and has developed a comprehensive PCV results framework to be used for regular monitoring purposes. Some additional health metrics have been added to ensure more thorough and comprehensive monitoring and tracking of progress in the AMC. The Secretariat will also continue to implement the recommendation of the evaluators to regularly review and update performance indicators, and will aim to set new targets and incorporate new indicators in line with the new Gavi strategy 2016-2020.

A results framework for Gavi-supported pneumococcal vaccine and the AMC has been developed during the reporting period. 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 (based on 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

	2009	2010	2011	2012	2013	2014	2015*
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	-
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[xvii]	1[xviii]	16	24	38	40	50
Coverage of PCV in AMC-eligible/Gavi-supported countries***	0%	1%	5%	10%	19%	n/a**	n/a
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	n/a**	n/a

Source: Gavi Secretariat

** Year-to-date through 31 March 2015*

*** WUENIC coverage data and WHO-reported number of immunised for 2014 will be available in July 2015*

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

Pneumococcal vaccine coverage performance in countries continues to be closely monitored. In 2013, 3rd dose coverage amongst 73 Gavi-eligible countries was 19%, based on the WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) data[6], published in July 2014. The current projection for 3rd dose coverage in 2015 is 40%, in line with the 2015 Gavi Strategic Goal target.

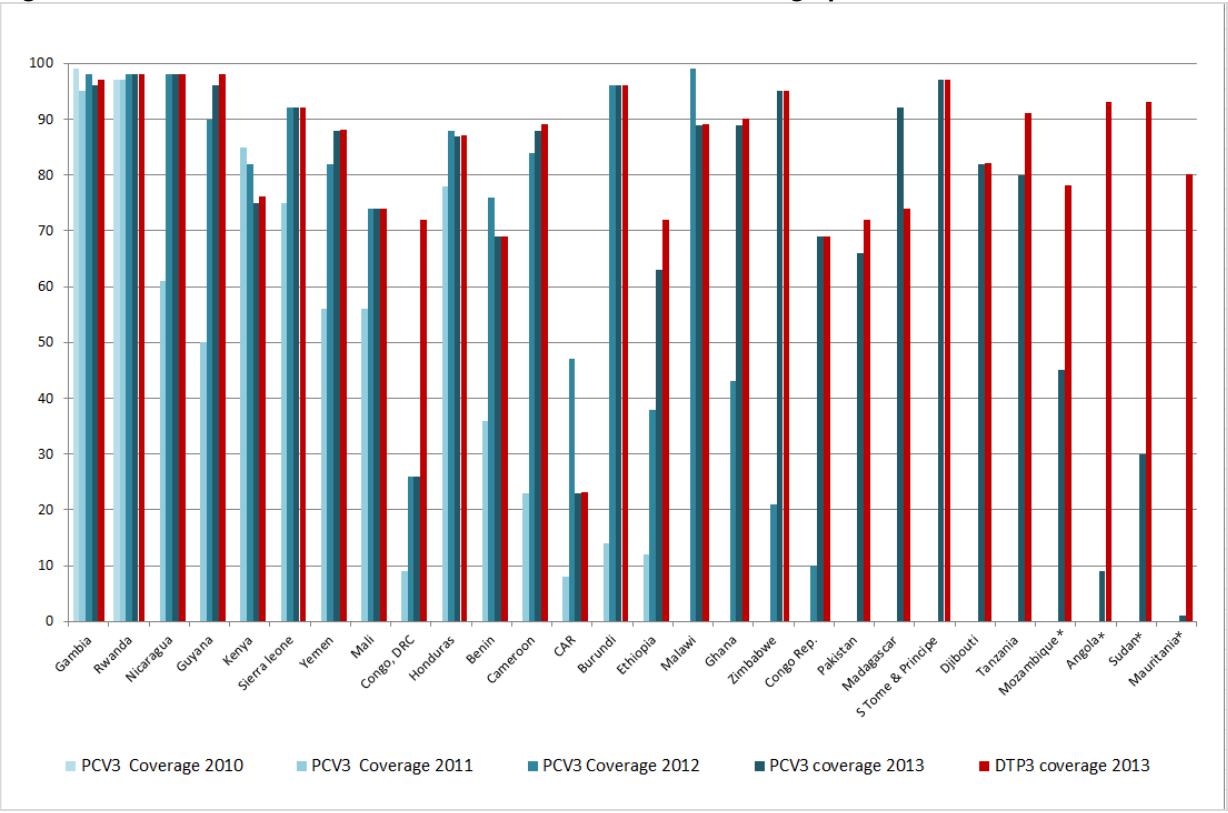
Figure 5 shows the PCV 3rd dose coverage versus DTP[xix] vaccine 3rd dose coverage in 2013 (WUENIC July 2014 data). The coverage data demonstrates that countries continue to successfully introduce PCV into their routine systems, with PCV 3rd dose coverage generally in line with DTP 3rd dose coverage by the second year of implementation. The main exceptions to this are phased introductions and mid-2013 introductions, where PCV 3rd dose coverage is still lower than that of DTP3. One area that will be closely monitored moving forward 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, one country (Nepal) has chosen to move the PCV 3rd dose administration to a later visit (9 months, with measles first dose), to avoid three injections at the 3rd DTP visit. However, the potential implications for PCV impact are not known. Further studies are being carried out to ensure that this change does not affect the immunogenicity of PCV.

[xvii] *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.*

[xviii] *Same as above.*

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

Figure 5. 2010-2013 PCV 3rd dose vs. 2013 DTP 3rd dose coverage performance[xx]



4.2. AMC Impact Evaluation

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

It is hoped that as a result of the additional time, the impact evaluation will have more relevant evidence available on the outcomes and impact of pneumococcal vaccination and country experiences (e.g. more years of PCV 3rd dose coverage estimates, more data from impact assessments, targeted studies, post-introduction evaluations and the full country evaluations). The Request for Proposals (RFP) for this independent evaluation was published in March 2015, and will be commissioned in Q2 2015 following a competitive selection process. A final report is expected in late 2015. AMC stakeholders and partners were widely consulted on the evaluation questions, design options and other methodological issues.

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

4.3. Full Country Evaluations

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

The introductions of PCV in Mozambique, Uganda, and Zambia were evaluated as part of this project and findings were reported on in the FCE Annual Report in 2013. Evaluation findings indicated that these three countries faced a number of common challenges with their introductions. The report also included a number of recommendations for the Alliance and, as a result, the Alliance published a management response to the evaluation recommendations on the Gavi website in June 2014.

The 2014 FCE Annual Report reports on findings related to PCV implementation in these three countries in 2014, and will be published on the Gavi website in Q2 2015 along with the Alliance management response; implementation will continue to be evaluated until 2016. The introduction and implementation of PCV in Bangladesh will also be evaluated through this project and reported on in the 2015 FCE Annual Report.

The work in 2013 relied mainly on process evaluation methods (including document reviews, participant observation, key informant interviews and after-action reviews). From 2014 onwards, this has been complemented with data from other evaluation components including, but not limited to, health facility surveys, household surveys and administrative data.

Results and findings from these evaluations will be made available on the Gavi website throughout the evaluation period[7].

4.4. Estimates of the impact of pneumococcal vaccination

In 2011, a multidisciplinary group with expertise in mathematical modelling was convened by Gavi, the Vaccine Alliance and the Bill & Melinda Gates Foundation to estimate the impact of vaccination in the 73 Gavi countries. A description of the methods and results from this first round of modelling was published in the journal *Vaccines* in April 2013[8]. Gavi impact estimates are updated biannually using similar methodology with the most recent round completed in early 2014. 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, and the economic benefits of vaccination (e.g. cost of illness averted). Based on current projections (SDF v.10), PCV use will avert an estimated 1 million future deaths among children vaccinated in Gavi countries by 2020. A peer-review publication with the latest impact modelling methods and estimates of economic benefit is anticipated in 2015.

4.5. Special studies on pneumococcal vaccines

Gavi is currently funding a number of special studies to help facilitate evidence-based decision making in support of the introduction and continued implementation of pneumococcal vaccines in developing countries. Studies will assess the impact of PCV on health and economic outcomes and monitor potential changes in pneumococcal serotype epidemiology. The status of these studies and key findings are provided in Annex 5.

Assessments under the PneumoADIP and the initial VI-TAC grants, which included pneumococcal vaccine effectiveness and impact studies in Kenya and South Africa, economic impact evaluations of pneumococcal vaccines in Ghana and The Gambia, and an evaluation of different PCV dosing schedules, concluded in 2013. PCV effectiveness studies in Kenya and South Africa will be continued through December 2015 under the current VI-TAC grant. The assessment of PCV impact on disease in the Gambia, funded initially by the PneumoADIP and subsequently by the Bill and Melinda Gates Foundation is ongoing.

These Gavi-funded special studies have continued to evolve the PCV evidence landscape. 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 has also shown that a variety of flexible PCV dosing schedules effectively reduce pneumococcal disease, consistent with results from the randomised controlled trials of these vaccines. In 2014, the Kenya and South Africa vaccine effectiveness studies produced several key publications indicating substantial effectiveness of PCV against vaccine serotype and all invasive pneumococcal disease (IPD) among children, as well as the broader scope of PCV impact, including herd protection and reductions in antibiotic resistant disease. The results from the impact study in Kenya have shown that widespread use of PCV may provide herd protection against pneumococcal disease by reducing transmission in both vaccinated and unvaccinated individuals[9]. Results from South Africa have shown that routine use of PCV protects children against IPD[10]. In addition, South African data has also shown routine use of PCV is effective against invasive bacterial pneumonia at a magnitude similar to that measured in randomised controlled trials, and routine PCV use is likely responsible for a significant decline in antibiotic-resistant invasive disease in the very young[11].

Assessments commissioned by Gavi to evaluate the impact of PCV in early adopting Gavi countries in Asia continued in 2014. These studies are assessing a range of outcomes, including impact on morbidity (e.g. invasive pneumococcal disease, radiological pneumonia and hospitalised pneumonia), changes in transmission (nasopharyngeal carriage), economic benefits and long-term disability in study sites in Pakistan, Nepal, Lao PDR and Mongolia. An additional study component was added to the study conducted by Oxford University in Nepal in order to evaluate the immunogenicity of the novel PCV schedule being implemented in the country (see section 4.1). Gavi recently contracted the US Centers for Disease Control and Prevention (CDC) and Agence de Médecine Préventive (AMP) to assist Burkina Faso in assessing the impact of PCV introduction on pneumococcal meningitis and changes in serotype distribution. Pneumococcal vaccine effectiveness studies will also be conducted in Bangladesh and Mozambique as a component of the Full Country Evaluations (FCE) work. Data collection for these studies began in late 2013 and early 2014, with all studies successfully reaching enrolment targets for 2014 and several beginning data analysis in 2015. Results of these studies are anticipated in 2016-2017.

These assessments of pneumococcal vaccines in selected epidemiologic settings will help to further assess the health and economic impact of vaccination on the burden of pneumococcal disease among Gavi countries. The findings of these studies will be key inputs to the planned AMC Impact Evaluation.

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 50 countries have now introduced pneumococcal vaccines in their national immunisation schedule.

5.1. Communications overview 2014-2015

Gavi continues to highlight and explain the AMC in relevant communications materials, particularly around pneumococcal vaccine launches. 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.

A major Gavi-supported study was published in the Pediatric Infectious Disease Journal (PIDJ) supplement. The "PCV Dosing Landscape Study" – led by the US Centers for Disease Control and Prevention, Johns Hopkins' International Vaccine Access Center and the University College London's Institute for Child Health – represents the most comprehensive review of dosing schedules to date. Outcomes from this analysis were shared with the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) and helped to inform WHO 2012 position paper on PCV use.

Another ground-breaking study was pivotal to develop communication materials that were broadly disseminated to the media, partners and stakeholders. Published in Lancet Global Health, researchers from Kenya found that widespread use of PCV reduces carriage of the pneumococcal bacterium in both vaccinated and unvaccinated individuals and is therefore expected to provide herd protection against pneumococcal disease. The research was conducted by KEMRI, Johns Hopkins Bloomberg School of Public Health, University of Oxford, Kenya Ministry of Health and the London School of Hygiene & Tropical Medicine. It was funded by Gavi and the Wellcome Trust.

On World Pneumonia Day 2014, Gavi highlighted the record number of children protected against the leading cause of pneumonia as countries strengthen their immunisation programmes. The latest figures released by Gavi on the 6th World Pneumonia Day showed that in 2013 alone, 15 million children were immunised with pneumococcal conjugate vaccine (PCV), bringing to 25 million the total of children who have received PCV since the first Gavi-supported introduction in 2010.

A number of pneumococcal vaccine launches were marked with press releases or feature stories in 2014, including a particular focus on Liberia.

5.2. Communications outlook for 2015-2016

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

The AMC impact evaluation will be a key moment for communicating about the mechanism and what it has helped Gavi and developing countries to achieve. A full communications plan will be developed and relevant media and other communications stakeholders will be briefed.

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.

5.3. Donor & stakeholder communication

In 2014, additional efforts were made to provide updates to AMC stakeholders, through regular AMC stakeholder calls and an annual AMC stakeholder meeting. These provide opportunities to exchange information and input on key issues. These included updates on the strategic demand forecast and implications, PCV roadmap development, revised disease burden and impact estimates progress on implementation, the progress on AMC targets and supply and rollout of vaccines. With regards to vaccine introductions, AMC donors were kept informed of progress and invited to participate in the vaccine launch events.

In May 2014, Gavi attended the event at IFAD that was co-organised with the Ministry of Economy and Finance of the Italian Republic (MEF), and the World Bank called "Pull Mechanisms: From the Health to the Agricultural Sector". Given the success of the AMC for pneumococcal vaccine, there has been interest in exploring the application of AMC mechanisms to other areas including, agriculture research and smallholder agriculture. The event at IFAD aimed to showcase the experience of AMCs from the perspective of different stakeholders (donors, recipient governments, International Finance Institutions and Development Finance Institutions, commercial banks and private sector agricultural suppliers, processors and value chain operators, agriculture and farmers associations, NGOs and civil society representatives) and provided a platform for discussing the feasibility and challenges of this instrument in smallholder agriculture in developing countries.

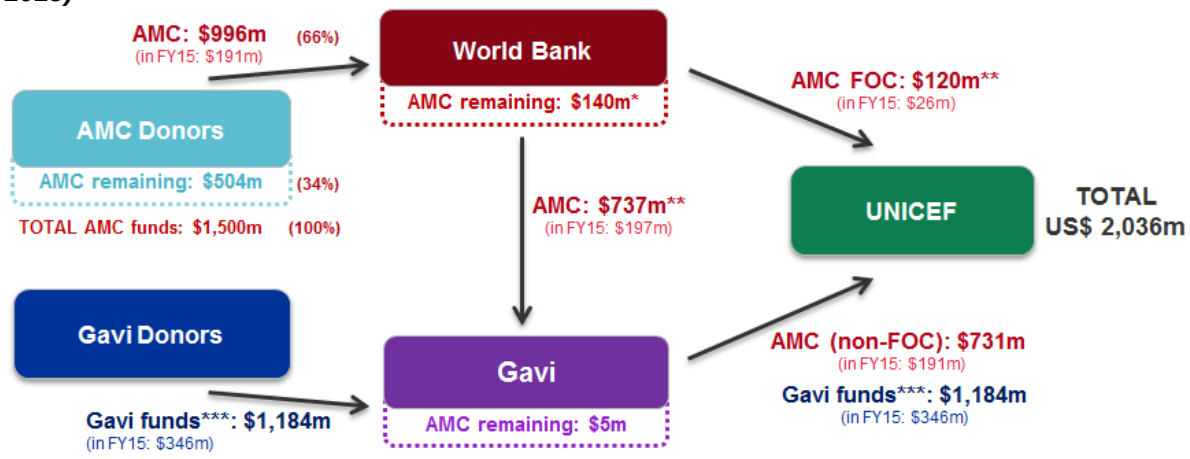
6. Financial Activities

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

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 6. Summary of AMC Financial Process Flow and funds disbursed (inception to 31 March 2015)



'FY15': AMC Fiscal Year 2015 (1 April 2014 – 31 March 2015)
** Includes $52m of Canadian Initial Funds, not yet available for disbursement*
*** Includes US$ 10.5m conversion from FOC to regular / 'non-FOC' funds, effected after receipt of funds from the World Bank (see footnote ii in text)*
**** 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.

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

6.1.1. Donor contribution receipts

As of 31 March 2015, the World Bank had received a total of US $996 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 March 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	370	265
Russian Federation	80	48	32
sub-total:	**765**	**468**	**297**
On Demand Donors			
Canada	200	200	-
Norway	50	50	-
United Kingdom	485	278	207
sub-total:	**735**	**528**	**207**
Total	**1,500**	**996**	**504**

Source: The World Bank

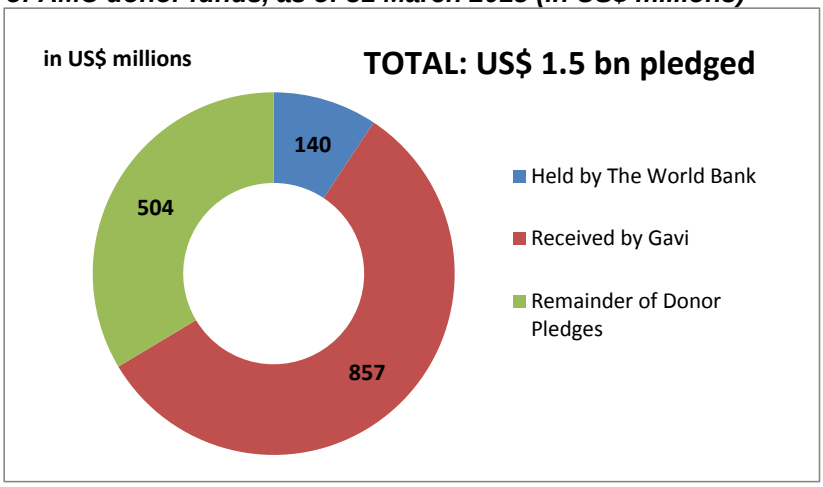
The World Bank has recorded the AMC donor funds in its financial statements as designated assets, with a corresponding liability to provide the funds to Gavi for the purchase of pneumococcal vaccines subject to the terms and conditions of the AMC. To enhance the predictability of AMC funding, the World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

AMC donor funds: inflow to Gavi

As of 31 March 2015, the World Bank had disbursed US $857 million (US $737 million to Gavi and US $120 million directly to the UNICEF procurement account relating to the Firm Order Commitments)[xxii]. Of the US $857 million, US $223 million was disbursed from 1 April 2014 – 31 March 2015 (US $197 million to Gavi and US $26 million directly to the UNICEF procurement account relating to the Firm Order Commitments). This leaves a balance of US $140 million held by the World Bank, of which US $88 million is available for immediate disbursement to Gavi (see figures 6 and 7).

Figure 7. Status of AMC donor funds, as of 31 March 2015 (in US$ millions)



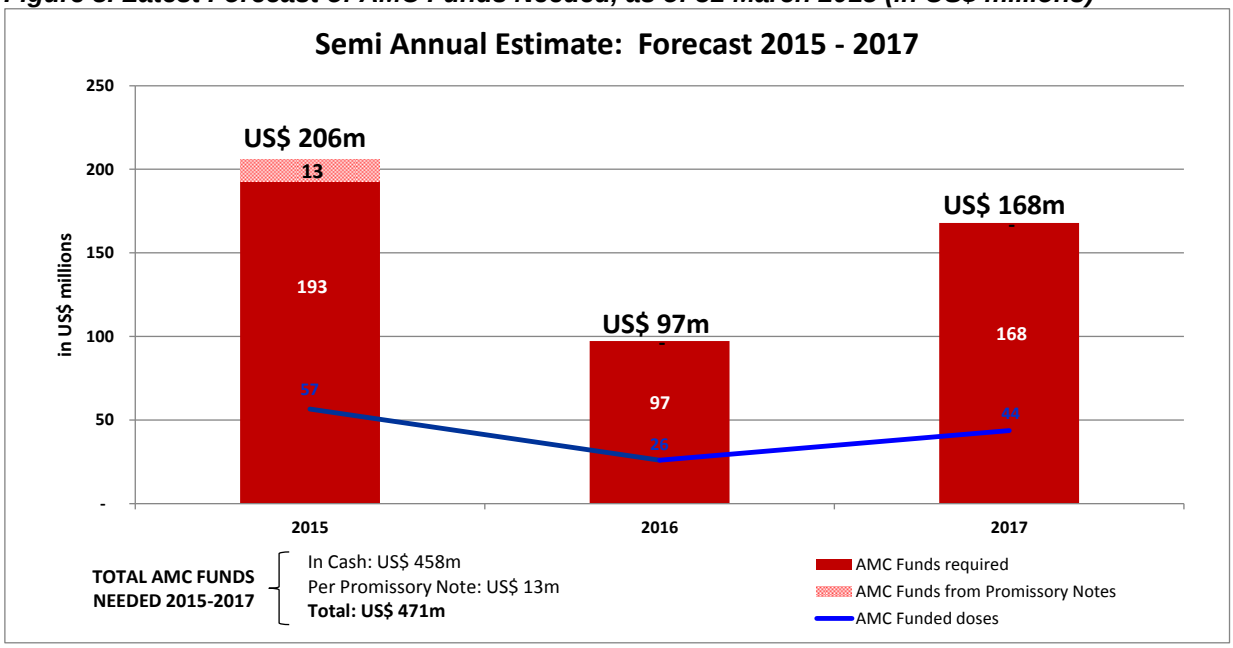
Source: Gavi Secretariat

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 the reporting period (in May 2014 and in November 2014), the latest of which forecasted a need for US $471 million of AMC funds, including US $13 million from Promissory Notes[xxiii], to procure 126 million doses of the pneumococcal vaccine between 1 January 2015 and 31 December 2017.

[xxii] *During 2014, the first GSK supply agreement received all of its AMC top-up funds without requiring the final tranche of FOC funds allocated to the agreement (US$ 10.5m), which had already been transferred by the World Bank on September 30, 2013 to a dedicated FOC bank account. As such, the full US$ 10.5m was converted to regular / 'non-FOC' AMC funds to be used for vaccine purchases under all supply agreements under the AMC that are still entitled to receive AMC top-up. The totals for FOC and 'non-FOC' funds have been thus adjusted by this US$ 10.5m throughout this report.*

[xxiii] *Each supply agreement contains a minimum purchase obligation known as a 'Firm Order Commitment' (or 'FOC' - see also Section 6.2), a portion of which is paid from AMC funds. In accordance with UNICEF's procurement process, FOC funds must be transferred to a dedicated UNICEF procurement account prior to the signature of a supply agreement. However, the Promissory Note allows the AMC portion of the FOC funds to be transferred directly from the World Bank to the UNICEF Procurement Account as per an agreed upon schedule.*

Figure 8. Latest Forecast of AMC Funds Needed, as of 31 March 2015 (in US$ millions)



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

6.2. UNICEF procurement: outflow of AMC donor funds

From 1 April 2014 to 31 March 2015, US $564 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US $218 million was from the AMC funds to pay for the AMC top-up portion of the vaccine purchase. The remaining US $346 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[xxiv]. Total funds include the transfers relating to the AMC-funded portion of the minimum purchase obligation, also known as the Firm Order Commitment (FOC), on the GSK & Pfizer supply agreements amounting to US $26 million (see Figures 6 and 9). From inception of the programme through 31 March 2015, a total of US $2,036 million has been disbursed for the procurement of pneumococcal vaccines through the AMC (US $851 million was AMC-funded and US $1,184 was Gavi-funded).

Six supply agreements have been signed under the AMC programme, to date.[xxv] The AMC funds allocated under the first Pfizer agreement and the first GSK agreement, both signed in 2010, 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 three of the four remaining supply agreements (the second Pfizer, the second GSK and the third Pfizer) will be fully disbursed during 2015. The remaining supply agreement (the third GSK) will continue to receive AMC funds through 2016.

In total, as at 31 March 2015 US $344 million has been transferred to Gavi's 'UNICEF procurement account' regarding the FOCs for the six existing signed supply agreements and related Promissory

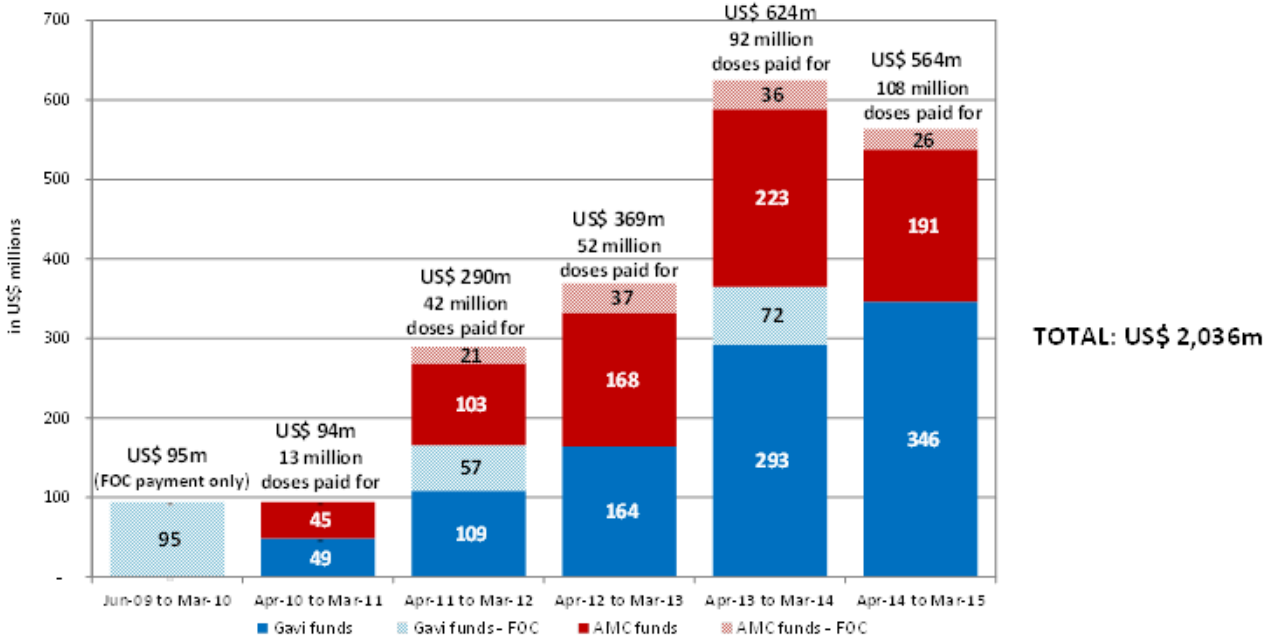
[xxiv] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US $0.19 per dose), in addition to the cost of the vaccine itself. These costs typically include the cost of syringes, safety boxes and freight.*
[xxv] *For details refer to Section 1.2 and Annex 1*

Notes. Of this amount, US $223 million represents the Gavi-funded portion of the FOCs and US $120 million represents the AMC-funded portion of the FOCs. Of the US $344 million transferred, US $263 million (approximately 76%) has been utilised and this represents the draw-down of already transferred FOC funds relating to the first five supply agreements.

Figure 9. Total cash disbursements to Gavi's 'UNICEF procurement account', (inception to 31 March 2015, in US $ millions)[xxvi]

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	TOTAL	of which: AMC / Gavi	of which: FOC	of which: Non-FOC
AMC Funds - FOC	-	-	21	37	36	26	120	851	120	
AMC Funds	-	45	103	168	223	191	731			731
Gavi Funds - FOC	95	-	57	-	72	-	223	1,184	223	
Gavi Funds	-	49	109	164	293	346	961			961
TOTAL:	95	94	290	369	624	564	2,036		344	1,692



TOTAL: US$ 2,036m

Source: Gavi Secretariat. Note: For the period April 14 – March 15, "108 million doses paid for": the total number of doses has increased from the previous year while the overall amount paid has decreased. This is due to a higher proportion of doses being procured under the Gavi-funded tail price only (46.5m doses [43% of total doses] for FY 2015 vs. 20.7m doses [23% of total doses] for FY 2014). Some numbers may appear not to add due to rounding.

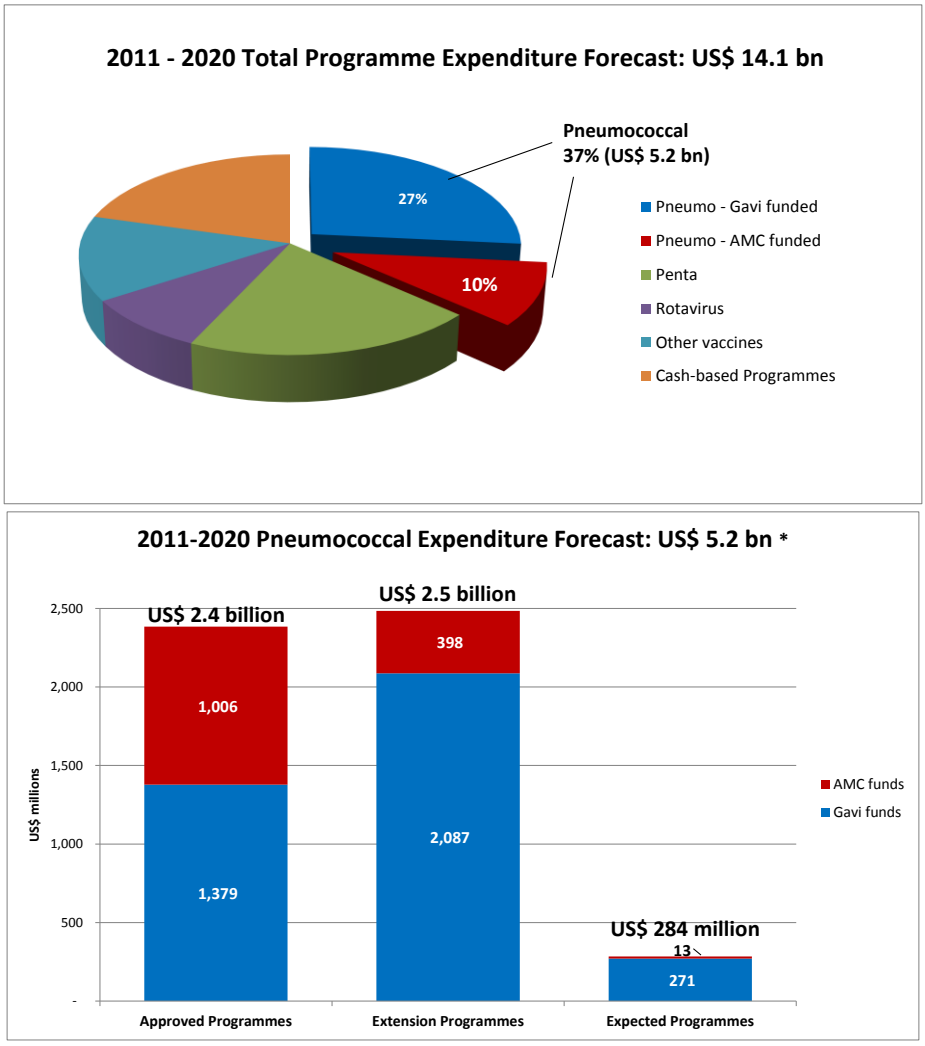
[xxvi] *Includes all CTNs received from UNICEF as of 20 February 2015.*

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

At the December 2014 Gavi Board meeting, an update was presented of Gavi's Long Term Financial Forecast.[xxvii] Total programme expenditures are projected to be US $6.3 billion and US $7.8 billion for the 2011-2015 and 2016-2020 periods, respectively; an overall total of US$ 14.1 billion for the 2011-2020 period. Of this US $14.1 billion, pneumococcal vaccine expenditures are anticipated to amount to US $5.2 billion, representing approximately 37% of total programmatic expenditures (see Figure 10).

For the 2015 and 2016 programmatic years, 53 countries had been approved to receive financial support for the procurement of pneumococcal vaccine. The 2015 commitments amount to US $704 million and 2016 commitments amount to US $181 million. The commitments are included as part of the total 2011-2020 "Approved Programmes" amounts presented in Figure 10 below.

Figure 10. 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 v10.0 and the latest supplier assumptions.*

[xxvii] *December 2014 Board Paper entitled "Board-2014-Mtg-3-Doc 09 Financial Forecast and 2015 Programme Funding Envelope Approvals "*

7. Challenges and Future Priorities

Country demand for the pneumococcal vaccines has been high, with 58 (79%) of the 73 Gavi-supported countries already approved for introduction. With 50 countries having introduced PCV since programme start in 2009, the priorities moving forward will be focused on supporting the 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, especially as countries start to graduate from Gavi support. Reducing the price of pneumococcal vaccines and ensuring proper balance of supply and demand remain key priorities.

7.1. Supporting country implementation and measuring impact

As the supply situation has now stabilised, efforts are focused to ensure that the eight remaining Gavi-approved countries are ready to introduce pneumococcal vaccines and that technical assistance is provided where appropriate to ensure high quality and continued acceleration of implementation. Alliance partners are reviewing country introduction status and coordinating technical assistance activities, with the aim of identifying and resolving issues with the support of the partners working at the country level.

Another priority is to support the application, introduction and implementation of pneumococcal vaccines in some of the AMC-eligible countries that have not yet applied for pneumococcal support. Although some of these AMC-eligible countries are not considering introducing pneumococcal vaccine in the near future (e.g. due to low disease burden), and others are not eligible to apply due to >70% DTP 3rd dose coverage eligibility criteria, there is a subset of countries that remains eligible and where burden of disease is high.

Vaccine programme implementation in countries that have already introduced PCV will continue to be closely monitored to identify issues in coverage performance. Lessons drawn from these countries can inform future pneumococcal vaccine introductions, as well as the roll-out of other vaccines. Broader efforts are on-going at Gavi to support health systems strengthening work, and in particular supply chain management, to improve coverage performance of routine immunisation programmes and ensure programmatic and financial sustainability in countries. 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.

A focus on gathering evidence on vaccine effectiveness and impact will continue, through Gavi-supported special studies. The AMC Impact Evaluation is also taking place in 2015 to assess the achievements of the AMC pilot. The results of this will be reported in the 2016 AMC Annual Report.

7.2. Managing supply and demand

Thanks to the AMC, manufacturers have entered into 10+ year supply agreements, which is unique for a Gavi-supported vaccine. This provides assurance that manufacturers would invest in scaling up production capacity and that supply would be available to meet long-term demand from countries. 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 contracted quantities. The coming years will demonstrate the ability of the limited supplier base to continue to meet the requirements. As the demand increases to 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.

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). So far, AMC procurement mechanisms achieved a 'tail-price' reduction of at most 6% from the initial 'tail-price' cap of USD 3.50/dose. Thus, the price of the vaccine is currently challenging for sustainable pneumococcal vaccination in most Gavi-supported and Gavi-graduated and graduating countries.

8. Conclusion

With the eight introductions in AMC-eligible countries during the reporting period, the 2015 target for number of pneumococcal introductions was reached in November 2014, more than one year ahead of schedule. 50 AMC-eligible countries have now introduced pneumococcal vaccines, and eight more are planning to introduce in the next two years.

Therefore, the pneumococcal vaccines procured through the AMC have an increasingly significant reach and impact. Third dose PCV coverage was 19% in 2013, a 9 percentage point increase from the previous year, and is projected to reach 40% 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.

Although the supply situation has improved with the addition of contracted doses in the Third Supply Agreements, the limited supply base remains a concern; therefore, the balance of supply and demand will continue to be carefully managed.

Furthermore, as countries enter the route to graduation from Gavi support, programme sustainability also becomes an area of increased focus for the Alliance. Gavi will continue to support special studies and continue to encourage countries to demonstrate the impact of pneumococcal vaccines in order to ensure that countries sustain PCV programme implementation in the years following graduation.

Annex 1 – Membership of the AMC Secretariat

Team	Staff member
Vaccine Implementation	**Carol Szeto** (until November 2014) Senior Programme Manager **Johanna Fihman** (November 2014 – January 2015) Senior Programme Manager **Melissa Ko** (February 2015 – present) Senior Programme Manager (Maternity replacement for Johanna Fihman) **Sara Sá Silva** Vaccine Programme Manager
Resource Mobilisation	**Ariane McCabe** Senior Manager
Finance	**Eric Godfrey** Senior Manager, Financial Planning, Analysis and AMC
Monitoring & Evaluation	**Laura Craw** Senior Programme Manager, Grant Performance Monitoring
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

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[xxviii] 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.

[xxviii]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 remain unallocated following the completion of the second Call for Offers and will be available for successive rounds of calls for offers.

Third AMC Supply Agreements

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

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

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

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

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

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

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

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

Annex 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	**Carol Szeto** (until November 2014) Senior Programme Manager, Vaccine Implementation, Country Programmes **Johanna Fihman** (November 2014 – January 2015) Senior Programme Manager, Vaccine Implementation, Country Programmes **Melissa Ko** (February 2015 – present) Senior Programme Manager, Vaccine Implementation, Country Programmes (Maternity replacement for Johanna Fihman) **Sara Sá Silva** Vaccine Programme Manager, Vaccine Implementation, Country Programmes
PATH	**Candace Rosen** Senior Policy and Advocacy Officer (representing VI TAC)[xxix]
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 **Gideon Chelule** Contracts Manager **David K. Mutuerandu** Contracts Manager **Sonia Freitas** Contracts Specialist (alternate member)
WHO	**Carsten Mantel** Leader – Priority Area New Vaccines and Innovation

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

	Hemanthi Dassanayake-Nicolas Technical Officer – Strategic Information Group, EPI **Alejandro Ramirez Gonzalez** (October 2014 – present) Technical Officer – Programme Operations, EPI **Isaac Gobina** (October 2014 – present) Technical Officer – Programme Operations, EPI

Source: Gavi Secretariat, as of 31 March 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 March 2015

Annex 5 – Summary of Gavi investments in PCV impact assessments

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

Study	Status of Activities	Key findings
A. WHO Surveillance		
Coordinated global surveillance networks for Invasive Bacterial Vaccine Preventable Diseases (IB-VPD)	Ongoing	The RV and IB-VPD surveillance networks represent the largest Gavi surveillance investment. In 2013, the WHO initiated a number of activities to strengthen the quality and use of the data generated through the global RV and IB-VPD surveillance networks with guidance from an informal technical advisory group (ITAG). The ITAG assisted WHO in a Strategic Review of the RV and IB-VPD surveillance networks in September 2013 to critically assess the networks and provide recommendations for the future vision for the networks, with a focus on improved data quality, enhanced country ownership and transition of the network to support country monitoring of the impact of new vaccine introductions (Hib, PCV, Meningococcal A, RV).
B. VI-TAC Special Studies		
1. Grant A-4: January 2009 - September 2013		
Landscape analysis of PCV dosing	Nine-paper supplement published in the January 2014 issue of *Pediatric Infectious Diseases Journal*. Presentations given at ISPPD 2012.	The available literature shows that each of three schedules (3+1, 3+0 and 2+1) all showed significant reductions in pneumococcal disease (IPD and/or pneumonia), and many programs also used catch-up campaigns. Choice of schedule should balance practical considerations and epidemiology, but achieving high coverage should be a primary goal to ensure herd protection. Varying study designs and epidemiologic settings made direct comparison of impact between schedules difficult.
Effectiveness of PCV7 against IPD (South Africa)	Publication in *Vaccine* 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* on effectiveness of PCV in this case-control study.	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, but insufficiently so for HIV-infected children. This may indicate the benefit of a booster dose for HIV+ children on this schedule. In addition, HIV+, malnourished, sick, and poor children are at increased risk of pneumococcal disease.
Effectiveness of PCV against presumed bacterial pneumonia	Measuring effectiveness in HIV-infected and HIV-uninfected children. Publication in *Vaccine*	In a matched case-control study, PCV7 was 39.2% effective (95% CI: 8.46-59.6%) in preventing presume bacterial pneumonia

Study	Status of Activities	Key findings
(PBP) (South Africa)	2012 highlighting study contribution to S. African policy-making. Implications: This study can inform the evidence gap on the impact of PCV on x-ray confirmed childhood pneumonia in developing-country settings. Poster displayed at ISPPD 2014. Manuscript submitted to *Thorax* in Q4 2014.	(defined as consolidation on chest X-ray) in children 3 months to 2 years of age, under conditions of routine use and using a hospital control group for comparison. The effectiveness estimates were of similar magnitude to those found in the more controlled environment of randomized trials to measure vaccine efficacy. This is the first published study on the impact of PCV on pneumonia in conditions of routine use in Africa or South Asia.
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. Presentations at the International Rotavirus Symposium and 8th Vaccine & ISV Conference. Manuscript under development for both RV (planned for submission Q1 2015) and PCV (completion of first draft by in Q3 2015) and study arms.	Results of the RC study arm show a 47% reduction in diarrheal hospitalizations in children under 5 years of age following rotavirus vaccine introduction. The reduction was most marked in children under one year of age, and reductions occurred in both HIV-infected and HIV-uninfected children. The pneumonia study arm is still working to sort through significant data complexity in order to reach final conclusions.
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 was completed (see Key Findings). Poster displayed at ISPPD 2014. Manuscript for the cost of pentavalent and pneumococcal conjugate vaccine delivery in the Gambia before and after introduction published in April 2014 in *Vaccine*. Manuscript for economic burden of gastroenteritis in Ghana in development and submission expected by Q2 2014. Manuscript for the Gambian pneumococcal economic impact study is expected to be complete Q2 2015.	Economic impact of PCV introduction in The Gambia: The total incremental cost for transition to pentavalent and introduction of PCV together in The Gambia in 2009 amounted to $1,616,943 or $24.22 per fully-immunised child. Savings from the switch from tetravalent to pentavalent vaccine slightly offset the large additional cost of introducing PCV. The Gambian gov't assumed 16% of the added systems costs of the two vaccine schedule changes, while donor agencies contributed the remainder – Gavi (52%), UNICEF (31%), WHO (1%, plus significant staff time contributed for training).

Study	Status of Activities	Key findings
2. Grant A-11: September 2012 – December 2015		
PCV10 Impact (Kenya)	This is a continuation from the PneumoADIP PCV impact evaluation in Kenya. Implications: The inclusion of follow-on surveillance under VITAC provides the opportunity to establish a causal link between PCV10 and IPD incidence and generate additional data that will illustrate the effects of PCV introduction. 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.	Dramatic reductions in the incidence of vaccine-type invasive pneumococcal diseases (IPD) among children less than five years of age have been shown since PCV10 was introduced in 2011. As of December 2014, four years after vaccine introduction, there had been only one case of VT-IPD in 2014 among Kilifi Health and Demographic Surveillance System residents less than 5 years of age. The nasopharyngeal carriage study has shown that introduction of PCV10 in a developing country setting with a catch-up campaign has led to a two-thirds reduction in prevalence of vaccine-serotype pneumococci carried in both children targeted for vaccination & in older people who were not vaccinated.
PCV13 Effectiveness (South Africa)	This study is a continuation of B.1. The continuation extends the effectiveness of PCV13 in South Africa, which has replaced PCV7. Future publications expected.	Preliminary findings from B.1 reveal that use of PCV7 even in conditions of routine use and with high pneumococcal transmission, is highly effective for HIV-uninfected children, but insufficiently so for HIV-infected children. This may indicate the benefit of a booster dose for HIV+ children on this schedule. In addition, HIV+, malnourished, sick, and poor children are disproportionately struck by pneumococcal disease. The data on the PCV13 effectiveness study are still being accrued.
C. Hib Initiative Special Studies		
1. Grant: July 2005 – March 2014		
Invasive Bacterial Disease surveillance in India	Bacterial meningitis surveillance is ongoing at 3 sites. In addition to 1 paper in JID (above) 2 standalone papers have been published. 3 sub-studies are ongoing: retrospective analysis of stored CSF samples with real-time PCR assay, chart review at Chennai of all-cause pneumonia admissions to investigate potential decrease following Hib vaccine introduction, and NP carriage survey of Hib and *S. pneumoniae* at ICH.	Number of confirmed Hib meningitis cases at ICH, Chennai surveillance site has decreased by 82% since the vaccine was introduced in Tamil Nadu in Dec. 2011.
Hib and PCV impact in Pakistan	Bacterial meningitis surveillance is ongoing in 4 sites originally to measure the impact of Hib vaccine and has been extended to assess the early impact of PCV introduction on bacterial	Cases of Hib meningitis have almost disappeared since pre-Hib introduction time period and studies illustrate the long-term community impact of bacterial meningitis overall, including neurologic sequelae.

Study	Status of Activities	Key findings
	meningitis and nasopharyngeal carriage.	
D. PneumoADIP Special Studies		
1. Grant: March 2004 - December 2013		
PCV Impact in Kenya	Rolled over to VI-TAC.	
PCV Impact in The Gambia	Rolled over to VI-TAC in part (for economic analyses); additional continuation funding provided by GATES. This is a continuation of the Gambia PCV7 Impact study and is now evaluating the impact of PCV13.	
Cost-effectiveness of PCV catch-up	Analysis of the impact and cost-effectiveness of PCV catch-up among under-two year olds (current WHO recommendations) in Gavi-eligible countries. In this analysis, two models developed: a disease transmission model and an economic benefits model. Full integration of Kenya SIT model insights have been completed. Outputs of the cost-effectiveness model are pending. Auditing and evaluation have been completed for the disease burden and vaccine effectiveness sub-models and are ongoing for the resource utilization and costing sub-models. Preliminary results for the full economic benefits model anticipated by Q4 2015.	Preliminary results from disease transmission model found that rapidly increasing the protection in the community via catch-up campaigns not only leads to more rapid reduction in the IPD burden but also increases efficiency of the vaccine schedule in the first years after vaccination through rapid establishment of herd protection in the unvaccinated population. However, once routine vaccination has established herd protection, it is similarly efficient as catch-up campaigns. Any catch-up campaign, particularly among under two and five year olds, is likely to additionally prevent a high number of IPD for comparatively few extra vaccine doses in the first years after vaccination.
Economic value of vaccination in India	*The overarching goal of this analysis was to look at the potential health impact and costs averted through immunization with three vaccines—Hib, PCV, RV* vaccines. The project aimed to generate new evidence on the health and economic benefits of these vaccines *at the national level & in four states in India (Bihar, Delhi, Maharashtra, Tamil Nadu).* The analysis generated new evidence in 3 categories: (i) death & cases averted; (ii) disease costs averted; and (iii) productivity loss averted. 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%).

Study	Status of Activities	Key findings
E. Other Gavi Targeted Assessments		
1. PCV Effectiveness in Asia		
Impact of PCV-10 on IPD in Lower Sindh, Pakistan (Aga Khan University)	*Case-control study and IPD surveillance: Enrolment begun and field visits conducted at key sentinel sites except in Karachi due to security conditions. Sample sizes being re-calculated while plan of analysis is developed, with the potential for identification and inclusion of additional high-yield sites.* *NP Carriage: field work and serotyping complete; plan of analysis being developed with planned commencement of analysis in Q4 2014.* *Coverage Survey: Data is complete and cleaned – preliminary analysis begun.* *Vaccine Promotion: Implementation strategy being finalized; rapid formative research in selected districts proposed while detailed methodology, SOPs and analysis plans are being prepared.*	*Study findings anticipated in 2016.*
Impact of PCV on nasopharyngeal carriage in Nepal (Oxford University)	*PCV Impact (Healthy, Urban): Enrolment begun in April 2014; recruitment goals met for 2014. Amendment to collect samples in rural Eastern district approved in December and logistical planning begun with enrolment completion estimated for early 2015* *PCV Impact (Pneumonia): Continuous enrolment began March 2014 and there are currently 239 children enrolled. Urine is being collected and stored in case of successful development of a serotype specific urine assay, Serotyping of isolates has started.* *Surveillance: continues unchanged since 2005* *PCV Impact (administrative data): Anticipated to begin in 2015.*	*Study findings anticipated in 2018.*
Impact of PCV introduction on hospitalised pneumonia cases and nasopharyngeal carriage rates in Lao	*Pre-PCV13 data collection is complete as of 2014 and serotyping analysis of collected isolates has begun (projected to be available by mid-2015). Post-PCV13 carriage survey is in*	*Study findings anticipated in 2017.*

Study	Status of Activities	Key findings
PDR (Murdoch Children's Institute)	*planning stage and will commence in November 2015. The retrospective pneumonia review has been approved by all required governmental agencies and data collection has begun, but progress has been delayed due to a delay in release of funds, disorderly medical records, and change of personnel.*	
2. Centers for Disease Control and Prevention (2013-2014)		
Evaluating the impact of PCV in Burkina Faso	*An estimated 1800 retrospectively collected pneumococcal cultures and CSF specimens were collected from national meningitis surveillance from 2009-present day, while CDC has developed procedures for documenting PCV vaccination status of all PCV13-eligible cases of pneumococcal meningitis that has occurred since October 31, 2013. Data analysis plans are being developed.*	*Analysis of pre-vaccine introduction data anticipated in 2014.*
3. Full Country Evaluation (2013-2016)		
3.1 Evaluating the impact of PCV on nasopharyngeal carriage, IPD and x-ray confirmed pneumonia in Mozambique	*Data collection is ongoing.*	Study findings anticipated in 2016.
3.2 Impact of PCV on nasopharyngeal carriage in Bangladesh	*Nasopharyngeal carriage study to begin in 2014.*	Study findings anticipated in 2016.

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