ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

Annual Report

1 April 2011 – 31 March 2012

Prepared by the GAVI Alliance Secretariat

Contents

Abbreviations

AMC	Advance Market Commitment
AMT	AVI Management Team
AVI	Accelerated Vaccine Introduction
EC	GAVI Executive Committee
FOC	Firm Order Commitment
GAVI	GAVI Alliance
GNI	gross national income
IAC	Independent Assessment Committee
IRC	Independent Review Committee
M&E	monitoring and evaluation
NRA	national regulatory authority
NVS	new vaccine support
PATH	Program for Appropriate Technologies for Health
PCV	pneumococcal conjugate vaccine
PRG	Procurement Reference Group
PSA	Provisional Supply Agreement
PSF	Product Summary File
QSS	WHO Quality, Safety and Standards
SDF	Strategic Demand Forecast
TPP	Target Product Profile
UNICEF	United Nations Children's Fund
WHO	World Health Organization

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Background

Advance Market Commitments (AMCs) for vaccines aim to encourage the development and production of affordable vaccines tailored to the needs of developing countries. Following the announcement of the Governments of Italy, the United Kingdom, Canada, the Russian Federation, Norway and the Bill & Melinda Gates Foundation, who collectively pledged a total of US$ 1.5 billion to fund the programme, the pneumococcal AMC pilot was designed to stimulate the late stage development and manufacture of affordable pneumococcal vaccines for the poorest countries.

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

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

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

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

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

The Pneumococcal AMC entered its implementation phase on 12 June 2009. Since then, the first vaccines became available for procurement under the AMC terms and conditions and the first roll-out occurred in Nicaragua in December 2010. Within two years, nearly 70% of GAVI supported countries have planned for pneumococcal vaccine introduction and submitted applications to GAVI for financial support.

On 13 June 2011, the GAVI Alliance received a strong vote of confidence from the donor community as US$ 4.3 billion were pledged, bringing to US$ 7.6 billion the total resources available to GAVI for the period 2011 to 2015. Major public and private donors achieved a milestone in global health by committing funding to immunise by 2015 more than 250 million of the world's poorest children against life-threatening diseases. From a financial perspective, therefore, the GAVI Alliance is now well positioned to support countries in their efforts to accelerate the roll out of existing and new vaccines, reach more children in developing countries, and prepare and expand introduction of new vaccines.

The purpose of the report is to provide an update on AMC implementation activities, including procurement activities, delivery of vaccines, monitoring and evaluation activities, media and communications work, and all financial reporting. This report is the third pneumococcal AMC Annual Report[a] and covers all activities from 1 April 2011 to 31 March 2012.The report was developed by the

[a] The first and second pneumococcal AMC Annual Reports can be found on the GAVI website: http://www.gavialliance.org/library/gavi-documents/amc/

AMC Secretariat at GAVI, in collaboration with the World Bank and UNICEF Supply Division (SD), and was approved by the Independent Assessment Committee on 31 May 2012[b].

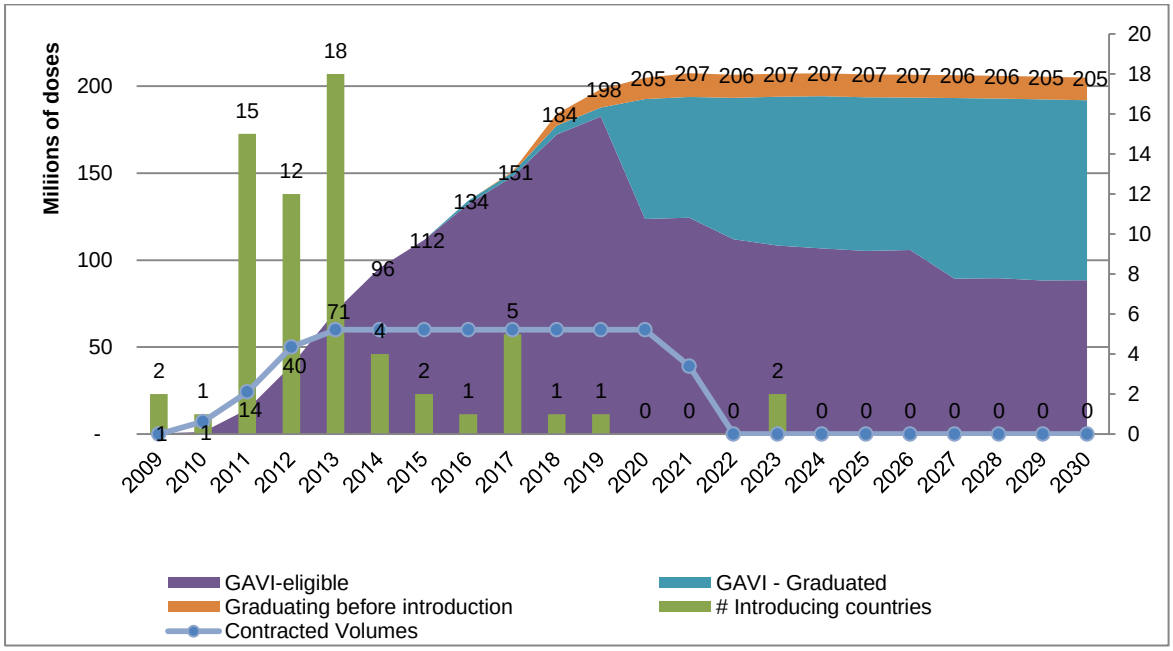
1. Procurement and introduction activities

1.1. Strategic Demand Forecasts

According to the AMC terms and conditions[1], the GAVI Alliance shall publish an updated Strategic Demand Forecast (SDF) on the AMC Website annually.The SDF outlines estimated demand for pneumococcal vaccines, estimated supply as contracted and the unmet demand. Based on the projected unmet demand, UNICEF may issue Calls for Supply Offers.

- SDF version 0.1 was published on the AMC website on 7 August 2009[2] and served as basis for the first Call for Supply Offers issued in September 2009.
- SDF v2.0 was presented to the GAVI Board in December 2010. The GAVI Board decisions on the newly adopted eligibility and graduation policies[c] led to significant changes to the SDF. As such, GAVI and UNICEFSD agreed to delay publication to allow for appropriate revision.
- SDF v3.0 was published on the AMC website on 11 March 2011 and served as basis for the second Call for Supply Offers issued in April 2011. This SDF reflects the latest policies approved by the GAVI Board including the suspension of the 70% DTP3 coverage filter – lowered to 50% DTP3 coverage for the May 2011 round of applications for New Vaccines Support.

Figure1. SDF v3.0 published in March 2011



[b] Note that as a public document, this report does not include any confidential information.
[c] Refer to page 8 of the 2011 AMC Pneumococcal AMC Annual Report

- SDF v4.0 was approved in July 2011.The SDF v4.0 was not published on the AMC website as a new procurement cycle was already in process.

SDF v5.0 was recently approved by the GAVI Secretariat and will be published in 2012 to serve as basis for the next Call for Supply Offers. An update will be provided in the 2013 Pneumococcal AMC Annual Report.

1.2. Call for Supply Offers

1.2.1. 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 GSK starting in January 2012 and Pfizer Inc in January 2013, and continuing for 10 years. Consequently, 15% of AMC funds were allocated to each manufacturer under this procurement round.

In addition to the above-mentioned PSAs, GSK and Pfizer agreed to provide in total 7.2 million, 24.2 million and 20 million doses in 2010, 2011 and 2012, as part of the AMC Capacity Development Period[d]. 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.

1.2.2. 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. UNICEF organised a pre-tender meeting on 10 March 2011 in Copenhagen to inform manufacturers about the AMC concept, including available funding for future contracts, the requirements for the forthcoming call and to provide an update on the introduction of pneumococcal conjugate vaccines (PCV) in GAVI countries and subsequent demand.

A new Call for Supply Offers was thus published on 8 April 2011 with the maximum target of 74 million doses by 2016 (see Figure1). UNICEF SD received four offers by 6 May 2011.

As per the Memorandum of Understanding with UNICEF, GAVI and UNICEF jointly determined the composition of a pneumococcal AMC Procurement Reference Group. With seven members (see Table 1), the role of the group is to provide advice to UNICEF throughout the procurement process, including

[d]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.

on the evaluation of bids, the structuring of awards and the allocation of supply, as well as on the monitoring of key indicators of relevance to pneumococcal AMC objectives. The Procurement Reference Group first met in person on 30 June 2011 in Copenhagen to review a summary of the proposals and the preliminary evaluation, and met a second time on 15 July via teleconference to provide final advice to UNICEF following the publication of the IRC recommendations on 8 July 2011.

Table 1.Membership of the pneumococcal AMC Procurement Reference Group

Name	Affiliation
Members	
Gregory Wallace (Chair)	Lead, Measles/Mumps/Rubella/Polio Team, National Center for Immunization and Respiratory Diseases, Centre for Disease Control
Lauren Franzel	Lead, Strategic Vaccine Supply, PATH
Dafrossa Lyimo	EPI Manager, Tanzania
Carsten Mantel	Medical Officer, Group Leader for the New and Underutilized Vaccines, WHO
Jon Pearman	Director, Accelerated Vaccine Initiative, GAVI
Gregory Widmyer	Senior Programme Officer, Bill&Melinda Gates Foundation
Paul Wilson	Assistant Professor, Global Health Program, Columbia University
Observers	
Natalia Antsilevich	Financial Officer, Multilateral Trusteeship and Innovative Financing for the World Bank
Johanna Fihman	Programme Manager, Accelerated Vaccine Introduction, GAVI
Aurelia N'Guyen	Director of Policy, GAVI

On 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 finalized 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(also see section 1.3.3).

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

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

As part of the supply agreements, manufacturers have agreed to provide in total 9 million doses for each of the years 2012 and 2013 as part of the AMC Capacity Development Period.

UNICEF has opted not to award the full quantities of the GAVI Strategic Demand Forecast for 2016 in response to this second tender. In order to incentivize 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.

52% of the AMC funds corresponding to US$780M remain unallocated and will be available for successive rounds of calls for offers.

Figure 2. Allocation of AMC funds

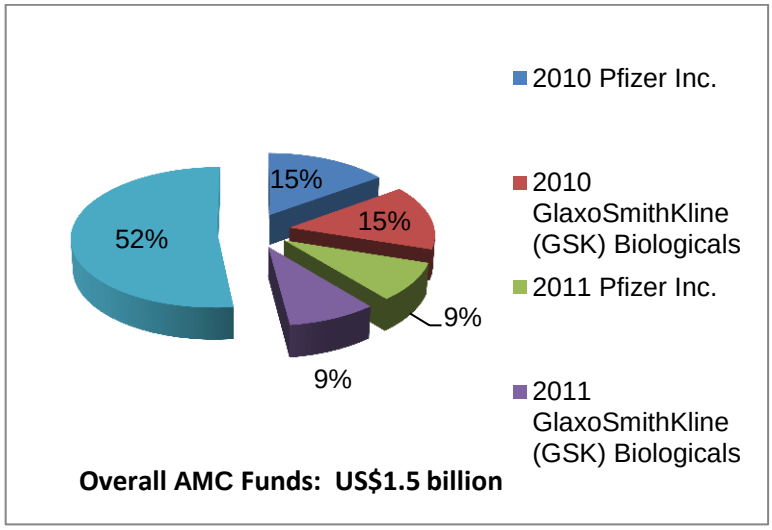


Table 2.Status on overall supply commitments

Manufacturer	Date of signature (week of)	Annual supply commitment (doses)	Trial price	Supply start date	AMC Funds allocated
GSK	23 March 2010	30 million	US$ 3.50	January 2012	US$ 225 million
Pfizer Inc.	23 March 2010	30 million	US$ 3.50	January 2013	US$ 225 million
GSK	12 Dec 2011	18 million	US$ 3.50	January 2014	US$ 135 million
Pfizer Inc.	12 Dec 2011	18 million	US$ 3.50	January 2014	US$ 135 million

1.3. Availability of pneumococcal vaccines

As of 31 March 2011, there are currently two pneumococcal conjugate vaccines (PCV) available for procurement under the AMC:

1.3.1. Pneumococcal conjugate vaccine, 10-valent

GSK launched a 10-valent PCV (PCV10) in Europe in 2009. PCV10 in a 2 dose presentation obtained WHO prequalification on 12 March 2010 and was deemed AMC eligible on 16 April 2010 by the AMC Independent Assessment Committee (IAC). PCV10 is a liquid vaccine in a novel presentation, as it is supplied in a 2 dose vial without preservative. Both doses are intended to be used within 6 hours of the vial being opened. This presentation requires training to ensure that the vaccines are used safely - i.e. technique used to withdraw multiple doses from one container avoiding contamination, and to discard unused doses after 6 hour maximum from extraction of the first dose. The same requirements apply to reconstituted vaccines without preservative. Due to the novelty of its presentation – liquid, multidose, without preservative -, the pre-qualification was first limited to Kenya until successful completion of a 12 months assessment of programmatic issues in two demographic surveillance sites as well as the

implementation of a Phase IV study to monitor Adverse Events following Immunisation (AEFIs) associated with potential mishandling of the product.[3] The first delivery to Kenya took place in September 2010.

In 2011, the WHO Quality, Safety and Standards (QSS) team – responsible for the prequalification process – set up a committee to assess the possibility to extend PCV10 use to countries other than Kenya, prior to data from the use of the novel presentation became available. The Committee approved the use of PCV10 to other countries provided that specific conditions were met by the supplier and recipient countries[e]. As a result, Ethiopia established such structure and subsequently introduced PCV10 in October 2011.

At the time of the writing of this report, following the assessment of data collected in Kenya and in Ethiopia WHO had confirmed that the PCV10 two dose presentation can be rolled out in GAVI countries, with a requirement for a strengthened training program to be in place before vaccine introduction and an assessment of training effectiveness implemented after vaccine rollout. GAVI, WHO and UNICEF are working together on the implementation of these conditions to be communicated to recipient GAVI countries. An update will also be published on WHO website.

1.3.2. Pneumococcal conjugate vaccine, 13-valent

PCV13 in 1-dose vial obtained WHO prequalification on 22 August 2010 and was deemed AMC eligible by the AMC IAC on 23 August 2010. UNICEF Supply Division started the procurement of PCV13 to GAVI-eligible countries in September 2010 upon IAC approval of the vaccine, with first delivery taking place in October 2010.

1.3.3. Country demand

A New Vaccine Support window was opened in 2011 allowing countries to apply by May 2011. An unprecedented number of countries applied for new vaccine introductions and specifically 29 countries requested support for pneumococcal vaccines. The record number of applications was the result of many factors: the lack of an application round in 2010; the temporary waiver of the 70% DTP coverage requirement; and a 'last opportunity' for graduating countries to apply. Following the May 2011 round, 47 of GAVI's 73 countries have now applied for support for pneumococcal vaccine.

Following the Independent Review Committee (IRC) review in July 2011, 18 countries were approved by GAVI's Executive Committee (EC)in September with13 planning to introduce in 2012 and five in 2013. Ten countries received a conditional approval and one country was asked to resubmit its application.

A second IRC meeting was scheduled in February 2012 to review the countries who were recommended for conditional approval in July 2011. An additional nine countries were recommended for approval and will be submitted for approval to the EC in April 2012 - which will lead to a total of 46 countries approved for pneumococcal vaccine introduction.

1.3.4. Supply availability

The current scope and pace of vaccine rollouts are unprecedented in GAVI's history. Given the scale up of demand, short-term supply for these vaccines will not be able to meet all requirements, and as a

[e] Refer to page 12 of the 2011 Pneumococcal AMC Annual Report available athttp://www.gavialliance.org/uploadedImages/Innovative_financing/Landing_page_highlights/AMC-Annual-report-2011_100.gif

result, some of the countries approved for new GAVI support will be unable to introduce the vaccine in 2012 or 2013.

It is challenging to balance supply and demand in the early stages of a new programme. For example, in the initial years of the introduction of pentavalent vaccine supported by GAVI, the manufacturing capacity required seven years to reach 40M doses. Thanks to the AMC, the early availability of considerable quantities of pneumococcal vaccines is an improvement with 63M doses on contract in 2012. However GAVI continues to encourage current manufacturers to accelerate capacity expansions even further to meet demand in developing countries, to reduce delays in introductions and thereby contribute to improving health. GAVI is also actively monitoring the pipeline development from potential future manufacturers.

For contracts entered into in 2011, both manufacturers will start supplying the Annual Supply Commitment Quantities from 2014. However, some doses were also offered to be made available under the AMC Capacity Development Period.[4] GAVI and its partners estimate that there will be 11 PCV introductions in 2012[f]. Three approved countries planning to introduce in 2012 will need to postpone vaccine introductions due to insufficient supply. Two countries decided to postpone their introduction from 2012 to 2013 – one due to in-country transportation issues, the other to wait for the availability of its first product preference.

The first priority remains the sustainability of programmes in countries that have already introduced. Considering the overall supply available, the approved countries planning introduction in 2013 are likely to face a year delay. In 2013, there should be at least one introduction. Further introductions will depend on the amount of additional supply that can be made available combined with the actual vaccine requirement in the introducing countries –delays in countries meeting their proposed introduction schedules have occurred in the past.

Based on the current supply available, all 37 approved countries will be able to introduce by 2014 at the latest.

As of 31 March 2012, the contracted supply for2012-2014 is as follows (see Table 3):

Table 3. Pneumococcal vaccine contracted volumes

Year	**2011**	**2012**	**2013**	**2014**
Current quantities on first contracts(in million of doses)	32	54	60	60
Doses contracted in 2011(in million of doses)		9	9	36
TOTAL	32	63	69	96

Source: UNICEF Supply Division

A new application round will be opened in 2012 and countries wishing to apply for support for pneumococcal vaccines are being alerted to the supply situation in the application guidelines. Additional contracts will be needed to meet new demand including from the nine countries recommended for approval by the 2012 February IRC. GAVI and UNICEF SD have agreed to issue a new Call for Supply Offers in the third quarter of 2012 to allow for consideration of the 2012 IRC recommendation in awards made to manufacturers. New supply agreements are expected to be signed early 2013.

[f] Of the 11 introductions, three countries were postponed from 2011 to 2012;eight countries were approved in September 2011. As described above, in total, five of the 13 countries approved in September 2011 are delayed to 2013.

In spite of the supply shortage, SDF v4.0 estimates that a total of 58 countries will have introduced pneumococcal vaccines by 2015.

1.4. Delivery of pneumococcal vaccines

1.4.1. GAVI-eligible countries approved for the introduction of PCV

A total of 37 countries are currently approved for introduction of PCV and an additional nine were recommended for approval by the IRC in February 2012.

1.4.2. Pneumococcal vaccine introductions

Out of the 19 countries that were approved prior to the May 2011 application round, 16 countries have introduced PCV. The remaining three countries were delayed to 2012. Congo Republic experienced delays in scaling up its cold chain capacity while Madagascar could not accommodate PCV13 due do the cold chain requirements. As a result, both Pakistan and Madagascar are expected to introduce PCV10 under the new conditions to be determined by WHO.

Table 4 – Pneumococcal vaccine introductions to date

Year	Country	Product	Status
2009	Gambia	PCV7 (donation)	Switched to PCV13 in June 2011
	Rwanda	PCV7 (donation)	Switched to PCV13 in August 2011
2010	Nicaragua	PCV13	Introduced December
2011	Guyana	PCV13	Introduced January
	Yemen	PCV13	Introduced January
	Kenya	PCV10	Introduced January
	Sierra Leone	PCV13	Introduced January
	Mali	PCV13	Introduced March
	Congo, DR	PCV13	Introduced April
	Honduras	PCV13	Introduced April
	Central African Republic	PCV13	Introduced July
	Benin	PCV13	Introduced July
	Cameroon	PCV13	Introduced July
	Burundi	PCV13	Introduced September
	Ethiopia	PCV10	Introduced October
	Malawi	PCV13	Introduced November

An analysis of the countries that have already introduced PCV suggests it took on average seven to eight months to introduce from the time the PCV products were deemed AMC eligible to launch in GAVI countries. This is the time taken for planning, training and other readiness activities. Three countries incurred minor delays beyond eight months due to the revised schedules for training activities, lack of supply availability, and insufficient time to implement cold chain expansion. It is worth noting that out of these 19 countries, five countries experienced delays due to cold chain issues.

Of the first GAVI countries that implemented pneumococcal introductions in 2011, several offered the vaccines to all children less than one year of age. Vaccinating all children under one could potentially lead to stock-outs at country level and intensify supply shortage at the global level as the approved applications are only based on a single birth cohort per year. These “mini catch-ups” are being closely monitored to collect data to assess actual demand levels. Given the current supply constraints, countries planning to introduce in the future are being advised not to conduct mini-catch-up campaigns.

1.4.3. Coordination of future introductions

In light of the increased number of introducing countries and considering the links between pneumococcal and rotavirus introductions the AVI sub group coordinates activities linked to the two vaccines. Indeed, the two products are being launched in many countries 'back to back' and in fact there are currently 15 countries that are planning launching pneumococcal and rotavirus vaccines within 24 months.

The Pneumo/Rota Operational Working Group (PROWG) ensures close coordination and improved information flow around pre-launch activities, day-to-day operational issues and actions for both pneumococcal and rotavirus vaccines. This includes:

- Monitoring of country readiness including expected introduction date, cold chain capacity, training, mobilization plans,
- Regular updates on implementation such as reports of faster (or slower) uptake in vaccine post launch.
- Country ranking and allocation of limited supply
- Communication on supply availability and supply options to countries.
- Regular updates on supply vs demand analysis

Table 5. Future pneumococcal vaccine introductions

Year	Country	Product	Status
2012	**Ghana**	PCV13	Planned April 2012
	Djibouti	PCV13	Planned June 2012
	Madagascar	PCV10	Planned July 2012
	Pakistan	PCV10	Planned July 2012
	Congo Rep	PCV13	Planned July 2012
	Zambia	PCV10	Planned July 2012
	Zimbabwe	PCV13	Planned July 2012
	Angola	PCV13	Planned October 2012
	Sao Tome	PCV13	Planned October 2012
	Tanzania	PCV10	Planned December 2012
	Mozambique	TBC	TBC in 2012
	Senegal	TBC	Postponed to 2013
	Sudan	TBC	Postponed to 2013
	Bolivia	TBC	Postponed to 2013
	Niger	TBC	Postponed to 2013
	Kiribati	TBC	Postponed to 2013
2013	**Armenia**	TBC	Approved for 2013 introduction
	Azerbaijan	TBC	
	Georgia	TBC	
	Moldova	TBC	
	Uganda	TBC	
	Bangladesh	TBC	Recommended for approval for introduction in 2013
	Guinea Bissau	TBC	
	Haiti	TBC	
	Lao	TBC	
	Lesotho	TBC	
	Mauritania	TBC	
	Nigeria (Phase 1)	TBC	
	Papua New Guinea	TBC	
	Togo	TBC	

Ghana will be the first country to introduce simultaneously pneumococcal and rotavirus vaccines. WHO and PATH are planning a series of assessments of the experiences of Ghana in planning and executing simultaneous launch of the two products in April 2012.

1.4.4. Serotype replacement

In response to the WHO Strategic Advisory Group of Experts (SAGE) recommendation that WHO monitor serotype replacement following the introduction of pneumococcal conjugate vaccine (PCV), WHO in collaboration with the AVI TAC conducted a systematic analysis of available data on pneumococcal serotype epidemiology following PCV7 introduction. The purpose was to document the occurrence and extent of serotype replacement following PCV introduction, assess factors that may have contributed to serotype changes following PCV introduction, and define important surveillance characteristics for monitoring serotype replacement. The conclusions were presented to SAGE in November 2011 where it was concluded that PCV introduction had resulted in overall Invasive Pneumococcal Disease (IPD) reductions in children under5 years despite increases in incidence of non-vaccine serotypes. SAGE therefore concluded that serotype replacement should not be an impediment to PCV introduction; and the observed increases in non-vaccine serotype IPD with the use of PCV7 are likely to be mitigated by the use of PCVs with broader serotype coverage – such as PCV10 and PCV13[5].

1.4.5. Review of proposed schedules for PCV vaccination

During its November meeting, the SAGE also reviewed the evidence in support of a number of different schedules which are currently used for PCV vaccination. Current recommendation is to give three primary doses. SAGE agreed that both the schedule with three primary doses and two primary doses plus a booster are acceptable for use under different scenarios.

2. AMC management structure

2.1. The AMC Independent Assessment Committee

The IAC serves a number of key functions. Most importantly, it has the mandate to review and approve the minimum technical requirements (TPP) that candidate products must meet to be eligible for AMC funding.[g]In addition, the IAC establishes when and if an adjustment of the pre-set long-term price of vaccines is necessary.

The IAC membership remains unchanged and comprises 11 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[6] A list of IAC members can be found in Annex 6.

[g]Also see section 3.2 on page 20 of Pneumococcal AMC Annual Report 2010 http://vaccineamc.org/files/AMCannualReport10.pdf

3. Monitoring and Evaluation Processes

3.1. AMC Lessons Learnt

In 2010, GAVI and the World Bank started working together on a document summarizing the experience and lessons learnt during the design and early implementation phases of the Pneumococcal AMC. This document is a first attempt to take stock of the experience to date and to encourage a constructive debate about the Pneumococcal AMC. It describes early lessons learnt on the selection of a target disease, on core design choices, and on processes related to the pilot Advance Market Commitment (AMC) for pneumococcal vaccines. While ongoing monitoring and evaluations scheduled for the coming years will provide further information about the value of the Pneumococcal AMC, this document highlights some of the key lessons to date and aims to provide a starting point to inform discussions about the potential applications of the AMC concept to other vaccines or health and non-health interventions. The document was published on the GAVI website on 8 October 2011.

An article on the same topic, entitled *'Advance Market Commitment for Pneumococcal Vaccines: Putting Theory into Practice', was* published in the November issue of the Bulletin of the World Health Organization under the 'Policy & Practice' section.

3.2. AMC Process and Design Evaluation

In 2007 the Department for International Development of the United Kingdom 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 four step evaluation process including:

- A baseline study to determine the point of comparison for future M&E, including the development of counterfactuals;
- Annual monitoring of both the AMC and the complementary activities required to support the public health goal of the AMC;
- A process and design evaluation about two years after the launch of the AMC to assess whether the AMC mechanism is working as expected and to obtain information on the AMC design issues; and
- Outcome evaluations every four years after the signing of the first AMC Supply Agreement. The outcome evaluations will focus on assessing the extent of achievement of the AMC objectives, as well as addressing design issues, as required. They will include an analysis of the counterfactuals. The first outcome evaluation is expected in 2014, given the signing of the supply agreement in 2010.

The AMC Baseline Study was published on 10 December 2010. The process and design evaluation is scheduled for publication in 2012. The evaluation will assess the extent to which the design of the AMC is valid and appropriate, given the AMC's objectives, and the extent to which the AMC is being implemented as planned. A further step in the evaluation will be to look at the pneumococcal vaccine AMC through the lens of whether future AMCs would be useful and, if so, to draw lessons on how these future AMCs should be designed. The evaluation will cover the design phase – starting in 2005[h] - and the implementation phase from June 2009 to December 2011

[h] An AMC for vaccines first gained attention in 2005 with the publication of reports by the Center for Global Development ("Making markets for vaccines") and the G8 Finance Ministers (Advanced Market Commitments for Vaccines – A new tool in the fight against disease and poverty, Tremonti Report, 2 December 2005).

The draft RFP was prepared by the Monitoring and Evaluation team at the GAVI Secretariat. Following a consultation with the AMC Stakeholders and with the CSO constituency, the Request For Proposal (RFP) was presented to the Evaluation Advisory Committee (EAC) for approval on 20 January 2012. The RFP was subsequently issued on 8 February 2012.

An Adjudication Committee meeting is scheduled on 10 April 2012. The committee includes five members: two independents, two AMC donors' representatives and one GAVI Secretariat staff. The final report will be delivered in October 2012.

4. Media and Communications

In 2011a total of 13 countries in the developing world began the introduction of pneumococcal vaccines thanks to the AMC. GAVI's media and communication team leveraged the vaccine launches to demonstrate the success of the AMC mechanism.

4.1. Media relations

GAVI works proactively not only to develop and strengthen relations with key reporters and to promote AMC stories in key media outlets, but also to identify and address any potential misunderstandings about how the AMC mechanism works before they arise. In addition, the team provides support to AMC stakeholders to respond to questions from journalists and other stakeholders (such as bloggers), and provides donors with appropriate communications updates and materials.

Media monitoring is used to capture news articles relating to GAVI (including those in which the AMC is highlighted) and also to identify further opportunities to leverage. Published articles are captured on a daily basis and are distributed both internally and externally, according to their relevance. GAVI works with its partners to respond promptly to critical articles that may create confusion or misunderstanding.

Overall, the coverage was generally positive and relatively widespread.

It is worth noting however that in the first half of 2011, questions were raised about price transparency, the price of pneumococcal vaccines, and potential conflict of interest in GAVI's governance structure. GAVI responded and directly with parties engaged and AMC donors, as well as developing a detailed Q&A explaining these issues. The issues had little impact in the media.

4.2. Online communications

The pneumococcal AMC website is systematically maintained to reflect the progress made and to provide target audiences and stakeholders with direct access to key documents relating to the pneumococcal AMC.

In June 2011, the media and communications team completed the migration process into a new andintegrated website.

The AMC is now better positioned on the GAVI website, which was revamped and launched in July 2011. With the integration into the GAVI site, the AMC now receives more visibility from a whole range of visitors who enter through the corporate site. The quality of online information about the AMC has also been improved thanks to the following:

- **Stronger search engine:** The revamped GAVI website allows users to find information and documents through a much more sophisticated search engine, improved navigation and key-word searches.
- **Dynamic data:** The new platform allows GAVI to be even more transparent and current with its data and documents about the AMC. Improved visuals help demonstrate AMC's impact in a more meaningful and engaging way.
- **Improved content:** The merging facilitates a "spring-cleaning" of sorts – allowing us to review all of the content currently on the sites and to ensure that the new site has the best and clearest content possible.

4.3. Multimedia

To highlight the implementation phase of the pneumococcal AMC and celebrate that pneumococcal vaccines are reaching children in developing countries in a sustainable manner, GAVI has developed two short films featuring the roll out process of the pneumococcal vaccines. The new films are:

- ***Fighting Pneumonia*:** provides information about the burden of pneumonia and highlights the rollouts of pneumococcal vaccines in Nicaragua and Kenya.
- ***World Pneumonia Day*:** raises awareness about the burden of pneumonia and pneumococcal disease and the potential of pneumococcal vaccines to have a great impact in children's lives.

4.4. Events

In order to strengthen the visibility of the AMC mechanism among target audiences, GAVI participated in a wide range of conferences and events worldwide in 2011. GAVI also partnered with countries and helped organize special events to mark and celebrate the roll out of pneumococcal vaccines in developing countries.

The rollout of pneumococcal vaccines in the developing world is underway across three continents. GAVI supported the introduction of the vaccine and showcased films, photographs and media materials to help promote the launches at the global level. M&C also organized a field visit and media trip to Malawi in November 2011 for top level reporters to witness the launch, which was closely observed by public health experts from around the world.

AMC donors were kept informed and invited to participate in the vaccine rollouts.

World Pneumonia Day

In addition, in 2011, GAVI developed a global plan to highlight World Pneumonia Day and help advocate about the importance of pneumococcal vaccines to help prevent millions of deaths. World Pneumonia Day (WPD) seeks to raise awareness of pneumonia as a public health issue and help prevent the millions of avoidable child deaths from pneumonia that occur each year.

Some of the activities included a reception in Geneva with GAVI donors and key partners, blogs written by advocates such us the President of Kenya, the Minister of Health from Rwanda, Bill Roedy, Seth Berkley, among others, a blog carnival, social media posts in Facebook and Twitter, a WPD page on the GAVI website, a viral film featured in partner's sites, a field trip with MPs to Bangladesh to see the burden of pneumonia and the need for vaccines, a media trip to participate in the launch of pneumococcal vaccines in Malawi, and more.

Pneumococcal vaccine launch in Malawi, November 2011

In the arms of his mother Janet, two-month old Bright MasamboChisale is the first baby in Malawi to be given a pneumococcal vaccine. Vaccinator Clement Saidi was proud to deliver the first vaccine in front the Minister of Health, Dr. Jean Kalilani, and a large crowd of onlookers, which included Malawian and international journalists.

5. Financial Activities

The financial structure of the AMC remains unchanged from the prior year. It is composed of the six AMC donors, the World Bank, GAVI, UNICEF, GAVI-eligible countries and eligible vaccine manufacturers.[i]

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

Prior to placing a purchase order with 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 within 20 days into GAVI's designated procurement bank account. These funds once

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

transferred can only be withdrawn by UNICEF. GAVI-eligible countries are obliged to co-finance the supply of the pneumococcal vaccine, in accordance with GAVI's standard co-financing policy. Countries make their payments to meet the co-financing requirement directly to UNICEF.

5.1. Donor Funds – inflow to the World Bank

The fixed-payment donors have together pledged a total of US$765 million to the pneumococcal AMC. The on-demand donors have pledged US$ 735 million (see Figure 6). The six donors combined bring the total available AMC funds to US$ 1,500 million, funds that are dedicated solely to the procurement of the pneumococcal vaccine.

Donor contribution receipts

As of 31 March 2012, the World Bank has received a total of US$ 531 million from AMC donors (see Table 6).

Table 6. Contribution receipts from AMC donors, as of 31 March 2012 (in US$)

	Grant Amount	Cumulative Receipts		Remaining Balance
Fixed Schedule Donors				
Italy	635,000,000	210,637,984	a/	424,362,016
Russia	80,000,000	24,000,000		56,000,000
Gates Foundation (BMGF)	50,000,000	30,000,000		20,000,000
On Demand Donors				
Norway	50,000,000	42,081,675		7,918,325
Canada	200,000,000	148,922,594		51,077,406
UK	485,000,000	75,117,780		409,882,220
Total	**1,500,000,000**	**530,760,033**		**969,239,967**

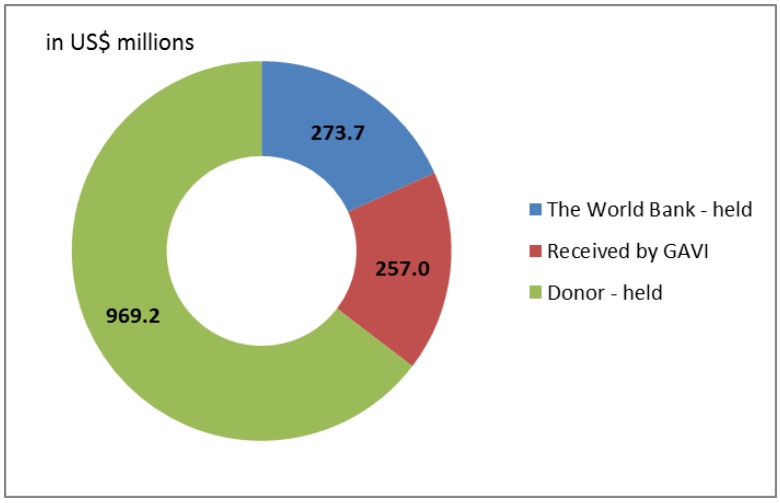
Source: the World Bank

The World Bank has recorded the AMC donor funds on its financial statements as designated assets, with a corresponding liability to pass through the payments 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 has made an additional commitment to pay AMC funds to GAVI even if these funds have not actually been received on schedule from donors. More specifically, the World Bank would commit to transfer funds to purchase AMC vaccines, 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 alsoprovides standard financial management and administrative services with respect to donor contributions, AMC commitments and disbursements.

5.2. AMC donor funds: inflow to GAVI

As of 31 March 2012, the World Bank has disbursed US$ 257 million to GAVI of which US$187.5 million was received from 1 April 2011 – 31 March 2012. This leaves a balance of US$273.7 million held by the World Bank, of which US$ 168.4 million is available for immediate disbursement to GAVI (see figure 3).

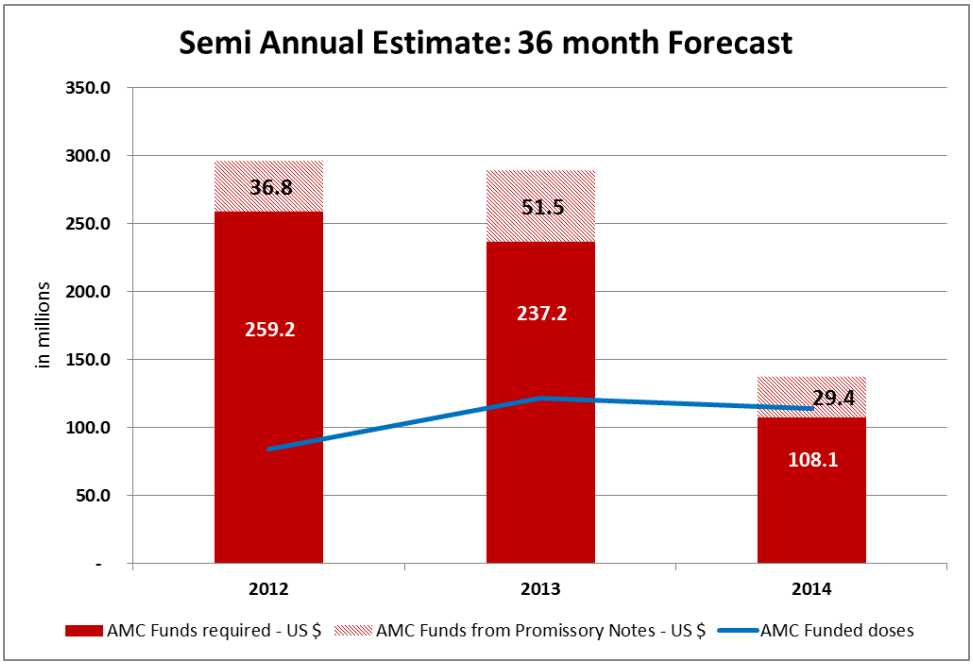
Figure 3. Status of AMC donor funds, as of 31 March 2012 (in US$ millions)



Source: GAVI Alliance Secretariat

As part of the reporting process, GAVI has submitted to the World Bank two Semi-Annual Estimates during the reporting period, the first in March 2011 and the second in October 2011. Based on the most recent Semi-Annual Estimate, submitted in October 2011, it is anticipated that US$ 722 million of AMC funds, of which US$ 117.6 will be from the signed Promissory Notes, are needed to procure 320.8 million doses of the pneumococcal vaccine from 1 January 2012 – 31 December 2014. Fulfillment costs are estimated at US$ 0.19 per dose.[j]

Figure 4.Latest Financial Forecast of AMC Funds, as of 31 March 2012



Source: GAVI Alliance Secretariat

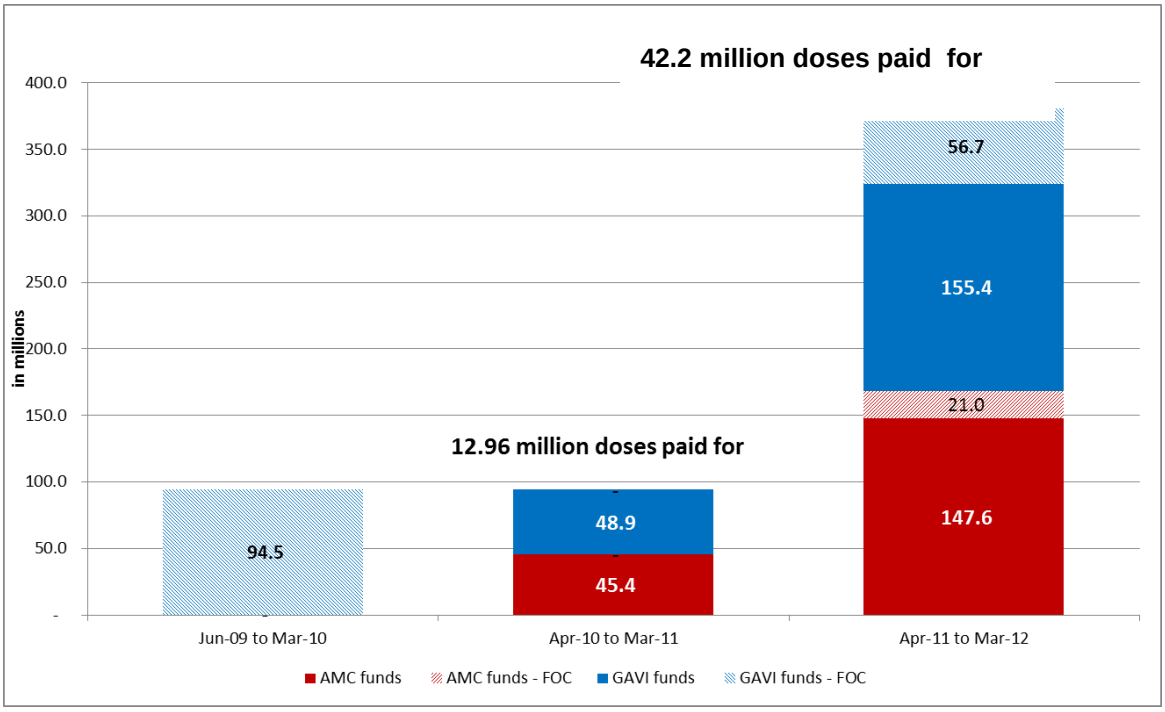
[j]Fulfilment costs are the extra costs incurred in supplying vaccines, in addition to the cost of the vaccine itself. These costs typically include the cost of syringes, safety boxes and freight

5.3. UNICEF procurement: outflow of AMC donor fund

From 1 April 2011 to 31 March 2012, GAVI has disbursed US $380.7 million to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US $168.6 million were from AMC funds. These funds include the transfers relating to the GAVI-funded portion of the minimum purchase obligation on the two new supply agreements, also known as the Firm Order Commitment (FOC), amounting to US $56.7 million and the AMC-funded portion of the FOC for year 1 on the GSK supply agreement signed in 2010 of US $21 million (see Figure 5).

In total, as at 31 March 2012 US $172.2 million has been transferred in relation to the FOCs on the four existing signed supply agreements and related Promissory Notes. Of this amount, US $151.2 million represents the GAVI-funded portion of the FOCs and US $21 million represents the AMC-funded portion of the FOCs. Drawdown on the transferred FOC funds for the supply agreement signed with GSK in 2010 began in Q4-2011 and will continue in Q4 of 2012 & 2013. The FOC for 2012 of 6M doses have been fully met. Drawdown on the FOC funds for the supply agreement signed with Pfizer in 2010 will begin in Q4-2012 (see Figure 5).

Figure 5. Total cash disbursements to UNICEF's procurement account, from inception to 31 March 2012



Source: GAVI Alliance Secretariat

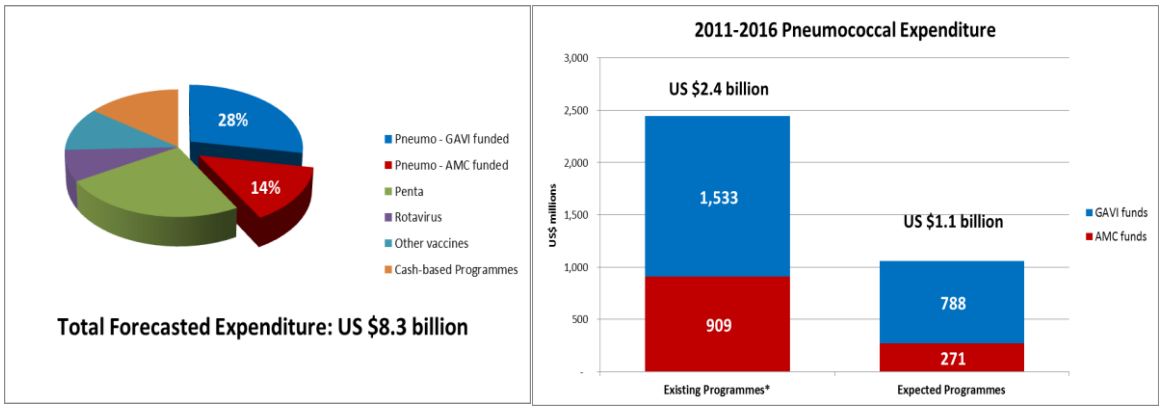
As of 31 March 2012, 32 countries had been approved by the GAVI Board to receive financial support for the procurement of pneumococcal vaccine for the 2012 programmatic year, with further 5 countries endorsed[k] for introduction in 2013. The 2012 approved financial support amounts to US$ 579.1 million and translates into the procurement of approximately 77.5 million doses of the pneumococcal vaccine.

[k]Endorsements constitute acknowledgement of the budget amounts but would not constitute a funding approval, decision, obligation or commitment of the GAVI Alliance

How the PneumococcalAMC fits in with GAVI's Long Term Financial Forecast

At the November 2011 Board meeting, an update was presented of GAVI's Long Term Financial Forecast[I]. For the period of 2011-2016, total programme expenditures are projected to be US $8.3 billion. Of this US $8.3 billion, pneumococcal vaccine expenditures are anticipated to amount to US $3.5 billion, representing 42% of total programmatic expenditures (see Figure 6).

Figure 6. Summary of Total Forecasted Expenditure 2011-2016



* Existing Programmes are defined as all GAVI Board approved, endorsed and extension programmes. Expected Programmes are defined as those which have received Conditional IRC approval or are forecasted projections based on Adjusted Demand Forecast v4.0 and the latest supplier assumptions

Source: GAVI Alliance Secretariat

6. Challenges and Future Priorities

6.1. Meeting country demand

The current scope and pace of vaccine rollouts are unprecedented in GAVI's history. GAVI isfully funded, the mainchallenge is now the availability of vaccines in the short term.

Thanks to the AMC, supply increased from zero to over 40 million doses within less than a year, and manufacturers have entered into 10 years supply agreements, contracting 63M doses in 2012, 69M in 2013 and 96M in 2014 and beyond. This is unique for a GAVI supported vaccine. However, the high levels of demand for pneumococcal vaccines cannot be fully met with short term supply availability, and therefore delays in 2012 and 2013 for a sub-set of countries introducing these vaccines are expected.

Discussions and close coordination with manufacturers are ongoing to understand key milestones and timelines for additional supply availability. At present, it is confirmed that all countries approved as of 31 March 2012 will be able to introduce in 2014 at the latest. A new Call for Supply Offers will be issued in the third quarter of 2012 to contract additional doses to meet new demand including from the 2012 round of application.

[I]November 2011 Board Paper entitled "Board-2011-Mtg-3-Doc 05: Updated long term financial forecast"

6.2. Exploiting the full potential of the AMC

The 2011 pneumococcal AMC Annual Report highlighted the risk that the target demand of 200 million doses annually may not be reached[m]this preventing the AMC from meeting its objectives. Following the recent rounds of application, the GAVI Board approved Nigeria[n] and Bangladesh for PCV introduction. As a result, among the large countries, only India has not yet applied for pneumococcal vaccine yet the recent introduction of pentavalent vaccine is a first step towards pneumococcal vaccine introduction. A GAVI task team is still working with the country to determine how GAVI can best support India in its decision making. GAVI and partners are now confident that the target demand will be reached during the AMC Offer Period which ends in 2020. However, the timing of emerging market manufacturer remains uncertain at this stage.

6.3. Coordination of pneumococcal vaccine introduction

The complexity of coordination of pneumococcal vaccine introductions increases with the number of approved countries. The issue of country readiness for introduction is all the more crucial in a supply constrained environment.

GAVI is working closely with countries to confirm their introduction timing and to align readiness for introduction with available supply. In some cases, this may require shifting their currently projected introduction dates into the future.

Through the AVI Country Readiness dashboard[o], GAVI and partners continue to assess countries' readiness to introduce especially focusing on large countries such as Pakistan – scheduled to introduce in 2012.

7. Conclusion

With the strong vote of confidence received from the international community on 13 June 2011, the GAVI Alliance is now well positioned to achieve this milestone of a quarter of a billion children receiving new vaccines. With the funding raised and the predictability associated with multi-year pledges, GAVI-eligible countries have received a strong signal of support from the donor community to accelerate the roll out of current vaccines, reach more children in developing countries faster than planned, prepare and expand introduction of new vaccines. GAVI and partners must now focus their efforts on strengthening countries' systems to enable them to roll out not only pneumococcal but also rotavirus vaccines - specifically with regards to cold chain and human resources availability.

With the early availability of pneumococcal vaccines, a total of 16 countries have already rolled out these lifesaving vaccines – including 10 during this reporting period. 11 countries will be introducing in 2012. Additional volumes have been secured through new Supply Agreements in 2011 and the level of demand has never been higher. It is estimated that approximately 3 million children have been vaccinated in 2011 with a projection of close to 9 million children vaccinated in 2012.

The short term supply availability will be the key challenge in 2013 and 2014. However in spite of the supply shortage, the SDF v4.0 estimates that a total of 58 countries will have introduced by 2015.

[m]See 2011 Pneumococcal AMC Annual Report page 26 section 8.5
[n]Nigeria was recommended for approval for the first phase of introduction. Conditions are still required by the IRC before the country can expand its introduction nationwide.
[o]See 2011 Pneumococcal AMC Annual Report page 14 section 2.5.4

Annexes

1. Composition of the Pneumo/Rota Operational Woking Group (PROWG)

Organisation	Team members
GAVI Alliance	**Johanna Fihman**, Programme Manager, AVI, Policy and Performance **Katherine Moore,** Senior Programme Manager, AVI, Policy and Performance **Rehan Hafiz**, Senior Specialist, Proposal Reviews, Country Programmes,
PATH	**Lauren Franzel**, Vaccine Market Analyst, Strategic Vaccine Supply **Lisa Menning**, Country Advocacy Officer
UNICEF PD	**Osman Mansoor**, Senior Advisor EPI (New Vaccines)
UNICEF SD	**Ann Ottosen**, Contracts Manager
WHO	**Hemanthi Dassanayake-Nicolas,** Technical Officer, New and Underutilized Vaccines **Carsten Mantel,** Medical Officer, Group Leader for the New and Underutilized Vaccines **Gill Mayers,** Technical Officer, New and Underutilized Vaccines

Source: GAVI Secretariat

2. IAC membership

Robin Biellik
Retired from PATH, consultant for WHO, Switzerland

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

Ingrid Callies
Adviser to the Vice-President for Medical Affairs, Institut Pasteur, France

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
Head, Public Private Partnership, Ministry of Health and Social Welfare, Tanzania

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

Tracy Lieu
Director, Center for Child Health Care Studies, Harvard Medical School, USA

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

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

SOURCES

[1] *Schedule 1: AMC Terms and Conditions. 5. GAVI Strategic Demand Forecast and Calls for Supply Offer. In: AMC Offer Agreement. Geneva, GAVI Alliance, 2011* (http://www.vaccineamc.org/files/amc_offer_agree.pdf, accessed 4 April 2011).

[2] *Strategic Demand Forecast v0.1* (http://vaccineamc.org/files/PneumoSDFv1_8_7_09.pdf, accessed 12 April 2011)

[3] *WHO Position Paper 30 April 2010* (http://www.who.int/immunization_standards/vaccine_quality/synflorix_2dose_statement.pdf, accessed 15 April 2012)

[4]*Refer to the Pneumococcal AMC Annual Report 2010 page 14- section 2.3* (http://vaccineamc.org/files/AMCannualReport10.pdf, accessed 12 April 2011)

[5]*The conclusions and recommendations of SAGE meetings are published in the WHO Weekly Epidemiological Record in English and French within two months of each SAGE meeting. http://www.who.int/wer/2012/wer8701.pdf, accessed 12 April 2012*

[6]*IAC membership* (http://vaccineamc.org/files/IACMembers2009.pdf, accessed 12 April 2011)