THE ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

PROCESS AND DESIGN EVALUATION

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DALBERG GLOBAL DEVELOPMENT ADVISORS

The Advance Market Commitment for Pneumococcal Vaccines
Process and Design Evaluation

Full Report
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Preface

Important notice

The GAVI Alliance commissioned this report, but the views expressed here are those of the authors only.

Throughout the evaluation process, our main point of contact at the GAVI Alliance has been Abdallah Bchir, Senior Specialist in Evaluation Policy and Performance. We are very grateful for Mr. Bchir's guidance and support throughout the evaluation. The GAVI Secretariat provided to us, through Mr. Bchir, the preliminary list of potential interviewees for the report; a database of internal documents, external publications, and press releases; and critiques and feedback on the report's findings. We have added additional interviewees and requested supplemental data as our research has progressed.

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Acronyms and Abbreviations

ADIP	Accelerated Development and Introduction Plan
AMC	Advance Market Commitment
AMC Secretariat	GAVI management team responsible for implementation of the Pneumococcal AMC
AMFm	Affordable Medicines Facility – malaria
AS	Applied Strategies
AVI	Accelerated Vaccine Initiative
BMGF	Bill & Melinda Gates Foundation
Capex	Capital Expenditures
CGD	Center for Global Development
CIDA	Canadian International Development Agency
COGS	Costs of Goods Sold
CSO	Civil Society Organizations
DALY	Disability-Adjusted Life Year
DCVM	Developing Country Vaccine Manufacturers
DFID	Department for International Development (United Kingdom)
DTP	Diphtheria, Tetanus and Pertussis
EEG	AMC Economic Expert Group
EMA	European Medicines Agency
FDA	Food and Drug Administration
GAVI	The GAVI Alliance (formerly Global Alliance for Vaccines and Immunizations)
HepB	Hepatitis B
Hib	*Haemophilus influenza* type B
HIC	High Income Country
IAC	Independent Assessment Committee
IFFIm	International Finance Facility for Immunisation
IRR	Internal Rate of Return
IWG	Implementation Working Group
LMIC	Lower Middle Income Countries
M&E	Monitoring & Evaluation
NPV	Net Present Value
OECD	Organisation for Economic Co-operation and Development

Pentavalent	Vaccine that covers DTP, HepB, and HiB
PAHO	Pan American Health Organisation
PATH	Program for Appropriate Technology in Health
PCV	Pneumococcal Conjugate Vaccine
PPV	Pneumococcal Polysaccharide Vaccine
PRG	Procurement Reference Group
PQ	Prequalification
R&D	Research and Development
RFP	Request for Proposal
SAGE	Strategic Advisory Group of Experts
SDF	Strategic Demand Forecast
TOR	Terms of Reference
TPP	Target Product Profile
UNICEF	United Nations Children's Fund (UNICEF SD: Supply Division)
WACC	Weighted Average Cost of Capital
WB	World Bank
WHO	World Health Organization

1. Executive Summary

Evaluation overview

Advance Market Commitments, or AMCs, offer a promising solution to the challenge of accelerating access to life-saving medicines. The idea of an advance market commitment was first articulated by economist Michael Kremer in 2000[1,2] and expanded upon in the 2005 Center for Global Development (CGD) publication "Making Markets for Vaccines."[3] The AMC concept was intended to address two perceived failings of global health markets. The first was that pharmaceutical manufacturers were incentivized to focus their research and development (R&D) on medicines for diseases that are more prevalent in lucrative markets, such as the US and Europe. There is much less incentive, and many more risks, to develop medicines for diseases that are more prevalent in low-income countries. Second, once developed, medicines often reach low-income countries a decade or more after their introduction in high-income markets. As a result, entire generations of children can go untreated or unvaccinated despite the existence of established products able to prevent millions of deaths.

The Pneumococcal Advance Market Commitment was the first attempt to translate the concept of an AMC to an actual market for vaccines. The aim of the Pilot AMC is to reduce childhood morbidity and mortality from pneumococcal diseases by minimizing the time between the initial development of the pneumococcal conjugate vaccine (PCV) and its introduction in low-income countries. Under the Pilot, six donors pledged 1.5 billion USD towards the purchase of 2 billion doses of PCV beginning in 2009. Since its launch, two suppliers have produced and distributed 82 million doses of PCV to 24 low-income countries.

This document is a *process and design evaluation* intended to offer insights and lessons to the international development community by appraising the design process, design decisions, and implementation of the Pneumococcal Advance Market Commitment to date. The Terms of Reference (TOR) for this evaluation, which are reproduced in Annex I, were developed by the AMC stakeholders and set out in the RFP document[4] dated February 2012. The TOR requires this evaluation to focus on 1) design process, 2) technical design elements, and 3) implementation, taking into account the available evidence for progress achieved toward the Pilot's objectives.

This evaluation focuses on how the key decisions that were made when designing and implementing the Pneumococcal AMC have contributed towards fulfilling the objectives of the AMC Pilot. Our analysis is limited to the immediate consequences of the Pilot's specific design choices, leaving the broader discussion of its overall impact to an outcome evaluation to be commissioned by the GAVI Secretariat in 2014. This evaluation utilized more than 440 documents, including the AMC Baseline study, more than 50 interviews, and a number of analytical methods to reach the conclusions that follow. Further discussion of the scope and methodology of this report are included in the Methodology chapter (Page 20).

Summary of analysis

1. Design Process

The design process for the Pneumococcal AMC Pilot (2005 to 2009) led to the successful development and launch of an innovative initiative, and raised significant new funds to purchase life-saving vaccines (Page 26). This included support from two countries that had not donated to GAVI before. Four factors contributed to the Pilot's successful launch. First, the AMC designers had a clear blueprint for their work, provided by the "Making Markets for Vaccines" report. Second, committed champions, including donors and the technical experts who developed the idea, maintained project momentum throughout the process. Third, the initiative garnered high-level political endorsement, particularly from ministries of finance. Finally, designers leveraged existing events, such as G8 summits, and organizations, such as the GAVI Alliance, the World Bank, UNICEF, and the World Health Organization, to drive the process forward.

Because the Pilot was the first AMC, its design process was driven by a "learning by doing" spirit (Page 29). These experiences provide lessons learned for designers of future such initiatives. Overall, the support of partner organizations – specifically the GAVI Alliance, UNICEF, the World Bank and WHO – played a key role in facilitating the launch and implementation of this Pilot. This AMC experience also yielded lessons for designers of similar, future initiatives. Setting clear objectives early in the design process, especially when working with a large Donor Committee, emerged as a crucial first step. Budgeting time for multiple rounds of iteration was also critical to moving efficiently through the design process, particularly when numerous working groups and partner organizations are involved. Finally, the importance of clear and timely external communication and consultation should be recognized by future designers as important to securing public support for the initiative.

2. Implementation

The implementation of this AMC is on track, and it is progressing towards its overarching objective of reducing morbidity and mortality from pneumococcal diseases in developing countries (Page 36). The Pilot has been implemented as designed, demonstrating the ability of the international development community to establish and administer an advance market commitment. While there are some areas for improvement, overall management of the AMC by GAVI, UNICEF, the World Bank, and the Independent Assessment Committee (IAC) has been effective and their roles have been fulfilled as planned. Some components of this AMC remain untested to date.

Overall, the design process and choice of design elements have contributed, at least in part, to increasing the supply and uptake of PCV (Page 43). Since this AMC's launch, two manufacturers – GlaxoSmithKline (GSK) and Pfizer – have invested hundreds of millions of dollars in expanding PCV manufacturing capacity. They have supplied enough PCV to satisfy demand from the 24 participating low-income countries, though temporary supply and demand imbalances have occurred. The launch of this AMC, and the momentum it created, appears to have contributed to the creation of a longer-term market for PCV, as participating suppliers have expanded capacity and additional manufacturers have expressed interest in joining the initiative. Uptake of the PCV vaccine by low-income countries has accelerated after the launch of the Pneumococcal AMC.

Moving forward, implementers face several challenges (Page 47): ensuring that meaningful indicators of progress are defined and regularly reported, determining a methodology that will enable the evaluators in 2014 to attribute any observed changes in trends to this AMC, and managing the market entrance of additional manufacturers. These challenges can be addressed by strengthening existing monitoring and evaluation frameworks, systems, and processes that ensure indicators are measured, communicated, and used to guide further implementation decisions. Implementers should also develop a clear plan to maximize the benefits from a third or fourth manufacturer's market entry.

3. Design elements

This AMC was also designed to test elements of the AMC concept laid out in the "Making Markets for Vaccines" report. As part of this evaluation, we gave in-depth consideration to the roles of the most important or controversial design elements: the Pilot's pricing structure, its legally binding commitments on donor pledges, its limited purchase guarantees on long-term procurement contracts, and its target product profile. The roles of other design elements are addressed in Appendix IV.

a. Pricing

The AMC pricing structure was designed by the Economic Expert Group (EEG), Implementation Working Group (IWG), and donor committees. Manufacturers are required to provide GAVI with 10-year procurement contracts at a price no higher than $3.50 per dose, a level referred to as the "tail price ceiling." Funding for these purchases comes from the GAVI general fund and, to a limited extent, from individual country co-payments. Manufacturers also receive a $3.50 top-up subsidy on the first 21% of doses in each contract, paid out from the $1.5 billion AMC fund.

The Pneumococcal AMC's pricing structure has been a focal point of public discussion regarding the initiative (Page 50). Critics have charged that the Pilot provides excessive profits to multinational suppliers who already have access to high-income country markets. This evaluation considers the goals, constraints, and tradeoffs faced by the AMC's designers, and analyzes whether the AMC has achieved a reasonable pricing structure. According to interviews, AMC designers stressed that some of their price structure priorities were:

- Save lives by minimizing the time between PCV's licensure in high-income markets and its introduction in low-income countries
- Ensure supply security by engaging both GSK and Pfizer
- Test the broader AMC concept
- Set a single price ceiling across all manufacturers

Whether or not the Pilot's pricing structure was "reasonable" can be evaluated against several benchmarks (Page 51). For instance, the Pneumococcal AMC's prices for PCV are more than 90% lower than those paid in high-income markets, though such tiered pricing is in line with pricing for other GAVI products. The Pilot's prices are also substantially lower than the $10-20 proposed by manufacturers during initial discussions, though it is unclear the extent to which those proposals represented negotiation stances. The pricing structure can also be evaluated in light of the incentives and returns provided to manufacturers, where the discussion becomes more nuanced. The optimal price would be just high enough to incentivize producers to participate – in other words, provide a profit above costs

that would cover risks, opportunity costs, and other factors. Although manufacturers do not share detailed information regarding their internal decision making process, information described in detail in the body of this report suggests that the internal rate of return (IRR) needed to incentivize suppliers fell in the 10-20% range.

Our analysis of the appropriateness of the AMC's tail price ceiling is broken down into four questions in our report (Page 61):

Given what was known at the time of the AMC design, was the AMC's tail price ceiling set to a reasonable level to attract the two existing manufacturers? We used a Monte Carlo approach to model the uncertainties the AMC designers faced when setting the tail price ceiling. The model indicates that at the $3.50 tail price ceiling, there was a 60% chance that a manufacturer with unit costs in the high part of the estimated range would have participated in this AMC. Given the designers' specific constraints and approach, the Pneumococcal AMC's tail price ceiling was therefore likely set appropriately to achieve the goal of dual supplier participation.

Given what we know today, what can we say about the returns that suppliers are earning? In order to determine the internal rate of return (IRR) that a supplier is earning from this Pilot, one needs information on their costs and revenue over the lifespan of this Pilot. These calculations depend on information that is not available today, such as the total revenue each supplier will earn over the course of the AMC Pilot and confidential data on the cost of producing the vaccines. Therefore, we developed a range of scenarios in which we used the latest estimates of the most likely revenue and cost ranges. These scenarios were developed through extensive input from experts as well as by reviewing any publicly available information that would help us to develop reasonable estimates. In order to develop return estimates, we applied these scenarios to the quantitative models developed during the AMC's design stages by the IWG and further refined these models with new information that is available today, notably the total capital investments multinationals have made in expanding their PCV production capacity. Our analysis, assumptions, and results are detailed in the report's main text and in Appendix III. Under the majority of the scenarios that we simulated, manufacturers earn returns that are at or above the target range described on the previous page of 10-20%.

Under what conditions would companies have competed in the GAVI market without receiving the AMC's top-up $1.5 billion subsidies? Whether manufacturers would earn returns high enough to participate in GAVI markets without the Pneumococcal AMC depends on their unit costs. According to our model, a multinational manufacturer with unit costs in the low end of the estimated range that sold a total of 750 million doses at $3.50 or above would have earned returns between 10-20%, even allowing for a wide range of investment costs. The substantial revenue potential of the GAVI market therefore may have been enough to attract low-cost manufacturers without additional subsidies, though whether sufficient demand would have existed without the momentum created by this AMC is an open question. However, manufacturers with costs in the high end of the estimated range would have had returns in the 10-20% target range only if they could have sold doses at $4.00 or above and their investment costs were $150 million or below.

If competition in future tender rounds results in tail price reductions, will this lead to significant cost savings? This AMC is structured so that firms can compete by bidding under the tail price ceiling, so it is

possible that, over time, prices will drop. However, in the first two tender rounds both manufacturers bid at the $3.50 cap. Some interviewees have indicated that they expect prices to drop only when a third supplier enters the market and creates competition, around 2017. The price could further decrease if implementers opt out of existing contracts in favor of lower-cost suppliers. However, it is unclear to what extent such action would fit under the spirit of these provisions. Additionally, the ability of this AMC to take full advantage of these terms is dependent on the degree to which low-cost manufacturers can rapidly scale capacity.

b. Additional design elements

Legally binding commitments on donor pledges (Page 67)

Legally binding commitments on donor pledges were a key element of the Pilot. Designers and implementers have indicated that such commitments were seen as essential, both for providing tangible guarantees to manufacturers and, more broadly, for building momentum with countries, donors, and suppliers around the initiative. Three of the four registered manufacturers interviewed concurred with this assessment, though all three expressed a strong preference for firmer commitments in the future through agreements such as guaranteed purchase contracts.

From a purely financial and legal perspective, this AMC's guarantees were relatively weak, because funding was dependent on both demand materializing and, more importantly, tail funding. In particular, the uncertainty of GAVI's 2011 replenishment round created risk for suppliers. However, interviewees have emphasized that the momentum created by the legally binding commitments meant that the funding round was more likely to succeed, and that PCV would have been given priority in the event of budget cuts.

Evidence from manufacturer behavior is ambiguous. GSK appears to have begun planning for a large-scale production plant in Singapore, targeted at low-income markets, before the discussions around this AMC began. However, it is undear how the evolution of the Pilot and legally binding commitments affected their subsequent investment decisions. Because Pfizer and other low-income country vaccine manufacturers appear to have made their decisions to invest in capacity or research for GAVI markets after the announcement of this AMC, we have no evidence on how they would have acted in the absence of legally binding commitments.

Purchase guarantees (Page 74)

Whether the Pilot's long-term tender contracts should be firm purchase guarantees, as opposed to purchase options on the part of UNICEF/GAVI, was strongly debated during the Pneumococcal AMC's design. Ultimately, only 6% of the value of the AMC contracts (on an NPV basis) was guaranteed to producers. Both GSK and Pfizer have indicated that, while they believe purchase guarantees can play an important role in reducing risks and costs, the relatively small size of the Pilot's commitments made them largely irrelevant to corporate decision-making. However, recent experiences with purchase guarantees for other vaccines, such as the rotavirus vaccine, suggest that, under the right circumstances, large-scale commitments can be extremely powerful levers for donors to gain better pricing.

Target product profile (Page 76)

Overall, both public health experts and industry representatives interviewed agreed that the Pilot's target product profile (TPP) forms an appropriate standard for PCV products targeted at low-income countries, particularly in terms of its serotype coverage requirements. Several interviewees praised the TPP for striking an appropriate balance between setting a high bar to ensure vaccine effectiveness and still allowing low-cost producers to compete. The TPP also proved useful in inspiring and supporting similar guidance for other prospective vaccines.

While the TPP has not played a significant role in shaping GSK and Pfizer's products, other suppliers indicate it has provided them with useful guidance for product development. However, they also indicate that for competitive reasons they will aim to outperform the minimum threshold set by the TPP. Though it is impossible to evaluate the counterfactual, manufacturer interviews also suggest that the TPP's serotype requirements have not restricted competition in the PCV market for low-income country vaccine manufacturers.

The TPP faced a significant issue regarding the use of multi-dose vials without preservatives, a new presentation for which field practice was not well-established. This caused delays and frustration. The development of pneumococcal protein vaccines also demonstrates the potential challenges faced by developers of TPPs for earlier-stage products, particularly when understanding of the underlying science is evolving in parallel with the product development. The experience of the AMC TPP suggests several lessons for future AMCs, detailed later in this report.

Capping individual manufacturers' share of the AMC (Page 80)

Some interviewees suggested that this AMC should have included explicit caps on existing manufacturers' share of the subsidy to ensure new entrants would not be shut out. AMC designers decided against such caps out of concern they might restrict competition by limiting the market share that aggressive suppliers could gain. No new evidence has come to light regarding how this dynamic will play out in practice.

4. Lessons and considerations for future AMCs

Translating the AMC concept into a pilot yielded many insights for future reference (Page 81). This was the first AMC implemented, and designers navigated many unknowns during its development. Designers of future development programs should first determine the type of market mechanism or solution that fits the problem at hand, taking into account the pragmatic realities of a market, and design tailored, nuanced solutions accordingly.

If designers of future development programs determine an AMC is an appropriate solution, designers should then consider several lessons to guide their design (Page 82). First, find strong project advocates to drive the design process and launch. Second, plan in advance to develop the AMC in an iterative fashion, rather than a fixed, sequential manner. Third, identify the risks private sector participants will face, and decide and make clear who will bear which risks between the private sector and the funders. Fourth, take into account the challenges of growing supply and demand simultaneously in a new market. Fifth, recognize that pricing the award is one of the most challenging aspects of designing an AMC, and plan accordingly – factoring in the need for robust data gathering. As the AMC moves towards implementation, designers may leverage existing organizations and events to

move the process forward and communicate as needed with both civil society organizations and the broader public. Finally, throughout the AMC, designers should set clear targets and track progress for monitoring and evaluation purposes. These lessons as well as other information from this Executive Summary are described in further detail in this evaluation report. A broader discussion of this AMC's impact will be discussed in an outcome evaluation commissioned by the GAVI Secretariat in 2014.

2. Introduction

Overview of the Advance Market Commitment concept

The idea of an Advance Market Commitment, or AMC, was first articulated in 2000 by economist Michael Kremer in a series of National Bureau of Economics working papers.[5,6] A few years later, in 2005, a Center for Global Development (CGD) working group led by Kremer, Ruth Levine, Alice Albright, and Owen Barder published a detailed blueprint for potential AMCs entitled "Making Markets for Vaccines."[7]

The AMC concept was intended to address two perceived failings of the global health system at the time of its publication. First, market incentives led manufacturers to focus only on research and development (R&D) for vaccines that could be sold at a high profit margin in the U.S. and Europe, rather than to direct R&D resources towards fighting diseases whose burden mostly fell in low-income countries. Second, even globally applicable vaccines often reached low-income countries a decade or more after their introduction in high-income markets; in some cases, such as that of the Haemophilus influenzae type B (HiB) vaccine, an entire generation of children went unvaccinated despite the existence of established products able to prevent millions of deaths. The Pneumococcal AMC aimed to prevent this needless suffering by facilitating low-income countries' access to the pneumococcal conjugate vaccine (PCV) at the same time as its roll-out in high-income countries.

A vaccine AMC seeks to create a credible promise of funding for manufacturers to incentivize the development of new vaccines or expansion of production capacity for existing products needed in the developing world. Donors pledge to subsidize the purchase of initial vaccine doses at a sufficiently high price so that private sector manufacturers find a credible commercial case for investment. Such funding can be applied to spur research on both early-stage products, which require scientific progress and clinical trials, and late-stage products closer to regulatory approval, when manufacturers finalize capacity decisions for the product. Especially for early-stage products, this funding is not guaranteed to any individual manufacturer; rather, donors promise to subsidize a market where manufacturers compete to provide supply. The "Making Markets for Vaccines" working group estimated that it would cost $3 billion per disease to create an incentive comparable with expected revenues from medicines targeting high-income markets.

"Making Markets for Vaccines" argued that AMCs have several benefits relative to other forms of aid. The report contended that AMCs would enjoy unique advantages since funding would be purely contingent on success; if manufacturers did not develop an effective product, donors would not incur any costs. An AMC would offer equal incentives to all manufacturers, without the distortions that result from "picking winners" to fund too early in the process. If an AMC did successfully lead to the development of new vaccines, it would be an extremely cost-effective form of development assistance, costing potentially less than $15 for each disability-adjusted life year (DALY) saved.

Description of the Pneumococcal AMC Pilot

***Streptococcus pneumonia*, or pneumococcus, is the predominant cause of severe pneumonia worldwide, leading to approximately half a million deaths of young children each year.**[8] It also causes many other pneumococcal infections, including meningitis, septicemia, and otitis media (ear infections). Pneumonia from all causes is estimated to be responsible for 18% of annual deaths among children worldwide.[9] While adult vaccines against pneumococcus have existed for decades, until recently they were not appropriate for children under two years of age, who have less developed immune systems. In 2000, Wyeth received approval in the U.S. and in 2001 approval in Europe to market the pneumococcal conjugate vaccine (PCV) Prevnar-7 for infants.[i][10] However, the individual strains – called serotypes – of pneumococcus vary considerably across the globe. Several of the most significant ones for Africa and Southeast Asia, such as types 1 and 5, were not part of the seven included in Wyeth's product. Throughout the 2000s, both GlaxoSmithKline (GSK) and Pfizer, which had acquired Wyeth, conducted research into vaccines that could protect against a greater variety of worldwide strains. Still, it was unclear whether manufacturers would make the necessary investments to expand manufacturing capacity to meet the high volume requirements of developing markets.

The Pneumococcal Advance Market Commitment (AMC) was a first attempt to translate the concept of an AMC to an actual market for vaccines. It aimed to save the lives of millions of children by minimizing the time between the development of PCV and its introduction throughout the developing world. In February 2006, after pneumococcal disease was selected as the target disease, committees comprising donors, economists, and technical experts met to design the details of the Pilot AMC. In 2007, the AMC donors agreed to commit $1.5 billion towards the initiative. The final design, announced in July 2008, stated the following overarching goal and objectives:

> **Goal:** To reduce morbidity and mortality from pneumococcal diseases and, specifically, to prevent an estimated 7 million childhood deaths by 2030.
>
> **Objective 1:** To accelerate the development of pneumococcal vaccines that meet developing country needs (e.g., by serotype composition and vaccine presentation) as specified in the Target Product Profile, (TPP).
>
> **Objective 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, represents value for money and incentivizes manufacturers to scale-up production capacity to meet developing country vaccine demand.
>
> **Objective 3:** To accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers, including binding commitments by participating companies to supply the vaccines at low, long-term and sustainable prices after AMC finances are depleted.
>
> **Objective 4:** To test the effectiveness of an AMC as an incentive mechanism for needed vaccines and to learn lessons for possible future AMCs.

[i] FDA approval year: 2000; EMA approval year: 2001.

Under the Pilot AMC, donors pledged 1.5 billion USD to fund the AMC subsidy for the purchase of 2 billion doses beginning in 2009. Technical experts created a Target Product Profile (TPP) that defined the desired attributes of the vaccine manufacturers needed to produce in order to participate in the AMC. Subsidies would be provided in the form of frontloaded top-up payments of $3.50 per dose for the first 21% of doses supplied. In exchange, manufacturers were required through 10-year contracts to commit to selling PCV that met TPP criteria to low-income countries at a price no greater than $3.50, referred to as the "tail price ceiling".

The Pneumococcal AMC also leveraged several established development institutions as part of its implementation. The GAVI Alliance ("GAVI"), which was started as the Global Alliance for Vaccines and Immunisations in 2000, was chosen to house the AMC Secretariat and administration functions because of its experience working with both donors and countries to manage the funding and implementation of vaccine programs. UNICEF Supply Division was asked to manage procurement of PCV via long-term contracts.[ii] The World Bank was given responsibility for holding donors' annual payments in trust for GAVI and transferring money to GAVI on a quarterly basis, as well as providing a further guarantee of donor funding by putting such pledges on its balance sheet.

Because the Pneumococcal AMC was the first attempt to test how the concept of AMCs would unfold in practice, it was designed as a pilot program. Since many of the Pilot's elements were being tested for the first time, much of the design and implementation work was conducted in the spirit of "learning by doing". Consequently, the lessons learned from this AMC ideally will contribute to the development of successful innovative financing programs in the coming years.

[ii] UNICEF was asked to handle PCV procurement after a review of alternative procurement options.

3. About this evaluation

Evaluation objectives and scope

This document is a *process and design evaluation* intended to contribute to the international development learning agenda by offering insights and lessons from the appraisal of design decisions, design process, and implementation to date. The Terms of Reference (TOR) for this evaluation, which is reproduced in Annex I, were developed by the AMC stakeholders and set out in the RFP document[11] dated February 2012. The TOR asks that this evaluation focus on 1) design process, 2) technical design elements, and 3) implementation, and examine available evidence of how these design elements contributed to progress toward Pilot objectives.

Furthermore, this evaluation extracts lessons from the design and implementation of the Pneumococcal AMC and generates insights, such as success factors and potential barriers, that can be applied to future development programs or AMCs.

To achieve the latter, we aimed to understand:

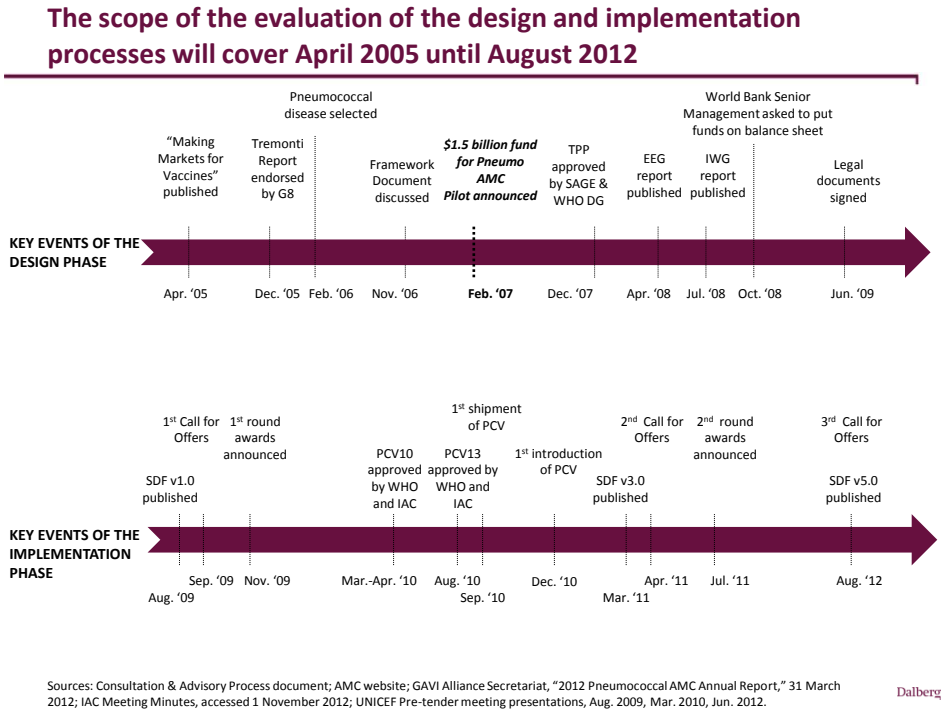
- Which features of this AMC's design, process, and implementation effectively enabled progress towards the Pilot's intended objectives? In what ways could these features have been improved?
- What implications and lessons learned can inform future efforts to develop AMCs or other innovative finance mechanisms?
- What are the success factors and potential barriers for future AMCs?

This evaluation exclusively explores whether the design and implementation of the AMC Pilot has been effective at achieving its stated goals of spurring PCV vaccine development, expanding supply, stimulating uptake, and testing the concept of AMCs in an overall effort to reduce morbidity and mortality from pneumococcal diseases in developing countries. Our analysis is limited to the immediate consequences of the Pilot's specific design choices, leaving the broader discussion of its overall impact to an Outcome Evaluation to be commissioned by the GAVI Secretariat in 2014. Thus, the evaluation of AMC's success in achieving several of its target outcomes, such as the number of children vaccinated or the rate at which country demand for PCV has increased, is out of the scope of this report.

Exploring the broad range of alternative AMC structures is also outside the scope of this evaluation. Critics have questioned whether other approaches may have achieved better value-for-donor funds. For instance, critics have argued that donors should instead drive greater technology transfer between multinational and developing-world vaccine producers, push for vaccines for other diseases such as malaria or polio, focus more on strengthening in-country health systems, or consider alternative health interventions.[12,13] This evaluation will not explore such structures in detail, aside from noting the lack of existing counterfactuals in a few areas.

This process evaluation will cover the AMC Pilot's design phase, from 2005 to 2009, and the implementation phase, from June 2009 through 2012.

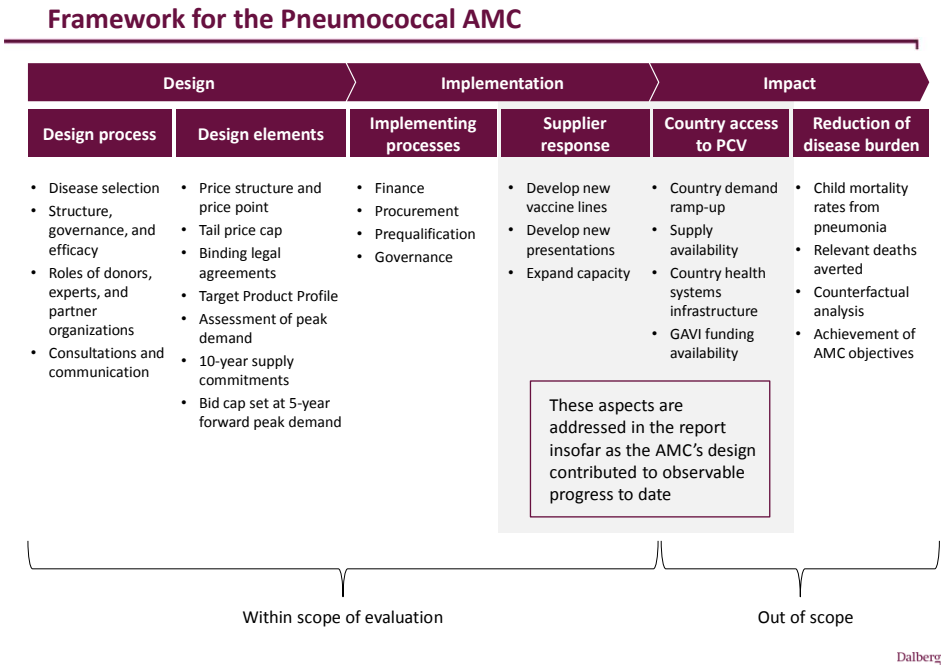
Figure 1: Evaluation of the design, process, and implementation will span April 2005 through August 2012



Evaluation framework

This evaluation is structured around three main lines of inquiry as per the TOR: process, design elements, and implementation.

Figure 2: Evaluation framework



Process: The first area of inquiry explores how well the process of designing the Pilot was executed, and how this process contributed to the AMC's outcomes to date. As specified in the TOR, this evaluation covers the following processes:

- Disease selection
- The processes' structure, governance, and efficacy
- Roles of donors, experts, and partner organizations
- Expert and stakeholder consultations and communication
- Major success factors and tradeoffs

Design: The second line of inquiry examines how specific AMC design elements (including but not limited to those listed below) contributed to the Pilot objectives. As specified in the TOR, the evaluation reviews the following major design elements:

- The AMC Pilot's price structure and price point
- The tail price ceiling
- The importance of ensuring donor funding was guaranteed by binding legal agreements
- The appropriateness of the Target Product Profile
- The importance and accuracy of the assessment of peak demand at 200 million doses
- The 10-year supply commitment requirement
- The limited 3-year purchase guarantee on contracted doses

Implementation: The third area of inquiry assesses the implementation phase and emerging insights from such efforts to date. This section considers the effectiveness, efficiency, timeliness, transparency,

and responsiveness to contextual changes and external factors in both the design and implementation processes. The evaluation assesses the following aspects of implementation:

- The extent to which the AMC has been implemented as designed
- Procurement
- Prequalification
- Governance
- Areas of implementation that have worked well and challenges during implementation

Key definitions

In this report, "GAVI Alliance" and "GAVI" are used interchangeably to refer to the global health partnership founded in 2000 and currently implementing the Pneumococcal AMC. "GAVI Secretariat" refers to the GAVI staff responsible for GAVI's day-to-day operations; it is accountable to the GAVI Board. The "AMC Secretariat" is the administrative body of the AMC, held by the GAVI Alliance Secretariat.

"Partners" or "partner organizations" refer to institutions that work with GAVI to deliver on aligned mission and objectives. In this evaluation, the partner organizations refer to the World Bank, the United Nations Children's Fund (UNICEF), and the World Health Organization (WHO). "AMC stakeholders" include the World Bank, UNICEF, and the six AMC donors.

The subject of this evaluation, the Pneumococcal Advance Market Commitment Pilot program, is also referred to as "this AMC," "the Pilot," or "the Pneumococcal AMC". This is to distinguish the program from references to non-specific advance market commitments for other sectors or target products; in the latter case, we refer to them as "AMCs".

Finally, the term "AMC designers" is used throughout this report to refer to members of both the technical and donor committees who from 2005 through 2009 participated in the design phase and established the parameters of the Pilot. "AMC implementers," on the other hand, refers to members of the GAVI Alliance, UNICEF, and World Bank who are currently executing the mechanisms of this AMC.

4. Methodology

Analytical approaches

The evaluation will build on insights from the AMC Baseline Study, annual monitoring reports, all formally published documents within and outside of the AMC Secretariat, as well as the internal documentation of GAVI and the AMC Secretariat, including unpublished literature[iii] on the topic.

Table 1: Description of specific lines of analyses and evidence sources

Evidence source or specific analysis	Description
Desk review of documentation	Reviewed more than 440 internal documents, external publications, press releases, and critiques produced between 2005 and 2009 as part of the Pilot's design process.
Mapping of design process and decision-making	Mapped design process, design elements, and corresponding decision points and modifications over time using documented evidence and meeting notes.
Compared planned versus actual outcomes and timelines	Conducted analyses comparing actual versus planned outcomes and timelines for the design process, implementation, and implications from design elements.
Leveraged case studies and comparators	Researched and mapped similar multi-billion dollar initiatives in global development, e.g. IFFIm.
Compared to counterfactuals from other vaccine markets	Researched and analyzed other vaccine markets as imperfect counterfactuals for pneumococcal vaccine.
Reviewed existing economic models and analyses	Closely examined and tested the assumptions made by the various economic models, e.g. AMC-FIRM and EEG models. Comprehensive review of the assumptions and NPV analyses that drove pricing decisions.
Conducted standardized interviews	Conducted 54 telephone or in-person interviews with key individuals involved in the Pilot categorized into six groups (see table below). All interviews were based on a standardized questionnaire, which was tailored based on the knowledge and background of the individual interviewee. Interviewees were given supporting documents introducing this evaluation's terms of reference, scope, and context.
Conducted quantitative analysis	Conducted statistical analysis on quantitative data gathered from surveys.
Conducted scenario modeling	Modeled outcomes given hypothetical tail price scenarios. Monte Carlo simulation used to model multiple unknown variables over a range to understand implications on manufacturer incentives, returns, and decision to participate in the AMC. NPV modeling of AMC to manufacturers given a range of assumptions. Based inputs on information from public AMC committee reports, internal models, documentation developed during the design process, public documents, and press releases, in addition to recent manufacturer interviews.

[iii] This includes draft reports, memos, and confidential information.

Evidence source or specific analysis	Description
Examined costs and financials	Analyzed available costs and financials data to assess the performance and efficiency of AMC implementing bodies.
Conducted quantitative surveys	Conducted surveys with key stakeholders, who were asked to rate certain elements of the AMC on a numerical scale.
Reviewed general documentation and original design process assumptions	Analyzed supply landscape at the time of AMC development, macro-level global health context, country demand assumptions, expected GAVI funding needs, expected vaccine cost estimates and capital expenditures.

Table 2: Interviewee grouped by stakeholder group

Stakeholder Group	Number of interviews	Organizations of Interviewees
Donors	9	Bill & Melinda Gates Foundation, Italian Department of the Treasury, UK Department for International Development (DFID), Canadian International Development Agency (former)
Technical Experts and Advisors	13	Applied Strategies Consulting, PneumoADIP at John Hopkins University (former), Center for Global Development (former and current), Columbia University, Dartmouth University, Clinton Health Access Initiative, Stanford University, Seattle & King County Department of Public Health, Harvard University, Covington & Burling LLP, AMC Economic Expert Group (former), AMC Implementation Working Group (former), AMC Advisory Group (former), AMC Procurement Reference Group members
GAVI Alliance and Secretariat	10	GAVI Alliance and Secretariat (current and former members)
Partner Organizations	7	World Health Organization, World Bank, UNICEF
Manufacturers	12	Merck (former), Serum institute of India, Panacea Biotec, Pfizer, GlaxoSmithKline (GSK), Instituto Butantan, The Biovac Institute, China National Biotec Group Company Ltd., Wyeth (former)
Civil Society Organizations and External Experts	3	Médecins Sans Frontières (former), Oxfam America, Plahte J. Plahte Research & Consulting

We contacted for interviews individuals from a wide array of organizations and positions related to the AMC design process and implementation, including vocal critics of this AMC. Some individuals and organizations declined to take part in this evaluation and, in general, did not state their reasons; hence, their perspectives are reflected only through publically accessible reports. A comprehensive list of individuals interviewed is included in the Annex II of this report; additionally, 15 individuals from 12 organizations were contacted for interviews, but were not available or declined to be interviewed.

Important notes on methodology

In light of data limitations and the complexity of evaluating a program in progress, we implemented measures to ensure an objective, inclusive, and transparent report. For instance, we sought multiple, documented confirmations of our findings from different sources. This process is detailed below in "Evaluation process". We recognize that interviews, by nature, often yield subjective information, and participants may characterize the same element or process differently. Additionally, for the purposes of this evaluation, interviewees were often required to recall events as far back as seven years. Thus, we will note any instances when our conclusions are supported only by statements from interviews, without corresponding evidence in written documents.

Furthermore, this evaluation will at times present both positive and negative findings on a certain topic, which may preclude the possibility of drawing neat and concise takeaways. This decision is intended to contribute to a more objective critique, and directly reflects the multifaceted findings from our research and the complex nuances of an initiative still in the implementation phase. Note that detailed technical analyses are available in the Appendix to improve the conciseness of the report.

Evaluation process

During the course of this evaluation, the GAVI Secretariat provided us with access to its time, expertise, and AMC-related documentation.

- We began by reviewing more than 440 Pneumococcal AMC-related internal documents, external publications, press releases, and critiques.
- We conducted interviews with a wide range of stakeholders. Interviewees were selected with the goal of maximizing the diversity of perspectives and opinions on this AMC. We chose not to interview any in-country health or government representatives, as we were advised by the GAVI Alliance this would not be necessary. Please refer to Annex II and III for a full list of interviewees and individuals contacted for interviews.
- Next, we sought to fully verify and substantiate via documentation the information obtained from interviews and to build our corresponding hypotheses through factual verification sourced as much as possible from documented evidence. Findings derived only from a single informant are clearly noted in the text.
- We conducted additional data analyses, secondary research, and ongoing interviews to validate, revise, or add nuance to our key hypotheses.
- We submitted a preliminary draft of the evaluation to the GAVI Secretariat, who circulated the draft to a group of this AMC's stakeholders and experts for a review of factual findings and process assessments. Reviewers were given one month to provide feedback and factual corrections; in early December, we presented findings to this AMC's stakeholders in Dar es Salaam, Tanzania, and received feedback verbally as well.
- We recognize that inherent conflicts of interest may exist in this situation, particularly in areas where we point out potential improvements in implementation performance based on input from parties involved in implementation. Thus, we made revisions and additions based only on corrections of facts and factual findings, and conducted additional research and analyses to

substantiate claims made in feedback. We have incorporated other feedback insofar as it provides reasonable grounds to further explore the thinking behind our conclusions.

- On January 10, 2013, we submitted the Final Draft.

Pricing-related modeling process

To answer the question of whether this AMC's pricing was appropriate, we developed various quantitative models to plot implications for manufacturer incentives, given ranges for multiple variables. The detailed descriptions of these models can be found in Appendix 3. The overall process for building our pricing analyses follows:

- Building upon the original models used by the Economic Expert Group (EEG) and Implementation Working Group (IWG), we incorporated additional information learned during this evaluation's research and analysis phase.

- We presented the assumptions, results, and implications of the pricing models to select members of the EEG and IWG to verify model assumptions and validity.

- We revised the assumptions and parameters for our model as we obtained new information and feedback from manufacturers and members of the EEG/IWG.

Methodological limitations

As evaluators in the present day, we encountered difficulties in quantifying and accounting for the distinct global context at the time of design. The differences between the time when the Pilot was designed and present day introduce a range of confounding factors. For instance, gradual changes over time in the emphasis on and funding for global health issues, in the dynamics between private sector companies (e.g. vaccine manufacturers) and international organizations, and in GAVI's role and prominence are difficult to measure. The general appetite for funding global health programs and vaccines, in particular, is difficult to capture through the documents preserved for this evaluation. Since current evaluators do not have contextual evidence, we have tried to gain some perspective via interviewee recollections and perceptions.

There is a lack of suitable counterfactuals and control scenarios to compare against the Pneumococcal AMC and its various design elements. For instance, we cannot evaluate this AMC's design and implementation against the actual counterfactuals of not having a Pneumococcal AMC or the Pneumococcal AMC in altered form. Furthermore, it is difficult to separately attribute and measure the benefit of the Pneumococcal AMC's overall funding from its specific design elements and process.

Broadly, multiple stakeholders and differing perceptions within a complex process introduce various biases to an evaluation. The Pilot design process was a difficult undertaking by many stakeholders. The complexity of the process introduced a risk that participants may have only partial information about any given decision, or may remember details incorrectly, as some interviewees were asked to recollect events three to seven years prior. Moreover, interviewees, speaking with the benefit of perfect hindsight about the complex process and design of the Pneumococcal AMC, may inadvertently "overfit" aspects of past intentions, data, and process with present reality. There is also a tendency for individuals to unconsciously filter information based on their preferences. In our case, proponents of this AMC process and design may recall positive aspects of the design over shortcomings, while critically-inclined participants may recall shortcomings more precisely.

To control for this, the evaluation team contacted and/or interviewed stakeholders with a diverse range of viewpoints from a wide array of organizations and positions related to the Pilot, including vocal critics. The evaluation attempted to ensure that experts without an interest in this AMC were included in the interview process to avoid skewed results and to put the responses of stakeholders into perspective. Some individuals and organizations declined to take part in this evaluation; hence, their perspectives are reflected only through publically accessible reports.

Since the Pneumococcal AMC is still in the implementation stage, we recognize the potential conflicts of interest for various interviewees who are currently involved in this process or related activities; thus, we have attempted to verify interview content with documented evidence.

Statistical biases in our interview process may include:

- **Non-response bias:** This bias may affect our conclusions if individuals who declined our interview requests differ greatly in the outcome variables from those who responded.
- **Selection bias**: We began the interview process by working with the relevant individuals identified by the GAVI Secretariat. This list was supplemented with a great number of additional names as our research progressed. However, we cannot guarantee the final list was comprehensive of every possible viewpoint.

Additional limiting factors include possible conflicts of interest in providing data and a general lack of available data. The latter factor particularly includes a lack of access to sensitive or proprietary information, such as manufacturers' fixed and variable costs, capital expenditures, and profit margin requirements; even if we were able to examine such data, it is likely that these costs will vary widely across manufacturers. In addition, vaccine producers may face a conflict of interest in providing such information. These drawbacks inhibited our ability to evaluate the extent to which manufacturers are incentivized by the Pilot's price ceiling. In the previous methodology section, we outlined the ways in which we sought multiple confirmations across data ranges and various scenarios.

Additional data-related challenges include a lack of consolidated databases for key information and processes, e.g., the lack of consolidated information on PCV WHO prequalification dates or PCV shipment data per country. Occasionally, multiple sources for the same data (e.g. vaccine introduction dates, volume contracted versus offered) did not always match. In such cases, we have attempted to follow up with the source authors to understand and resolve the discrepancies. Finally, while we relied as much as possible on documented information, due to the lack of details in written records, we supplemented our research with findings from stakeholder interviews. We have noted in this report the areas where no documentation was available and findings rely on interviews alone. We believe we have implemented these controls sufficiently to generate meaningful lessons about this AMC's design process, design elements, and implementation.

5. Design Process

Relevant TOR Questions addressed in this section:

- **Question 5:** To what extent is the AMC management structure – such as the placement of the AMC within the context of the GAVI Alliance, and the setup of an Independent Assessment Committee – relevant to the achievement of the AMC objectives?
- **Question 6:** To what extent was the AMC Donor Committee an effective and efficient way to oversee the AMC design phase?
- **Question 7:** To what extent was the role of different partner organizations appropriate, effective and efficient during the design phase?
- **Question 8:** To what extent were expert and stakeholder consultations adequate during the design phase?

Key findings:

Overall, the process of designing the Pneumococcal AMC (2005 to 2009) was successful in developing and launching an innovative initiative and raising significant funding for vaccines. Four factors contributed to the AMC's successful launch: 1) a clear blueprint provided by the "Making Markets for Vaccines" report; 2) consistent and committed project champions, including the Italian government, the Canadian government, the Bill & Melinda Gates Foundation, the World Bank, and WHO; 3) high-profile political endorsement; and 4) reliance on established organizations and structures. The design of the management structure, as discussed in the following chapter, also made positive contributions toward this AMC's objectives.

The Pneumococcal AMC Pilot was the first AMC ever designed. As such, its design process relied on a participatory approach, driven by a "learning by doing" spirit. Overall, the support of partner organizations – specifically the GAVI Alliance, UNICEF, the World Bank and WHO – played a key role in facilitating the launch and implementation of this Pilot. This AMC experience also yielded lessons for designers of similar, future initiatives. Setting clear objectives early in the design process, especially when working with a large Donor Committee, emerged as an important reflection. Budgeting time for multiple rounds of iteration is also critical to moving efficiently through the design process, particularly when numerous working groups and partner organizations are involved. Finally, the importance of clear and timely external communication and consultation should be recognized by future designers as important to securing public support for the initiative.

When assessing the design process for a new initiative such as the Pneumococcal AMC, it is important to recall that the Pilot was a new idea shaped by a diverse coalition of stakeholders. The Pilot design process involved the creation of new funding arrangements, procurement processes and legal structures

to accommodate the AMC concept. As such, the process relied on a participatory and "learning by doing" approach. Furthermore, no single institution was responsible for driving the initiative forward. Instead, the Pilot was the result of several very different organizations working cooperatively and flexibly to take and enact decisions.

Within this context, the design process culminated in several notable achievements, including:

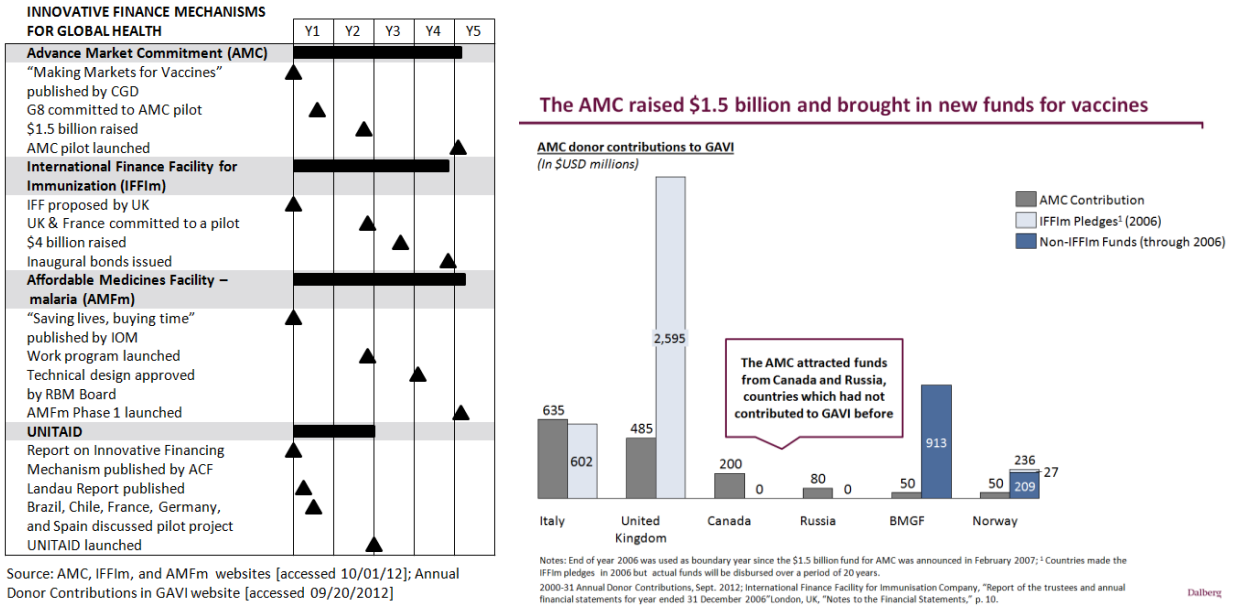
- **Transforming an idea into an operational pilot within an acceptable time period.** The four years required to design and launch this AMC is comparable to the timelines of other recent, multi-billion dollar multilateral financing initiatives, such as the International Finance Facility for Immunization (IFFIm) and Affordable Medicines Facility – malaria (AMFm).[14,15,16] However, recent health initiatives have required less time to launch. In just two years, the governments of Brazil, Chile, France, Norway, and the United Kingdom created UNITAID, a funding agency for treatments and diagnostics for HIV/AIDS, malaria, and tuberculosis in low-income countries.[iv,17,v] Initiatives to negotiate procurement deals for rotavirus vaccines and intra-uterine devices took as little as eight and two months, respectively.[18] Overall, however, novel programs like this AMC likely take longer to establish operational pilots.

- **Attracting new funds for vaccines.** Canada and Russia, two countries that had never before contributed to the GAVI Alliance, contributed a combined $280 million to this AMC.[19] Interviewees stated that these funds would not have been contributed to global health or international development if not for the AMC.[20]

[iv] UNITAID has an annual budget of approximately $300 million.

[v] A partial explanation for this difference could be the fact that UNITAID does not directly handle procurement or project implementation, and no specific procedures had to be defined before its launch.

Figure 3: The Pneumococcal AMC timeline and funds raised



Source: AMC, IFFIm, and AMFm websites [accessed 10/01/12]; Annual Donor Contributions in GAVI website [accessed 09/20/2012]

Source: AMC, IFFIm, and AMFm websites [accessed 10/01/12]; Annual Donor Contributions, GAVI website [accessed 09/20/2012], IFFIm annual financial statements 2006.

Success factors

This AMC's design process reveals four factors that contributed to its success; they offering lessons for translating future novel program ideas into reality:

1. **A clear story and blueprint.** The "Making Markets for Vaccines" report provided both a clear story for what the AMC was intended to achieve and what steps were necessary to accomplish these goals. Individuals interviewed for this report suggest this was because the report was viewed as highly credible—it was financed by an independent organization and developed through an intense 18-month consultative process. The Pilot designers referenced the paper repeatedly for guidance through a complicated multi-stakeholder development process.[21] In the end, elements of this AMC closely matched the ideas laid out in "Making Markets" five years before.

2. **High-profile political endorsement**. The momentum behind the AMC process originated in 2005, when the idea of an AMC for vaccines caught the attention of Gordon Brown, then British Chancellor of the Exchequer. A technical expert involved in the design process recalls, "Once Gordon Brown decided to support the AMC, the idea became real in the eyes of other potential donors and the industry."[22] Soon after, the Pilot garnered the endorsement of the G8, making various ministers of finance accountable for its progress.[23] The AMC value proposition was particularly attractive to these ministers because it represented a potentially elegant economic solution to a pressing need. A donor representative summarizes, "The Italian Ministry of

Finance became interested in the AMC for two main reasons: the AMC was about fixing incomplete markets and it was about an innovative idea."[24]

3. **Consistent and committed project champions**. Several highly committed project champions took ownership of the initiative and assumed the lead in driving the process forward. Italy took an early leadership role in 2005, contributing nearly 50% of the Pilot's subsidy funds while reaching out to other ministers of finance to bring in new donors.[25] "Russia joined the AMC after a personal intervention from the Italian Minister of Finance, Mr. Tremonti," explains an interviewed stakeholder.[26] Afterward, the design process benefited from the sustained engagement of three donor champions: the Italian government, the Canadian government, and the Bill & Melinda Gates Foundation. These organizations anchored the design process and provided continuity throughout the design phases.[27] The World Bank also helped facilitate the Pilot design by convening donors, industry stakeholders, the AMC disease selection panel, and the GAVI Alliance, and also provided financial management support. Additionally, the regular consultation of World Health Organization health experts and external technical experts, who guided the design process from inception to final design, ensured that the Pilot was grounded in a current and nuanced understanding of PCV development.

4. **Established partner organizations and structures.** Designers[vi] of the Pneumococcal AMC relied on established structures and the capabilities of existing organizations to facilitate the design and launch of this AMC. This precluded the need for additional time and funding to set up a new organization to implement the Pilot. This AMC leveraged the GAVI Alliance's experience managing the procurement and distribution of vaccines to developing countries, the World Bank's expertise in financial management services, UNICEF's vaccine procurement experience, and the WHO's technical experts and TPP design protocols to transform the AMC concept into a reality. "The AMC presented to donors not only a compelling argument to address a problem, but also practical ways to implement it," says a technical expert involved in the design process.[28] In sum, the participation of multiple partner organizations improved the efficiency of the Pilot design process and rollout.

Insights into design challenges

The Pilot design process also offers insights into the challenges of orchestrating an AMC and lessons in how to resolve them. Designers of this AMC faced several consideration factors related to the selection of the vaccine for subsidization and to the negotiation of tradeoffs between various AMC objectives:

- **The initial AMC concept explored incentivizing the development of either an early-stage or a late-stage vaccine; the Pilot ultimately chose a late-stage product.** For the selected pathogen, pneumococcus, there were already late-stage products in development.[29] As a result, the Pilot did not focus on incentivizing development of early-stage products, but rather on incentivizing companies to build manufacturing capacity for existing vaccines. Because of the high-income

[vi] The term "designers" is used throughout this report to refer to members of both the technical and donor committees that together established the parameters of the AMC Pilot.

markets that existed for PCV, some interviewees felt that that the Pilot focused on a product less suited to the overall AMC approach. They suggested that future initiatives should include economists alongside public health experts in early design stages, to ensure the product's specific market context is taken into account when selecting the disease. Selecting the disease prior to setting the Pilot objectives (see Figure 4) also prevented experts from fully assessing how the market context would impact the AMC's outcomes and goals.[vii]

- **The breadth of the Pilot's objectives resulted in necessary but difficult trade-offs between its various goals during the design and implementation phases.** Interview findings indicate that donors carefully negotiated the AMC objectives for years, so as to accommodate all participants' preferences (see Figure 5). One interviewee suggested having a broad set of goals final was deliberate, as a means of maintaining support among donors with different priorities and visions for the Pilot. However, this engendered trade-offs, as the Pilot strived to achieve different goals, such as the need to test objectively the concept of an AMC (Objective 4) and the goal of finding the best way to rapidly increase the availability of PCV (Objective 2). In addition, the goals do not clearly indicate how to divide incentive funds between existing PCV manufacturers and new manufacturers seeking to join the PCV market, as discussed in the Implementation chapter.[viii] Some designers found it challenging to align clear objectives early in the design process, particularly while working with the large and diverse donor committee. AMC stakeholders expressed in interviews for this evaluation they clearly understand the objectives and the ways in which they should be implemented today.

- **Designers did not make clear the greater priority placed on scale-up near-term production capacity versus incentivizing new producers in the long-term. This had effects on both the AMC's internal structure and external communication.** Interviews with designers of the pneumococcal AMC have made clear the priority they placed on ramping-up PCV distribution to children in low-income countries as quickly as possible, an approach which implicitly favored existing manufacturers. However, because the greater relative emphasis placed on this objective was not made explicit, the Pilot's structure and external communication did not reflect this thinking. Instead, the Pilot's stated goals gave equal weight to Objective 1 (accelerating the development of vaccines) and Objective 2 (scaling up capacity). Interviews confirm that external observers have different interpretations of how the Pilot is meant to incentivize second-generation producers, and manufacturers themselves have various perspectives on its value (described in more detail under the Implementation chapter). One interviewee suggested these competing views may be the result of some designers' weak understanding of the development timeline of DCVMs in the early stages of the design process. Later literature suggests the AMC designers did not clearly communicate to external observers how the AMC would balance short-term and long-term goals.[30] One interviewee from a civil society organization commented that

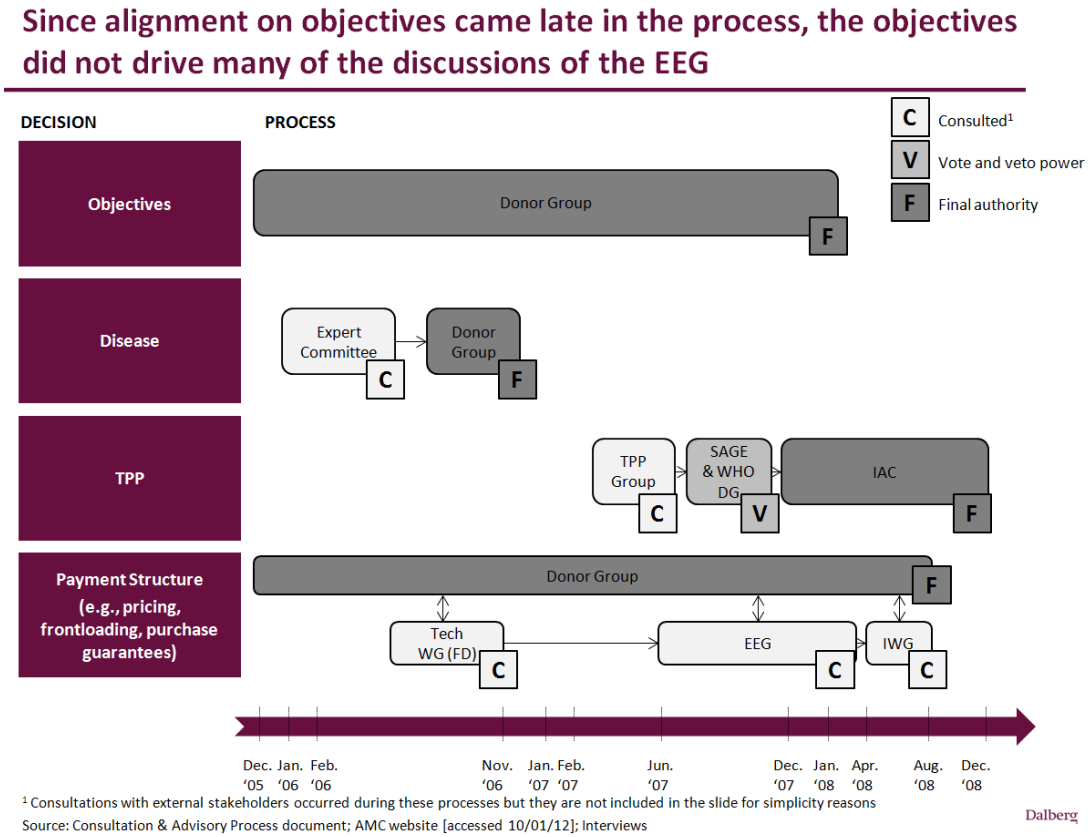
[vii] The "Terms of Reference for AMC Expert Group Report on Options for Modifications to AMC," dated 28 January 2008 is the first document to include the AMC objectives as defined in the legal documents.

[viii] The AMC objectives as described in the "Framework Document: Pilot AMC for Pneumococcal Vaccines," dated on 9 November, 2006 and in the original Export Group Terms of Reference from 27 June 2007 included the idea that "[the AMC] should engage emerging as well as multinational manufacturers." However, the AMC objectives defined in the Annual Reports do not make any reference to emerging manufacturers.

this confusion was a source of much of his group's early negative reaction to the Pilot, and that once it was understood that the Pilot's relative emphasis was on driving near-term procurement rather than stimulating long-term innovation much of the resistance abated.[31]

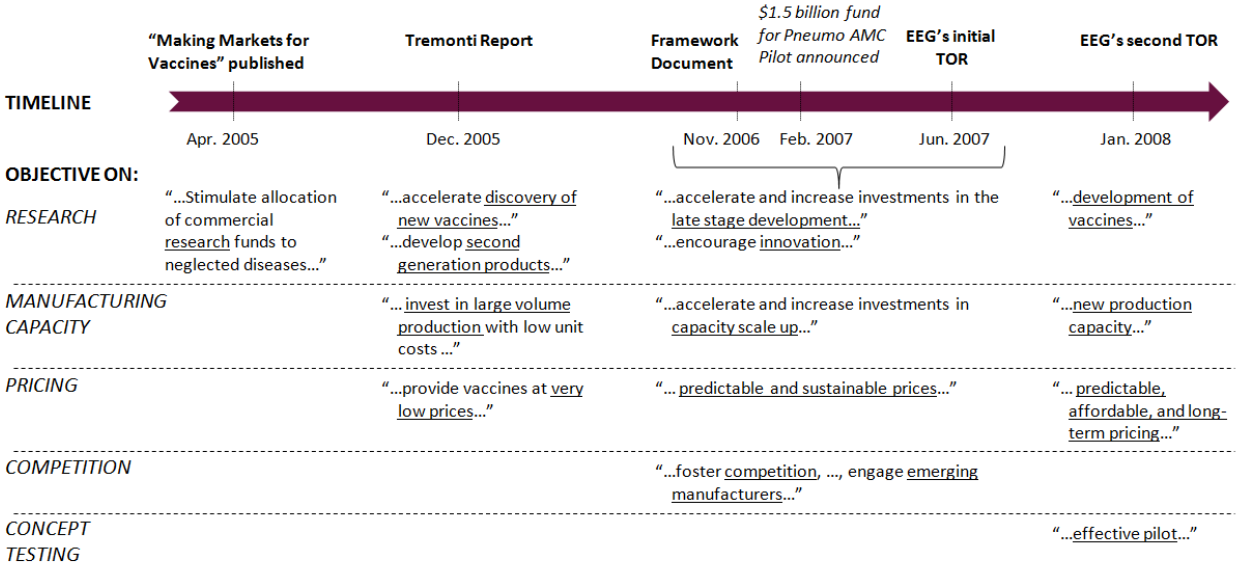
- **The seven-week timeline for selecting the target disease limited the AMC designers' ability to leverage all available data**. An Independent Expert Committee, with eight of its 13 members representing developing countries, selected pneumococcus as the Pilot's target disease.[32] Interviewees have noted that the 2006 G8 Summit imposed an extremely tight timeline on this process.[33] The selection of committee members, submission of background papers by disease expert groups, and the committee's final recommendation occurred over seven weeks.[ix] Some interviewees suggested the decision process may have been unintentionally biased towards diseases in late-stage research, for which more and better-quality data was available. Other interviewees suggested that it would have been helpful to involve in the decision-making a group comprising more than just global health officials.

Figure 4: Sequence of decisions for the Pneumococcal AMC Pilot



[ix] On 9 January 2006 the Committee had not yet been formed and on 27-28 February 2006 the Committee met in Paris to agree on its final recommendation.

Figure 5: History of the objectives for the Pneumococcal AMC Pilot



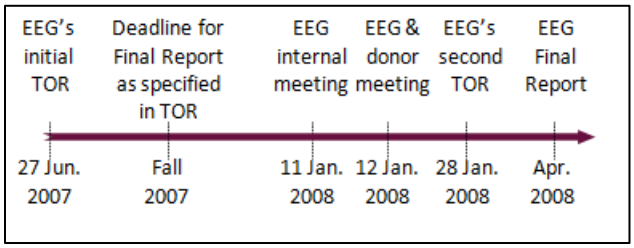
Sources: Making Markets for Vaccines; Tremonti report; Framework Document; TORs for EEG; Interviews

Finally, there were five ways in which the AMC design process, designer group, and communication could have improved:

- **Additional time should have been budgeted for iteration and review, given the number and diversity of stakeholders involved.** It was always unlikely the Pilot's designers would perfect the mechanism's structure in their first attempt. Originally, the design process was intended to be linear, with no time built in for testing and/or review of individual elements.[34] When a review finally did occur by the Economic Expert Group (EEG), it was in the process's final stages. The EEG was responsible for finalizing the details of the AMC design in 2007,[35] but they instead suggested certain design elements needed to be modified or revisited.[36] Donors subsequently rewrote the TOR for the EEG (see Figure 6), necessitating another review phase and resulting in a delay of six to eight months.[x] The new TOR established the broader structure under which this AMC would operate.[37] This all might have been avoided if small reviews or testing loops had been built into the original design timeline at regular intervals.

[x] The original planned date of completion for the EEG's work was fall of 2007. This was revised based on the second EEG TOR, which targeted completion by February 15, 2008. The final EEG presentation to the donor committee was April 1, 2008; resulting in a total delay of 6 – 8 months.

Figure 6: Timeline of the Economic Expert Working Group (EEG)



- **Designers should have recognized the tradeoffs between aligning with established partner organizations – which were seen as appropriate, effective and efficient – and the potential delays that could be caused by bringing on board established bureaucracies.** According to one interviewee, the decision to implement the Pilot via existing institutions may have led to a lengthier design process because the priorities, policies, and internal processes of these implementing agencies had to be taken into account. As one example, according to another interviewee the World Bank required more time than expected to approve the addition of the AMC commitments to its balance sheet, although this did not cause a delay or affect the AMC timeline according to the World Bank.[38] We have not uncovered written documentation proving that any delay was a result of any particular organization.[39] Despite logistical difficulties, overall, the partner organizations – specifically the GAVI Alliance, UNICEF, the World Bank and the WHO – strengthened this AMC's credibility and contributed to its successful launch and implementation.

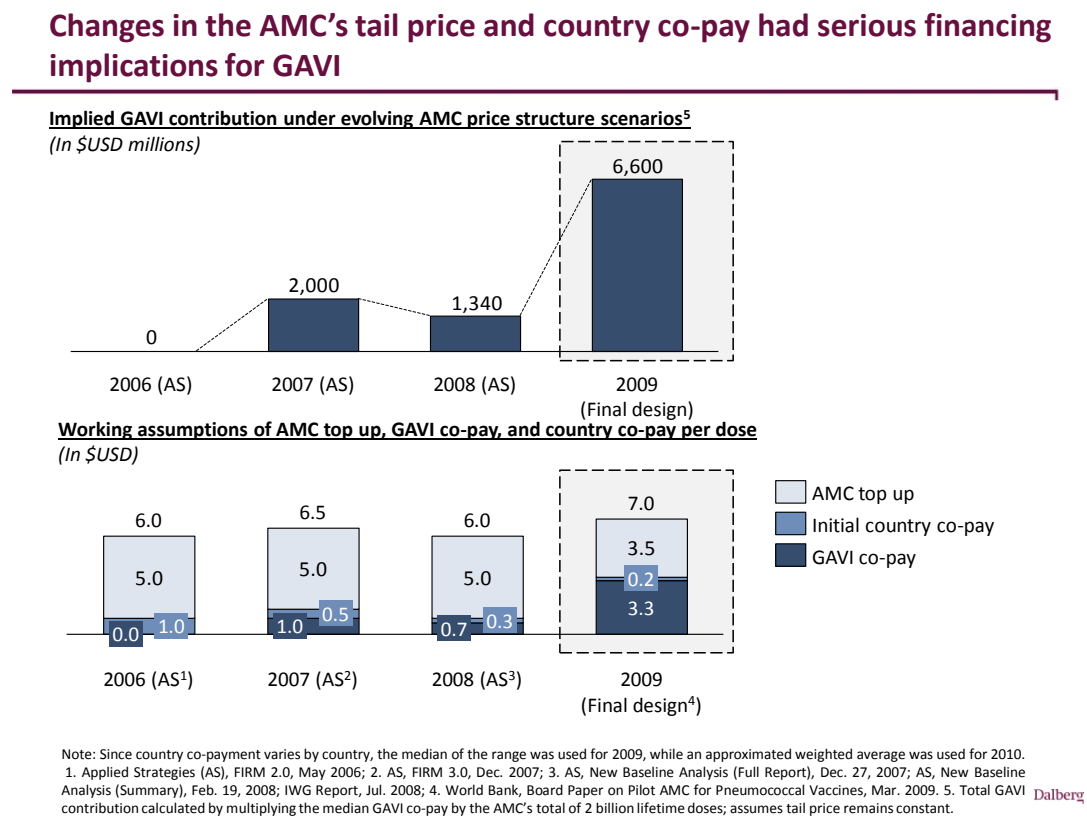
- **Designers should have involved more individuals with industry and deal-brokering experience to facilitate negotiations with manufacturers.** The AMC committees and working groups were designed to include expertise across a wide range of topics.[40] However, only one member of the EEG and IWG had prior vaccine industry experience.[41] Future initiatives should consider including a greater diversity of members with prior industry experience; the Pilot's designers dealt with much uncertainty due to the lack of accurate industry cost and profit estimates, and individuals experienced in negotiating and deal-making could have been of of particular value.

- **Understanding the role of all implementing organizations – particularly the role of the GAVI Alliance – could have prevented launching the Pilot before all of the necessary funds were secured.** The original AMC concept included a tail price ceiling low enough that developing countries would be able to cover the costs.[42] However, in the Pilot's final design, the tail price ceiling was raised to $3.50, far above initial estimates, and the co-payment required of countries was reduced by roughly 80%.[43] As a result, the GAVI Alliance became responsible for funding approximately $3.30 per dose in the initial contracts.[xi] These expenditures strained GAVI's business model severely and were a leading cause of its 2011 funding crisis.[44] Though interviews

[xi] Another effect of the large drop in the country co-pay was to render earlier concerns over initial uptake irrelevant. The $0.20 co-pay that GAVI-supported countries must provide has proven to be considered minimal relative to the perceived health benefits, and demand has surged far beyond initial estimates.

indicate this possibility was known at the time of the design, more emphasis should have been placed on anticipating and resolving potential challenges.

Figure 7: Changes in the AMC's tail price ceiling and country co-pay



- **The AMC Pilot design process featured several controversial decisions about the use of public funds to incentivize private firms – designers should have increased transparent and timely external communication about how decisions were made.**[45] Throughout the design process, civil society organizations voiced strong concerns about the risks of over-paying the private sector.[46] They pointed to the need for transparency regarding the models and assumptions that drove pricing decisions. However, this AMC's decision makers conducted their analyses and made decisions based on information that to date remains unpublicized.[xii] As a result, the reasoning behind major design decisions, such as the Pilot's payment structure, is still the subject of controversy.[47] Some experts involved in the design process expressed the view that the AMC Secretariat did not fully anticipate the attention this initiative would attract. For this and other reasons, suggest several original designers, the AMC Secretariat and decision-makers were not adequately prepared to communicate on the decision-making process.

[xii] The Implementation Working Group, composed of 2 GAVI representatives, 3 UNICEF representatives, 2 World Bank representatives, and 4 members of the Economic Expert Group, recommended the final price and payment structure.

6. Implementation

Relevant TOR Questions addressed in this section:

- **Question 9:** To what extent were the estimated costs of setting up and implementing the AMC in terms of finances and staff allocation reasonable and appropriate?
- **Question 10:** To what extent has the AMC been implemented as designed? What elements have been most difficult or require adjustment, if any?
- **Question 11:** To what extent has management by the implementing agencies of the AMC been efficient, effective, transparent, timely, and appropriately responsive to changes in context and external factors?
- **Question 12:** In what phases of the implementation process have the greatest costs been incurred? To what extent are on-going support costs reasonable and appropriate?
- **Question 13:** To what extent has the oversight process (e.g. IAC) been adequate?
- **Question 14:** To what extent have the complementary activities identified as necessary to stimulate demand and support the introduction of pneumococcal vaccines in GAVI eligible countries (including communication and outreach activities) been conducted as planned?

Key findings:

The implementation of this AMC is on track, and it is progressing towards its overarching objective of reducing morbidity and mortality from pneumococcal diseases in developing countries. The Pilot has been implemented as designed, demonstrating the ability of the international development community to establish and administer an advance market commitment. However, some components of this AMC remain untested to date.

Overall, the design process and choice of design elements have contributed to increasing the supply of PCV. Since this AMC's launch, two manufacturers have supplied enough PCV to satisfy demand from the 24 participating low-income countries, though temporary supply and demand imbalances have occurred. The launch of this AMC, and the momentum it created, appears to have contributed to the creation of a longer-term market for PCV, as participating suppliers have expanded capacity and additional manufacturers have expressed interest in joining the initiative. While there are some areas for improvement, overall management of the AMC by GAVI, UNICEF, the World Bank and the IAC has been effective.

Moving forward, implementers face several challenges: ensuring that meaningful indicators of progress are defined and regularly reported, determining a methodology that will enable the evaluators in 2014 to attribute any observed changes in trends to this AMC, and managing the market entrance of additional manufacturers. These challenges can be addressed by strengthening existing monitoring and evaluation frameworks, systems, and processes that ensure indicators are measured, communicated, and used to guide further implementation decisions. Implementers should also develop a clear plan to maximize the benefit of a third or fourth manufacturer's market entry.

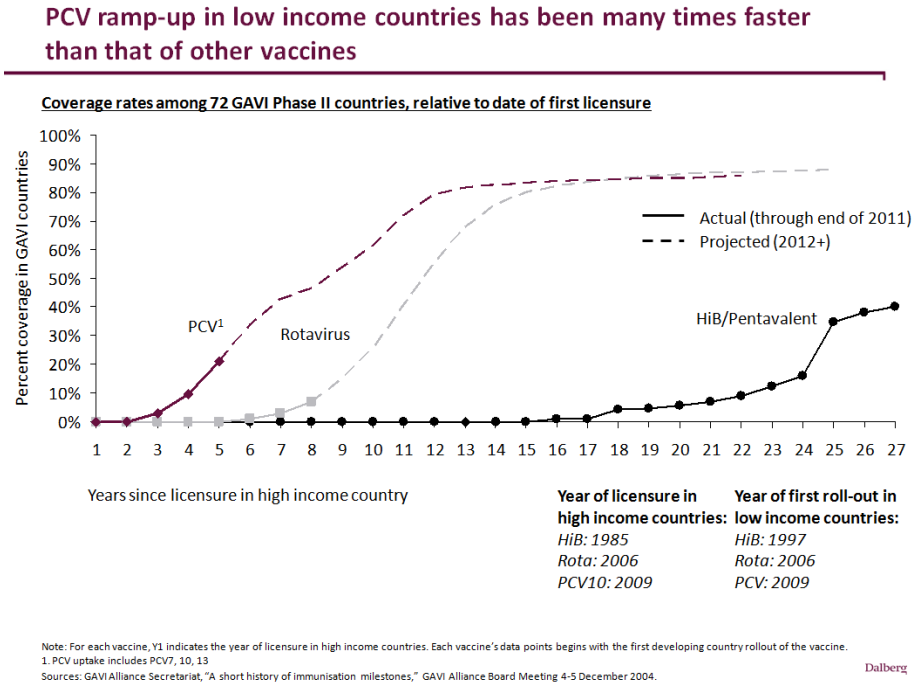
This chapter evaluates the elements of implementation covered by the Terms of Reference, but does not include an evaluation of this AMC's impact, including its role in reducing morbidity and mortality, as this will be the topic of the 2014 Outcomes Evaluation. Additional details on the efficient, effective, transparent, timely, and appropriate management of this AMC are included in Appendix II.

The AMC's progress towards its goals

The implementation of this AMC is on track, allowing the Pilot to progress towards its overarching objective of reducing morbidity and mortality from pneumococcal diseases in developing countries. To date, this AMC has contributed to the distribution of 82 million doses of PCV;[48] more than 900 million doses have been contracted, and by the end of 2012, 24 low-income countries have introduced the vaccine as part of their immunization programs. As of 2012, 51 GAVI-supported countries have applied for additional GAVI support to introduce PCV.[49] Two manufacturers are supplying pneumococcal vaccines which have been of suitable quality and quantity to meet the needs of low-income countries, and additional manufacturers have submitted bids indicating interest in supplying. A considerable increase in supply capacity has occurred over this time period, from 4.3 million doses in 2010 to more than 60 million doses in 2012.

PCV uptake in GAVI countries is occurring at a faster rate than that of other comparable vaccines, such as rotavirus and pentavalent. In the roughly three years since PCV10 and PCV13 were approved for use in high-income countries, 24 GAVI-supported countries have adopted PCV[xiii,50] as part of their national immunization programs. In contrast, only seven UNICEF-supplied countries introduced the rotavirus vaccine by the end of 2012,[xiv,51] though it was first licensed in high-income countries in 2006 and the WHO SAGE committee recommended its use in low-income countries in 2009.[xv] Both PCV and rotavirus vaccines were deployed in low-income countries significantly faster than Hib combinations (including monovalent HiB, now part of the pentavalent vaccine), which only began reaching these areas more than a decade after approval by U.S. and European regulators.

Figure 8: Rollout of PCV compared to rotavirus vaccine and HiB/pentavalent



The "AMC Outcomes Evaluation," scheduled for 2014, will assess progress in much greater detail. This report is an evaluation of this AMC's design process and design elements, and this chapter discusses how they have impacted implementation to date and addresses the implementation questions included in the Terms of Reference. Additional review of implementation will be covered by the 2014 evaluation, including a detailed review of progress towards the AMC Objectives and discussion of the Pilot's role in reducing morbidity and mortality.

[xiii] Adoption defined as delivery of PCV dose 3.

[xiv] Adoption defined as delivery of rotavirus vaccine's last dose.

[xv] WHO SAGE recommended introduction of rotavirus in 2007, including in developing countries. However, initially this was limited to countries in Europe and Latin America as clinical data were only available from these regions.

This chapter also discusses the extent to which: this AMC has been implemented as designed, the design process and design elements contributed to increasing PCV supply and country uptake, management has been effective, as well as the main challenges currently faced by implementers.

AMC Objectives

Goal: To reduce morbidity and mortality from pneumococcal diseases and, specifically, to prevent an estimated 7 million childhood deaths by 2030.

Objective 1: To accelerate the development of pneumococcal vaccines that meet developing country needs (e.g., serotype composition and vaccine presentation) as specified in the TPP.

Objective 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 incentivizes manufacturers to invest in scaling-up production capacity to meet developing country vaccine demand.

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

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

Extent to which AMC has been implemented as designed

This AMC has been implemented as designed and overall adherence to the program is being achieved. The roles originally crafted for UNICEF, GAVI, and the World Bank have been fulfilled as planned.

The Pneumococcal AMC demonstrated the ability of the international development community to establish and implement the key elements of an advance market commitment, which had never previously been tested. Creating an AMC required donors to provide funds in novel ways and develop new rules and committees to govern procurement processes. These commitments needed to have sufficient credibility to prompt private sector firms to invest hundreds of millions of dollars in vaccine production. The Pilot demonstrated the ability of donors and technical experts to deliver on many of these key elements, as delineated in the original "Making Markets for Vaccines" framework. The following list highlights some of the important features implemented as designed:

- Legal structures binding donors[xvi] to provide pledged funds if stated conditions (i.e. regarding total demand for PCV) are met
- Limited purchase guarantees over long-term contracts for manufacturers

[xvi] Italy, Canada, United Kingdom, Russia, Norway, and the Gates Foundation signed such legal agreements.

- Establishment of eligibility requirements for AMC-compatible products through a Target Product Profile (TPP)
- New governance structures to manage the administration of an AMC, such as the Pilot's IAC, as well as to leverage the experience of organizations such as the GAVI Alliance, UNICEF Supply Division, WHO, and the World Bank

Since the launch of the Pneumococcal AMC, the development community has launched other, similar innovative financing programs. While some of these programs have not yet been fully launched and evaluated, their existence suggests continued interest in results-based financing for development and that some were, at least in part, inspired by the successful launch and implementation of this AMC.

Figure 9: Additional innovative financing mechanisms

Innovative financing mechanisms for global development inspired by the Pneumococcal AMC

The Pneumococcal AMC concept encouraged other innovative financing mechanisms for development:

New AMC (Sector)	Description	Funder/ Implementer	Fund Amount	Target Products	Stage
AgResults initiative	Using AMCs and other results-based financing methods to advance agricultural development	Canadian and US governments, BMGF, WB	TBD	• Biocontrol products • Biofortified products • On-farm storage products	Early: specific pilots identified
Low Carbon Advance Market Commitments	Using pull mechanisms to drive private sector investment in low carbon, climate resilient technologies.	DFID	TBD	• Renewable energy products and tech deployment • Green mini-grids; large-scale, grid-connected renewable energy projects • Deployment of biogas for schools and hospitals	Early: ideas in development, implementing pilots (Rwanda)
Emission Reduction Underwriting Mechanism	Generate low carbon market by guaranteeing payment for performance in delivering emissions reductions	Copenhagen Green Climate Fund	Target of up to $100 billion by 2020	• Any emission lowering products • Further research pending	Research pending
Sustainable Energy Sources	Using a feed-in tariff AMC to encourage Non-Conventional Renewable Energy; attract private capital for provision of energy access infrastructure.	Sri Lanka government, Ceylon Electricity Board	Total unknown; 3-tier tariff for 20 years	• Electricity generation energy sources: biomass (dendro power), hydro, wind, municipal waste, agro waste, and waste heat recovery	Implemented

Sources: DFID, Low Carbon Advance Market Commitments, accessed 18 October 2012; Pisces, Policy Brief: Low Carbon Advance Market Commitments, 5 October 2010; Climate Change Capital, Advance Market Commitment/ Emission Reduction Underwriting Mechanism for Carbon and REDD, 01.06.10; Dalberg report on AgResults Initiative

Dalberg

Extent to which management has been effective

Overall implementation and management by GAVI, UNICEF, and the World Bank has been smooth and effective, as these organizations have fulfilled their roles as planned. A further discussion of AMC implementation regarding efficiency, effectiveness, transparency, timeliness, and responsiveness to changes can be found in Appendix II. The two most challenging areas of implementation – managing

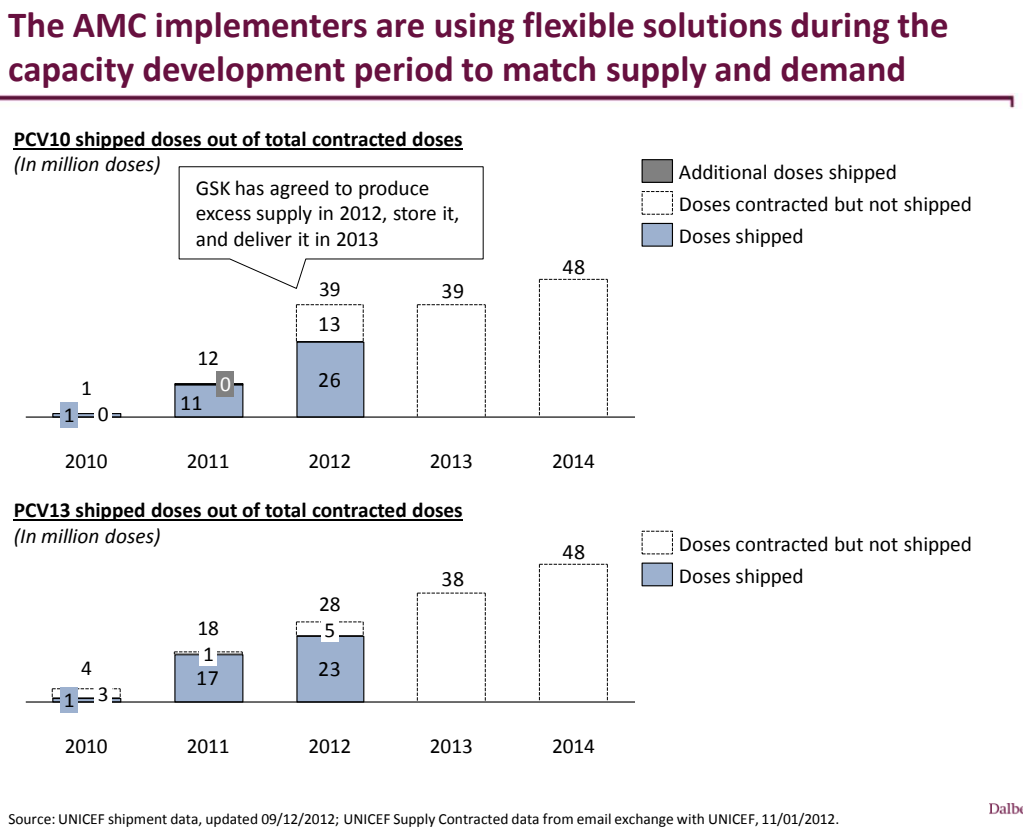
initial ramp-up during the Capacity Development Period and working with manufacturers to provide near-term demand forecasts – have been conducted effectively, as described below.

Managing the introduction of new vaccines is difficult, and while this AMC has been challenged by matching supply and demand during the ramp-up phase, effective implementation has contributed to its overall success. Because the PCV market has two distinct products – PCV10, produced by GSK, and PCV13, produced by Pfizer – implementation can be especially challenging. The Pilot's designers believed an important element of "market creation" was to provide countries with the ability to choose which vaccine they preferred, but this created situations of oversupply of one product and undersupply of the other. Specifically, despite a 12 million-dose surplus of PCV10 in 2012, Bolivia and Senegal elected to introduce PCV13, which delayed their vaccine introduction until early 2013, when sufficient supply became available.[52]

This AMC's use of a "Capacity Development Period," during which GAVI and UNICEF can procure doses ahead of the scheduled 2014 start date of AMC contracts, has helped alleviate supply issues during the ramp-up phase. The UNICEF Supply Division, which was asked to take on responsibility for managing PCV tendering and procurement via long-term contracts,[xvii] has also employed various creative solutions in the near term to match supply and demand. In 2012, GSK faced a surplus of 12 million PCV10 doses due to a delay in introductions by a number of countries. UNICEF, anticipating a supply deficit in 2013 and recognizing the importance of purchasing the contracted amount to incentivize GSK's continued capacity expansion, purchased the excess doses for delivery in the following year, taking advantage of the vaccines' longer shelf-life;[53] they are set to be delivered in 2013. This decision also helped compensate GSK for the costs of running high stock levels over the year end.[54]

[xvii] UNICEF was chosen after a review of alternative procurement options.

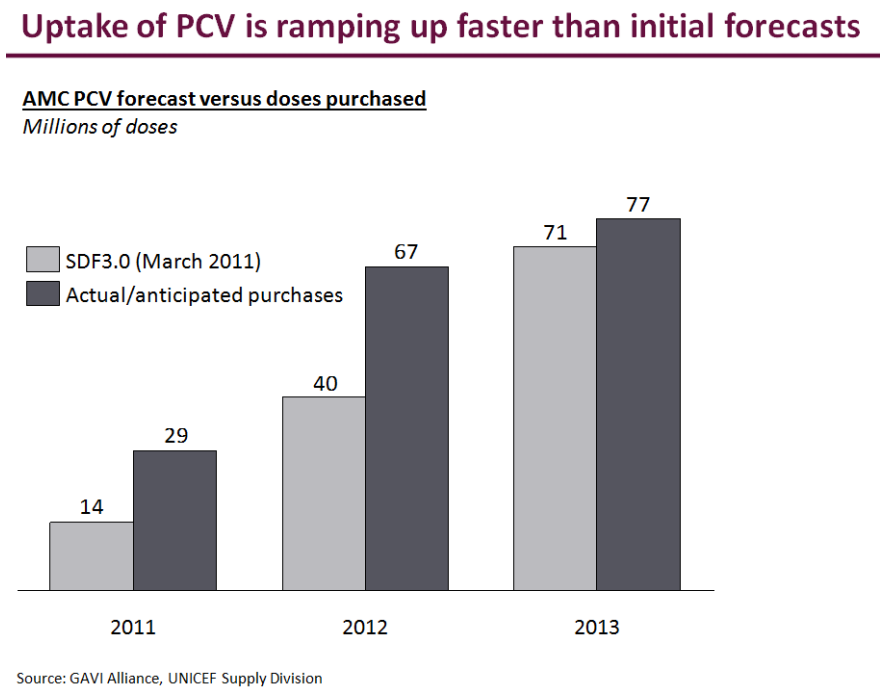
Figure 10: The AMC implementers are using flexible solutions during the capacity development period to best match supply and demand



Effective management of this AMC allowed PCV supply to increase steadily, and demand has grown more rapidly than originally forecasted. The Strategic Demand Forecast (SDF) version 3.0, released in March 2011, shortly after the AMC Pilot began, estimated a need for 14 million doses in 2011, 40 million doses in 2012, and 71 million doses in 2013. However, demand and supply have exceeded these predictions, with 28.9 million doses contracted in 2011, 67 million doses in 2012, and 77 million for 2013. The number of PCV doses shipped by UNICEF in the first eight months of 2012 alone is close to the latest SDF estimate for all of 2012.[xviii] While the Strategic Demand Forecasts are not expected to estimate short-term demand accurately, this comparison suggests that both supply and demand are ramping up faster than the forecasted pace.

[xviii] UNICEF shipped 30 million of doses from January to August 2012 (figures extracted from UNICEF website); the latest SDF estimated a total demand for 2012 of 34 million doses.

Figure 11: AMC PCV forecast in March 2011 versus doses purchased



Implementers have improved demand forecasts for manufacturers since the launch of the Pilot. Manufacturers have previously expressed frustration that the AMC's Strategic Demand Forecast (SDF) was inaccurate in the short term. The SDF was designed as a long-run forecast, so it does not have the resolution necessary to support near-term production planning. UNICEF and GAVI have made efforts to resolve this issue over the past year: UNICEF developed a separate, finer-grained, rolling monthly forecast to assist manufacturers during the ramp-up phase. Unfortunately, these separate forecasting mechanisms were not well explained and initially confused manufacturers. GAVI also developed an Adjusted Demand Forecast, which uses the actual GAVI-approved quantities. While participants on all sides have indicated that the current situation has improved in recent months, manufacturers have indicated that they would still welcome greater transparency and increased communication. Some suggestions for additional communication include more visibility on the application status of countries pending inclusion in this AMC.[xix]

This AMC's implementers have successfully adapted to major external challenges since its July 2009 launch. One of the most significant changes was the revision to GAVI's country eligibility requirements and graduation policies, which occurred in November 2009. Without adapting to take into account these new requirements, this AMC would have undergone a drop in peak PCV demand of 50 million doses, or 25%.[55] However, the GAVI Board and IAC adjusted the Pilot terms continue support for

[xix] Country application status information could include submissions, IRC recommendations, timing of introduction, vaccine/presentation preferences.

graduating countries,[xx] which brought expected peak demand back to the original forecast of 200 million doses per year.[56]

Oversight process of the IAC

The necessity and benefits of the IAC, the only body created specifically for this AMC, has not yet been proven. "Making Markets for Vaccines" envisioned this committee as an impartial oversight body for an AMC.[xxi,57] However, it has not met since August 2010. As some stakeholders pointed out, the minimal involvement of the IAC may potentially be viewed as a positive, since it suggests implementation is progressing smoothly. The IAC's role also includes reviewing ceiling price changes due to inflation, which will be required only later in the Pilot's timeline. One interviewee suggested there may have been a greater need for a decision-making body such as the IAC had existing institutions (UNICEF, the GAVI Alliance, WHO) not been well-suited for implementation.

Implementation progress to date

The design process, launch, design elements, and management of this AMC have contributed to its current outcomes. Briefly examining current supply and demand allows us to better evaluate the Pilot's implementation and management, as well as the design elements of the next chapter.

Since the launch of this AMC, two manufacturers have begun supplying PCV to meet the needs of low-income countries. Existing manufacturers – GSK and Pfizer – appear to have expanded PCV manufacturing capacity for the developing world following the Pilot's launch. In June 2009, GSK opened a new plant in Tuas Biomedical Park, Singapore, with potential capacity to produce up to 300 million doses a year. The plant, which GSK indicates is primarily intended to serve GAVI markets, began production in 2011.[58] However, as discussed further in the next chapter, GSK began planning for these investments before this AMC's design process began. Pfizer states that, spurred by this AMC, it has invested more than $100 million in expanding capacity to supply GAVI markets. This AMC has also sparked product innovation in the PCV market: Pfizer is currently working to develop a novel, mercury-free preservative specifically for GAVI markets. This preservative would enable the company to provide its doses in a multidose presentation requiring considerably less cold chain space than its current single-dose vial[59]—a major achievement for the global health community and this AMC.

The launch of this AMC and the momentum it created appear to have contributed to the creation of a longer-term market for PCV. At least two developing country manufacturers, Panacea Biotec and Serum Institute of India, have publically registered to supply PCV under the Pneumococcal AMC, signaling their intentions to provide doses when their products receive WHO approval. A senior executive at Panacea Biologicals explains that "the AMC has given us a crystal-clear signal that there will

[xx] The grandfathering of the AMC deal refers to the following agreements: 1) all GAVI-supported countries, according to the 2003 definition, will be able to access pneumococcal vaccines through GAVI at the AMC terms and conditions and have access to AMC funding; 2) graduated countries need to completely self-finance the vaccine price (tail price) once GAVI support has ended; 3) all countries must have achieved the DTP3 coverage above 70% in order to purchase under the AMC agreements.

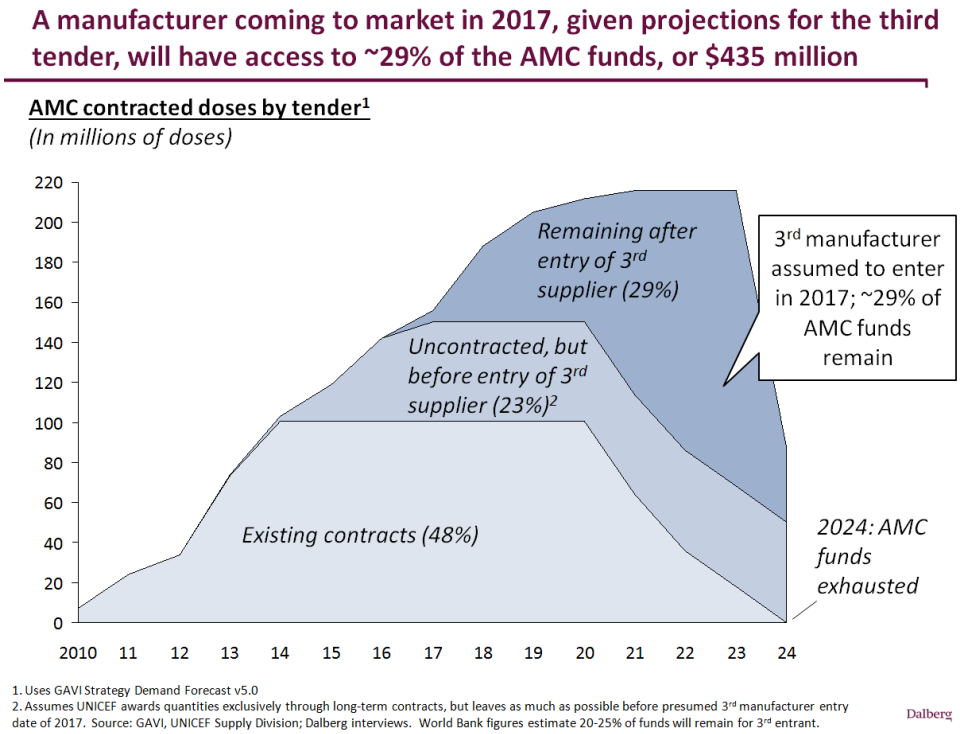
[xxi] In accordance with the roles originally envisioned for this entity (except for being "the main point of contact for manufacturers"), the IAC will: 1) determine whether a vaccine is AMC-eligible based on the TPP, 2) review and modify AMC prices if needed, 3) review and approve the progress of the AMC implementation, and 4) resolve disputes.

be specific demand [for PCV]. After the AMC was announced, the focus on our research program effectively tripled."[60] Additionally, a senior executive at Serum expresses interest in the momentum generated by the Pilot, noting that "the prospect of the long-term market that was being created [by the AMC] was a factor" motivating the company to register. However, the executive also points out that "though the discussion around the AMC was 'in the air' at the time, the AMC itself did not influence our decision to enter into PCV research in 2008. Our philosophy was that, whether the AMC came into existence or not, we were confident that we could make a product that GAVI would want to buy."[61] Several other manufacturers have also registered for the Pneumococcal AMC privately.[xxii] From the perspectives available, this AMC appears to be achieving precisely what it was designed to do: create momentum around purchase of an important vaccine, create demand certainty, and stimulate manufacturers to serve developing world markets in the long run.

On the other hand, the Pilot's structure may have deterred some manufacturers from participating, according to Plahte (2012).[62] Representatives from South Africa's Biovac Institute, Cuba's Centro de Quimica Biomolecular, and Brazil's Butantan were quoted publically stating that this AMC was irrelevant to their business plans, either because they perceived that its funds would not last until their research programs complete, or they considered its mandates on serotype coverage as overly broad for their target markets. However, these manufacturers have not since created regional versions of PCV for their home markets, suggesting that other factors, such as lack of funding, have limited their participation. Further discussion of these manufacturers' decisions and their reactions to the TPP are included in the design elements chapter.

[xxii] The names of these companies were not available for this report and thus representatives were not interviewed.

Figure 12: A 3rd manufacturer coming to market in 2017 will have access to a maximum of ~29% of the AMC funds, or $435 million



Even if a relatively smaller percentage of AMC funding is available to new manufacturers, the revenues to be realized are still significant. Assuming a third supplier enters the market in 2017, as depicted in the graph above, the manufacturer will likely have access to 29% of the $1.5 billion AMC top-up funding.[xxiii] This amount corresponds to subsidy payments of $435 million over eight years, or roughly $54 million a year on average (with the majority of revenues coming toward the end). A manufacturer that earns two-thirds of this remainder would earn annual revenues of $36 million[xxiv] in AMC top-up subsidies – comparable to the entire market size of GAVI's third-largest product by value, the measles vaccine. Such a manufacturer would, of course, also have access to the tail purchase revenues as well. Even if another second-generation manufacturer were to enter, this AMC's top-up subsidy would still represent tens of millions in revenue for both new manufacturers. Therefore, the Pilot's structure likely does offer an incentive to new manufacturers.

Since the launch of this AMC, the rate at which countries have approved and introduced PCV has increased. To date, 46 countries have been approved by the GAVI Board for PCV introduction; a further four countries have been recommended for approval and one country is conditionally approved by the Independent Review Committee. By the end of 2012, 24 countries had introduced PCV; GAVI estimates

[xxiii] This calculation assumes that tender rounds between 2012 and 2017 award 46 million doses in long-term contracts, enough to meet the requirements of the GAVI Strategic Demand Forecast version 5.0 through the end of 2016.

[xxiv] Based on volume as indicated in the figure below and only including top up subsidies of $3.5 per dose, this does not include additional revenue from the tail price.

that by the end of 2015 this total will reach 57 countries.[xxv] As of December 31, 2012, three of the countries approved for 2013 had already received supply.

It is difficult to discern which specific elements of the Pneumococcal AMC, including planned complementary activities, most contributed to increased in-country uptake. In particular, it is difficult to separate the effect of the Pilot's funding, versus its specific design features, in promoting adoption of PCV by GAVI countries. This AMC included many different factors working in tandem: a heavily subsidized country co-pay;[xxvi] a long-term predictable pricing structure for manufacturers and countries; and a highly public and visible campaign, driven in part by the momentum around this AMC's innovative nature and legally binding commitments. Several complementary activities, led primarily by the PneumoADIP program, aimed to promote country awareness and readiness. Such activities included a range of efforts to improve in-country cold chain capacity, train human resources, and rally political support for the introduction of PCV. Complementary activities also included communication and outreach; however, we were unable to assess whether such efforts – either by the PneumoADIP program or others – were conducted as planned, as details were not made available to us during this evaluation.

Lack of country readiness has been a major factor leading to delays in country introductions and thus has slowed country uptake. While 24 GAVI-supported countries have successfully introduced PCV as of December 2012, 14 countries planning introductions in 2012 and 2013 have experienced delays in introduction. According to the GAVI Secretariat, nine of these delays were related to country readiness alone, and an additional three delays were related to a combination of country readiness and gaps in vaccine supply.[63] Country readiness refers to changes in government, elections, cold chain infrastructure, staff changes, training, in-country financing, transportation issues or other factors. Only two country delays, Bolivia and Senegal, were related to gaps in vaccine supply alone; in both of these cases the delay was related to the unavailability of the country's preferred product, PCV13, while an alternative product, PCV10, was available for delivery.[xxvii]

It is difficult to determine whether different design elements would have led to a faster growth of PCV supply and demand. Country readiness appears to have played a significant role in limiting ramp up. According to UNICEF, even if supply for both products was readily available, not all GAVI-approved countries would be ready to introduce them immediately due to cold chain requirements, human resource capacity, etc.[64] PCV10 supply appears to be sufficient – GSK has the capability to produce up to 300 million doses of PCV using its Singapore plant, though they produced only 39 million doses in 2012. Pfizer, however, has not been able to keep up with demand for PCV13. In 2010, UNICEF contracted 6 million doses, but Pfizer only produced 4.3 million; in 2012 Pfizer was also unable to meet demand from all countries interested in introducing PCV13.[65] Although overall distribution between the two products will only be known once all countries have applied, on the whole, it appears supply has been the limiting factor for increased uptake of PCV13, and demand the limiting factor for the ramp up of PCV10. However, these mismatches are only expected to exist in the short term; demand for PCV10 on a dosage

[xxv] According to Strategic Demand Forecast v7.0.

[xxvi] This co-pay, which may be as low as $0.10, is significantly lower than had been envisioned in early iterations of the AMC, where discussions had centered around $2.00.

[xxvii] Senegal was offered PCV10 and specifically turned it down. As a result, while they requested introduction in July 2012, they will likely receive supplies mid 2013. Source: UNICEF, December 2012.

basis is actually greater than demand for PCV13, particularly in larger countries, which prefer PCV10's smaller cold chain footprint.[66]

Areas that remain to be tested

Some aspects of this AMC remain untested thus far. Given that this AMC launched only recently, observers cannot yet determine if certain aspects will unfold as designed. For example, several AMC stakeholders stated in interviews that the AMC tail price was expected to drop once a third manufacturer entered the market. Yet to date, only two manufacturers have provided supply under this AMC.

The set-up and implementation costs of this AMC appear to be reasonable, given available data, but evaluation of ongoing implementation costs cannot be conducted at the time of this report. Although we received limited data on the Pilot's set-up and implementation costs, the costs do not appear to be greater than necessary. This AMC's design process was on par with the timeline of other recent development initiatives, as described in the Design Process chapter. While there was a large number of staff members from multiple organizations involved in the Pilot's setup, interviewees stated this was reasonable and appropriate given the novelty of this initiative and the "learning by doing" design process.[67] We could not evaluate the areas of implementation that have incurred the greatest costs, as this requires access to implementers' internal current and historical cost data, which were not available for this evaluation; in particular, up-to-date information from 2011 and 2012 regarding ongoing implementation costs was not provided to us. Interviews with implementing organizations – the World Bank, the GAVI Alliance, and UNICEF – did not highlight any major issues with implementation costs to date.

This AMC tested the concept on one particular market, and has not yet demonstrated the impact of an AMC on other markets. AMC designers realized that the pneumococcal market had many specific features that might not apply to markets for other vaccines.[68] The level of market maturity, the supplier landscape, and the vaccine's complexity, for example, all contribute to the unique dynamics of an individual market. As a result, conclusions drawn from this Pilot regarding the effectiveness of the broader AMC concept and its specific elements may not hold when applied to other markets, vaccines, or early-stage products.

Main challenges facing implementers today

There are several primary challenges facing AMC implementers today: ensuring that meaningful indicators of progress are defined and regularly reported, determining a methodology that will enable the evaluators in 2014 to attribute any observed changes in trends to this AMC, and managing the entrance of additional manufacturers into the market.

Implementers should consider improving monitoring and evaluation indicators and adding clear progress targets. The M&E indicators and lack of targets developed during the design phase make it difficult to meaningfully track progress, guide strategic decisions, learn from any changes in trends and directly attribute them to this AMC. While certain benchmarks were set in the AMC Baseline Study, the

need for additional indicators and targets can be addressed by strengthening existing monitoring and evaluation frameworks, systems, and processes that ensure indicators are measured, communicated, and used to guide further implementation decisions. The indicators listed in the "Report of the Monitoring and Evaluability Study" could be expanded to include additional metrics that directly evaluate progress on AMC objectives, and relevant targets could be added. For example, in order to measure the Pilot's impact on in-country uptake, implementers could formally track, report, and differentiate between causes of delays for country introductions (e.g. country readiness vs. supply shortage) and set targets for the maximum number of countries experiencing delays. In addition, methods for integrating M&E results into implementation could be clarified. For instance, while UNICEF tracks the shipping of doses and their "on-time delivery", it does not track or publically present results regarding timeliness relative to targets, or the time required to complete payment procedures. Additionally, fund transfers and their rough dates are tracked, no exact target dates, beyond guidelines given in the original legal documents, are provided. Adding these metrics, as well as taking action to mitigate delays, could make implementation more effective moving forward.

AMC implementers should develop a clear plan for how they will maximize the benefit of the market entrance of additional manufacturers. Most stakeholders interviewed expressed the belief that PCV prices offered to GAVI and UNICEF will drop when a third supplier enters the market, if not sooner. However, this AMC's current contracting structure mandates the use of 10-year contracts, and as a result, only 29% of doses are expected to be available for contracting when the third supplier enters.

Uncertainty exists in the PCV market because future contracting plans are unclear. Some interviewees noted that the Pilot's contracts are structured as purchase options; implementers have the right to decline to purchase doses within existing contracts in favor of lower-cost offers. GAVI or UNICEF could also potentially use this flexibility to obtain more favorable pricing on existing contracts. However, once UNICEF enters into an agreement for a certain quantity annually, AMC funding would be committed and could not be redistributed to a new supplier. It is unclear to what extent such action would fit the spirit of these provisions, which have been represented in public communication primarily as insurance against potential low vaccine demand.[69] Additionally, GAVI or UNICEF's ability to take advantage of these terms depends on the ability of low-cost manufacturers to increase production levels rapidly to meet rising demand. These and other considerations are discussed further in the next chapter.

This AMC's implementers should communicate how they plan to respond to the entrance of new suppliers and take full advantage of any drops in price bids. As part of this communication, they should clarify whether they intend to exercise the option not to purchase doses through existing contracts, even if sufficient demand exists. Implementers should also begin exploring creative solutions to avoid the need for such measures, which could antagonize existing participants. For example, manufacturers may be willing to front-weight their contracts to provide supply earlier, before a third producer enter the market.[xxviii] Such a solution could represent a win-win: existing manufacturers would earn revenues up to 10 years sooner, and the Pilot's implementers would preserve their flexibility.

[xxviii] Essentially, this provision would serve a similar role as the Capacity Development Period, but extend from 2014-2017.

Additional elements of implementation and progress towards the AMC Objectives, including impact on morbidity and mortality, will be discussed in the Outcomes Evaluation scheduled for 2014. Additional information for this chapter, including an evaluation of the effectiveness, transparency, timeliness, and responsiveness of the Pilot to changes in context and external factors of implementation is included in Appendix II. In addition, an assessment of the existing GAVI annual M&E framework, along with suggested new indicators, can be found in Appendix II.

7. AMC Design elements

Price structure and price point

Relevant TOR Questions addressed in this section:

- **Question 2:** To what extent do specific AMC design elements (including but not necessarily limited to the AMC price and Tail price cap) contribute to the AMC objectives?
- **Question 4:** To what extent have assumptions underpinning the AMC at the time of its design proved to be robust and appropriate over time, including those related to vaccine cost?

Key Findings:

The Pneumococcal AMC's pricing structure has been a focal point of public discussion regarding the initiative. In particular, critics have charged that the Pilot provides excessive profits to multinational suppliers who have access to high-income country markets. The following section considers potential benchmarks for this AMC's pricing structure, examines the goals, constraints, and approach that its designers used when setting the tail price ceiling, and considers whether its tail price ceiling was set appropriately to reach its goals. We also introduce a model, an extension of the one used by the IWG, to estimate the incentives and returns manufacturers are earning from their participation in the Pilot.

We conclude that, given their constraints and approach, this AMC's designers set the tail price ceiling appropriately to maximize the chance that both existing manufacturers would participate. However, analysis using financial models created for this evaluation suggests that – under a range of reasonable scenarios regarding suppliers' unit costs, investments required, and total volumes – manufacturers may be earning financial returns greater than what was necessary to incentivize their participation in the Pilot. We also analyze under what circumstances manufacturers would have provided doses to low-income countries absent an AMC; we conclude that while the high revenue potential of the GAVI market would have offered low-cost manufacturers reasonable returns, returns for high-cost manufacturers would have been insufficient without some form of subsidy.

This AMC is structured so that firms can compete by bidding under the tail price ceiling, so it is possible that, over time, these profits could be eroded. However, in the first two tender rounds both manufacturers bid at the $3.50 cap. Some interviewees have indicated that they expect prices to drop only when a third supplier enters the market and creates competition, around 2017. Nevertheless, it is estimated that more than two-thirds of the Pilot's doses will be awarded before this date, so such reductions will most likely have little effect on the returns of existing manufacturers and provide minimal savings for funders.

The price could further decrease if implementers opt out of existing contracts in favor of lower-cost suppliers. However, it is unclear to what extent such action would fit under the spirit of these provisions. Additionally, the ability of this AMC to take full advantage of these terms is dependent on the degree to which low-cost manufacturers can rapidly scale capacity.

A key goal of the Pilot was to test the effectiveness and appropriateness of the design elements of the Advanced Market Commitment concept. The purpose of this section is to examine the consequences of the decisions that were made, so as to provide lessons learned that may inform future AMC design efforts. In this section, we evaluate the following key design elements: the pricing structure, binding legal commitments on donor pledges, limited purchase guarantees, target product profile, and lack of caps on manufacturer supply contracts. These design choices were made after extensive analysis by the AMC designers, though sometimes on the basis of very limited available information. In some cases the designers were faced with clear trade-offs, and they had to make decisions that would engender uncertain outcomes with associated risks and consequences. Further discussion of other design elements is included in Appendix IV.

How does the AMC's price outcome compare against various potential benchmarks?

The overarching goal of the Pneumococcal AMC was to accelerate the delivery of the pneumococcal conjugate vaccine (PCV) to millions of children at risk of a preventable disease; this AMC's price structure must be evaluated within this context. However, several types of benchmarks could be used to compare the appropriateness of its pricing:

- **Prices paid for PCV in high-income and middle-income markets**. In 2010, the public sector U.S. price for PCV13 was $92; the price for the Pan-American Health Organization (PAHO) was $20.[70] The Pilot's initial price of $7.00 represented 92% and 65% drops from these comparison points, with the tail price ceiling of $3.50 representing 96% and 83% reductions. However, other GAVI vaccines have also experienced similar price reductions through tiered pricing:[xxix] prices for monovalent hepatitis B, DTP-HepB, pentavalent, and rotavirus are all 88-98% cheaper than those charged to the U.S. public market.[71] GSK has also stated a commitment to the general principle of tiered pricing across several of its products.[72]

- **Initial manufacturer pricing indications when this AMC was being designed**, which were in the $10-20 range. However, it is difficult to discern whether such indications represented rigid positions or negotiating positions.

- **Cost per lives saved or DALY averted** relative to other vaccines or public health interventions. This was a guiding framework for this AMC's Implementation Working Group (IWG), which set the target rate at $100/DALY. Evaluating the cost-effectiveness of the overall Pilot on these metrics is outside the scope of this review, but is expected to be included in the AMC Outcome Evaluation scheduled for 2014.

- **Reasonable returns for manufacturers.** The primary motivation of this AMC was to incentivize manufacturers to conduct research or to expand capacity to meet the needs of low-income countries. The Pilot's pricing structure can thus be evaluated on the basis of whether it properly

[xxix] Monovalent hepatitis B and pentavalent experienced these reductions over a longer time period.

achieved the middle ground between ensuring that manufacturers earned commercial returns – i.e., were not motivated purely by corporate social responsibility or charity – and ensuring they did not receive profits over and above what was necessary to incentivize action.

Because the last of these perspectives is where much of the discussion around the Pilot's pricing has concentrated, it is the focus of the remainder of this section.

What would represent reasonable returns or incentives to manufacturers?

Target returns for manufacturers

Manufacturers typically require the internal rate of return (IRR) of new projects to meet certain target rates, called "hurdle" rates. Hurdle rates are constructed using a baseline rate required for any generic new project, and then adjusted based on a specific product's risks, size, context, nonfinancial returns, and other factors.

A common baseline used in industry is companies' weighted average cost of capital (WACC). In written communications, a spokesperson for GSK confirms that, "In order to ensure sustainability of the GSK commitment to make the [PCV] vaccine widely available to the entire population (including GAVI countries) the internal rate of return (IRR) or cash flow return on investment (CFROI) must be at minimum above the weighted average cost of capital of GSK." Bloomberg reports that over the past ten years, GSK and Pfizer's WACC has tended to vary between 6.5% and 8.5%, though with spikes as high as 12% during economically stressful periods.[73] The IWG assumed companies had a similar hurdle rate, 10%, when it modeled whether they would participate in the Pilot at various price points.

Risk and other considerations may also increase a project's specific hurdle rate above the baseline established by the WACC. While expanding capacity to meet this AMC likely represented less risk to pharmaceutical companies than typical early-stage research projects, it nevertheless required companies to commit resources towards a new and untested purchasing initiative for uncertain markets. Moreover, this AMC required companies to commit to provide hundreds of millions of doses over a 10-year time horizon without any formal guarantee these doses would actually be purchased.[xxx] This option structure, which was introduced as a risk-reducing measure for donors in case demand did not materialize, correspondingly raised the risk for manufacturers. Other considerations affecting manufacturer's target rates include the size of the market (smaller markets in revenue terms likely would require higher returns) and this AMC's intention to incentivize manufacturers not just to provide vaccines over the long term, but to ramp up production quickly. However, it is difficult to quantify the exact value of these adjustments, in large part because they vary considerably across manufacturers, markets, and products.

In the following analysis, we assume that required internal rate of return ("hurdle rate") for multinational manufacturers to participate in this AMC fell between 10-20%. This estimate is based on both the IWG's work and that of DiMasi et al (2003),[74] which states that, "we undertook an informal

[xxx] The AMC included limited purchase guarantees in early years, which amounted to 6% of each contract. These played a minimal role in suppliers' decision-making and incentives due to their small amount relative to other sources of payment.

survey of major pharmaceutical firms in mid-2001 with respect to the hurdle rate that they used in their R&D investment decisions. This survey of six firms yielded (nominal) hurdle rates from 13.5 to over 20%." The high end of this range provides a buffer of approximately 10-12% above manufacturer's WACCs. However, as noted above, the precise hurdle rate that each manufacturer would have used for this AMC depends on a number of factors that are difficult for external observers to measure.

In some parts of this report, we use the concept of Net Present Value (NPV), to translate future cashflows into present-day terms. These calculations require the use of a single discount factor. For consistency, we follow the example set by the IWG and use a rate of 10%. While, as discussed above, manufacturers may seek returns above this discount rate, this is equivalent to stating that they seek to do better than break-even on an NPV basis.

Indirect costs and benefits for manufacturers participating in this AMC

The direct profits from GAVI sales were not the sole consideration for manufacturers determining whether to participate in the Pilot. These considerations are difficult to quantify in a simple IRR calculus, but nevertheless represented real benefits and risks that may have affected internal decision-making. Such factors would include:

Benefits:

- **Allocated savings on other products due to economies of scale:** Manufacturers may be able to use their AMC-related investments in shared facilities to reduce the production costs allocated to other products that utilize the same distillation plants, filling lines, and other infrastructure. Based on the IWG report and interviewee estimates of manufacturers' fixed costs, such allocated savings could reach tens of millions of dollars per year.

- **Favorable publicity:** Manufacturers participating in this AMC would also benefit from the positive publicity provided by the high-profile nature of the Pilot. This benefit is especially noteworthy given frequent controversy over manufacturer prices and profits in both high-income and low-income markets.

Risks:

- **Financial opportunity costs:** Investments made by manufacturers in AMC-related capacity expansion used dollars and management time that would otherwise have gone towards other projects with different tradeoffs and risk/reward profiles.

- **Missed sales in higher-income markets:** Depending on their total production capacity and utilization, by devoting capacity to AMC markets manufacturers may have lost out on the opportunity to sell doses in higher-income markets. For these companies, the question regarding this AMC may not be simply one of whether or not to enter the GAVI market, but how they should allocate their product across markets with highly different profit margins.

- **Pricing in high-income markets:** Manufacturers may also have been concerned that, by announcing drastically reduced pricing for the GAVI Alliance, they would affect sales in the high-income markets that form the bulk of their returns. For instance, if Pfizer were to lose just 2.5% of its pricing power in non-GAVI markets for PCV13, it would have lost around $750 million in NPV over the 10-year lifespan of the Pneumococcal AMC, negating any profits resulting from the Pilot. In practice, this concern does not appear to have been realized, as Pfizer was able to raise its rates for PCV13 in the U.S. by 11% between 2010 and 2012.[75]

- **Pricing in PAHO countries:** Manufacturers also indicated in interviews that they were particularly concerned that supplying PCV to GAVI at extremely reduced prices would force them to sell the vaccine to PAHO countries at the same rate. As part of its standard contract, PAHO requires that manufacturers not sell equivalent products to other countries at lower prices (commonly called the "least-price clause"). Because a number of important middle-income Latin American countries are part of the PAHO consortium, this was viewed as a critical issue; resolving it proved to be a time-intensive process. PAHO provided a formal waiver for the Pneumococcal AMC only in August 2011, several years after the Pilot's other foundation agreements were signed.

What factors were AMC designers taking into account when setting the Pilot's price structure?

Determining the overall payment philosophy: Commitments for early-stage versus late-stage products

The original "Making Markets for Vaccines" report suggested two separate approaches for late-stage and early-stage products. In the former scenario, donors would be able to work with known suppliers with roughly established pricing structures; hence the report proposed signing direct contracts with specific manufacturers, citing pneumococcus as a specific example.[76] However, in the case of early-stage products, the eventual suppliers and their costs would be unknown. In these cases, the report instead suggested donors announce a more open-ended funding commitment at a price point they believed would deliver the best public health value.[77] To establish that target level, designers would take into account the anticipated costs of producing such a vaccine, but such figures would only be estimates, since by definition the product would not exist yet.

The Disease Expert Committee recommended that the Pilot focus on pneumococcal conjugate vaccines for the developing world, a product for which two multinational manufacturers (GSK and Pfizer) were already in late-stage research. However, largely because of the emphasis on testing the overall AMC concept, the Pilot design more closely matched the "Making Markets" vision for earlier-stage products. As explained in this section, some of the design elements were ultimately based more on the "Making Markets for Vaccines" vision, rather than on the needs of this specific market. Some interviewees have also indicated that adapting or retrofitting this approach caused challenges during the design phase.

Goals driving the payment structure

The AMC's price was decided upon by the IWG in conjunction with AMC donors. When deciding how to set the AMC's subsidy structure and tail price ceiling, these committees were working with a complex set of objectives. Each goal came with its own trade-offs and challenges:

Find a payment structure which will ensure millions of children are vaccinated in a timely manner. When the Pilot's designers developed its pricing structure, their highest priority was to save lives by minimizing the delay between when PCV was approved for use in high-income markets and when it was introduced in low-income countries. Historically, such lags have lasted up to twenty years, periods during which millions of children died from preventable diseases. Ensuring this delay did not happen for PCV was at the forefront of the designers' minds.[78] However, critics have charged that this meant that the majority of the AMC's spending would go towards higher-cost existing manufacturers.[79]

Provide pricing predictability by setting a single price ceiling. A central tenet of the AMC concept is to provide pricing predictability to allow manufacturers to plan R&D efforts and capacity expansions and countries and donors to forecast long-term program budgets. In adherence to this, the framework of the Pilot aimed to set a single tail price ceiling shared by all manufacturers, which designers indicated in interviews they expect to drop after a third manufacturer enters the market.

Such a tail price ceiling was envisioned by the original "Making Markets for Vaccines" report as part of an AMC for early-stage products. However, as GAVI's "Lessons Learned" white paper notes, "from an economic point of view it may have been more efficient to provide or negotiate tailored contracts with the two manufacturers, rather than shape a 'one size fits all' contract."[80] Several interviewees noted that the Pilot was designed in different circumstances than the original AMC concept: the Pilot's designers were considering established products, with identifiable manufacturers, each with roughly known production costs—none of which were foreseen at the time of "Making Markets". Because each supplier's per-dose costs reflect a different relative mix of capital expenditures, fixed operating costs, and variable costs, more bespoke contracts may have been better able to meet each manufacturer's specific circumstances, while still leaving room for new, lower-priced producers to enter in the longer term. Such an approach would have potentially fit the "Making Markets" framework for an AMC for late-stage products, but would not have been able to test the broader AMC concept.

Avoid a monopoly situation: This AMC's price-setters also had a strong desire to ensure both existing suppliers, GSK and Pfizer/Wyeth, participated. An expert involved in the design process explains, "We've seen in the history of vaccine marketplaces how vulnerable one becomes when there is a single producer. There was a tremendous amount of back-and-forth [during the design of the AMC] regarding the trade-off between setting the price very low and having only one or two manufacturers participate, versus setting it higher and having a more competitive landscape."[81] In interviews, several AMC designers indicated a broad set of reasons for why a monopoly was considered disadvantageous: it would have given excessive pricing power to one player; it would have risked supply breaks in the case of an unforeseen outage; and it would have led to complex political dynamics, as neither manufacturer wished to be uniquely prominent in front of their shareholders, civil society organizations, and the general public.

Despite significant uncertainties around manufacturers' cost structures, it was generally agreed that one of the two existing manufacturers had considerably lower marginal costs than the other—potentially even two-thirds lower. Thus, setting a single, shared price based on the higher-cost supplier meant providing considerable profits to the lower-cost supplier. This trade-off was known and acknowledged at the time.[82]

It is difficult to determine the price threshold at which the benefits of avoiding monopolies are offset by the higher costs. UNICEF has stated that it has incurred extra costs of at least 25% in ensuring a second supplier for the measles vaccine.[xxxi,83] Based on the designers' estimates of manufacturers' relative cost structures, the goal of attracting a second supplier for this AMC likely resulted in a 30-40% higher tail price ceiling.[xxxii] How actual pricing in a monopoly scenario would play out over time is difficult to gauge, particularly if a second low-cost manufacturer were to eventually enter in 2017.

Members of civil society have also indicated some tolerance for such arrangements, at least in the short term. A former staff member of Médecins Sans Frontières commented in an interview, "Personally, I'm not embarrassed that one manufacturer is making profits off of the fact that they might have a better, less expensive process. The key, however, is to make sure that this situation does not persist in the long term, and that competition is organized to ensure they will lower their prices or lose business."[84]

In the future, a potentially insightful, alternative example for evaluators might be the market for rotavirus, where long-term guarantee contracts at specific prices have been signed with GSK. The current implications are mixed: while rotavirus is being successfully rolled out across several low-income countries, GAVI overall is currently facing a supply shortage of GSK's product.[85] However, it is important to caveat that the rotavirus market had many distinct characteristics from that of PCV (for instance, it appears that GSK today has significant unused capacity for PCV, unlike rotavirus suppliers), and that it is still too early to tell how the dynamics of both will play out in the long term.

Incentivize early producers while allowing for later price declines: While designers recognized that second-generation suppliers would likely have lower costs than first-generation manufacturers, they considered it unacceptable to let millions of children go unvaccinated during the seven to 10 years it would take for new suppliers to build their PCV programs. The designers therefore set the Pilot tail price ceiling at a level designed to attract existing producers in early years. Because the pricing structure was specifically designed as a ceiling and not a fixed value, this AMC's designers hoped subsequent competition would drive prices below the cap.[86] Several designers indicated in interviews, however, that they anticipated such competition would only occur once a third manufacturer entered the market.

Some interviewees argued that this AMC's pricing structure did not set clear enough expectations for how its designers intended the market to evolve. For instance, despite its nature as a cap, the stated $3.50 tail price ceiling may have an anchoring effect on the price and make it easier for higher-cost incumbents to remain in the market in the long run. An alternative structure considered by designers

[xxxi] UNICEF states that 20% of its costs for measles in 2004-2006 went to ensuring a second supplier remained in the market; this translates to a 25% higher cost burden from the single-supplier scenario.

[xxxii] Dalberg analysis based on internal estimates of suppliers' relative costs used by the IWG and EEG. Assumes a single price shared across all manufacturers.

was breaking the Pilot into an explicit two-stage payout: a higher top-up ceiling price initially, justified by a lack of competition and the high capital costs faced by producers, followed a few years later by a lower ceiling to reflect anticipated competition. Such an approach would have the benefit of setting expectations for how the AMC intended the PCV market to evolve in later years. It may also have helped mitigate public criticism over the pricing structure. However, locking in price thresholds would also have had a disadvantage in potentially reducing purchasers' flexibility in the event that a lower-cost manufacturer did not arrive in time to the market.

Constraints around setting the price point

This AMC's designers also faced a broad set of constraints in their efforts to set the best possible price:

Strong priority on reaching an agreement: The Pilot's price-setters considered the costs of setting the price too low to be very high, as it would result in not achieving a pilot AMC and a lost opportunity to introduce a critical vaccine to the developing world. Conversely, while a too-high price would mean financial loss, they considered this outcome far preferable to not having an AMC at all. As a member of the IWG explains, "The losses from getting it wrong in different directions were very asymmetric. If buyers could have gotten the vaccine for a dollar less, some money would have been saved – but if buyers hadn't gotten a vaccine it would have been a real disaster for millions of children." The Pilot's donors would also face political costs from the failure of such a high-profile initiative. Because the public health and political costs of failing to strike the targeted deal were viewed as so high, the AMC price-setters faced a difficult trade-off: they had to choose between optimizing the price they would pay for PCV and maximizing the chance that they could sign deals with both manufacturers in the first place.[xxxiii]

This prerogative had a significant impact on the AMC's cost. Had the AMC designers been willing to risk only one manufacturer signing up, even as they targeted two, they would have been able to set the tail price ceiling lower. However, this also would have brought with it all of the inherent risks and disadvantages of a monopoly supply situation.

Information disadvantages: The Pilot's designers were at a severe information disadvantage relative to the suppliers, a situation faced by many purchasers in public health markets. They had no access to manufacturers' costs of goods, nor insight into the amount manufacturers would need to spend in order to expand production capacity to meet AMC demand. In contrast, manufacturers, of course, had a detailed understanding of their own finances.

To estimate the costs that manufacturers faced, the designers relied on research done by consulting firms Oliver Wyman and Applied Strategies. These estimates varied widely, ranging from below $1.00 to above $3.25 per dose.[87] In addition to varying considerably on cost estimates, even for the same manufacturer, the different studies did not analyze how these costs would scale with volume. Similarly, estimates of the capital investment required by multinational manufacturers ranged widely, from $50-400 million dollars.[88] The Pilot's designers also did not have insight into the opportunity cost that

[xxxiii] However, the AMC's designers also believed that, as a mitigating factor, at most prices under discussion the AMC would deliver relatively high value-for-money to donors relative to other potential uses of healthcare funding.

manufacturers faced when choosing to invest in expanding capacity for the developing world as opposed to other programs – or the potential savings they would have from building shared facilities or reaching economies of scale. When the IWG chose the final price ceiling, they used a model that estimated manufacturers' costs over a range of potential values, with the goal of ensuring that suppliers would at least break even in NPV terms, even under high-cost scenarios.

Unilaterally set ceiling price: This AMC's price-setters decided against engaging negotiating with the existing manufacturers in favor of announcing a single price ceiling. There were several reasons for this approach. First, and primarily, it was considered that any structure reached through detailed negotiations would not represent a market mechanism or "true AMC" and therefore would be contrary to the spirit of the Pilot; several interviewees cited this as an overriding concern. Second, donors sought to avoid perceptions of favoritism among existing or prospective suppliers, particularly as one of the two existing manufacturers was based in a donor country. Additionally, designers wanted to make sure that new manufacturers would be not be shut out of the market. Finally, antitrust and competitive concerns were considered: manufacturers would refuse to establish a shared price together for fear of legal liability. Because of these concerns, contact with manufacturers during the pricing process was limited to a small set of discussions and briefings.

However, the "one-shot" approach had disadvantages as well. Without the information revealed by the dynamics of offer- and counteroffer-based negotiations, AMC designers were unable to test their hypotheses regarding manufacturers' costs and price floors in any meaningful way. Moreover, the system built in a significant second-mover advantage for manufacturers. Both sides knew that once suppliers decided whether or not to accept this AMC's offer, buyers would not have a second chance to bid;[xxxiv] therefore, donors would need to make their initial offer high relative to their estimates of manufacturers' costs in order to ensure it was accepted the first time.

The AMC's final pricing framework

The Pilot's final pricing framework involved two distinct payment structures:

Top-up subsidy: Manufacturers receive a top-up subsidy, paid for out of the $1.5 billion in guaranteed AMC donor funding intended to offset the capital expenditures necessary to expand production capacity for this AMC. These funds are allotted to each supplier in proportion to the fraction of this AMC's 2 billion doses they provide.

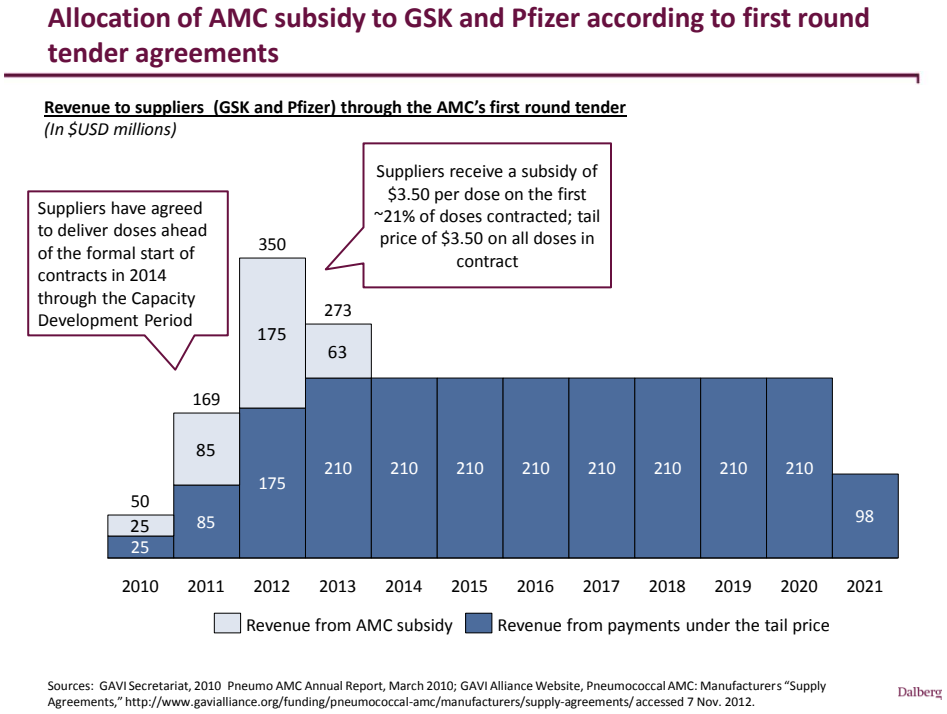
As a practical matter, these subsidy payments are made as a top-up payment of $3.50 for the first 21% of doses of each AMC contract. However, it is worth noting that because a manufacturer's proportion of the Pilot's total doses determines how much each manufacturer receives, the actual price is simply a proxy for the rate at which the subsidy is disbursed. For instance, a lower top-up price would simply mean the subsidy would be spread out over more doses. This somewhat complex pricing mechanism

[xxxiv] It is possible that the price could have been set in an iteratively higher fashion; however, interviewees indicated that at the time there was a belief that such an approach would have likely dissipated and eventually lost the momentum of the AMC process. Source: Dalberg interviews, 2012.

has proved to be a source of confusion and complicated efforts to explain this AMC to the broader public.[89]

Tail price ceiling: Manufacturers are also paid a "tail price," funded by the GAVI Alliance and individual countries, over the full set of doses of each long-term contract. These tail payments are intended to offset manufacturers' marginal costs of production. This AMC tail price was set at the ceiling of $3.50, with the hope that competition might drive it down further.

Figure 13: The AMC contract payment structure



Additionally, because the Pilot's contracts are not guaranteed, implementers may be able to decline to purchase doses through existing contracts in favor of those from lower-cost suppliers. The potential of this approach is discussed in a separate section below.

Introduction to pricing analysis and model

The following analysis is based on a model of manufacturer costs and revenues over time, used to estimate supplier IRRs from AMC-related investments. As its starting point, the model takes its structure from the work done by the IWG, with updated inputs to reflect improved information regarding this AMC's capacity development period, price structure, and long-term strategic demand forecasts. These inputs are then used to estimate manufacturer expenses, revenues, profits/cashflows, and returns under a range of scenarios.

While the fundamental underlying structure of our model is built off of the IWG's, it is worth noting that the two are used to answer different questions. The IWG was focused on identifying the price levels at

which manufacturers would earn returns above a 10% threshold. Our model analyzes the likelihood of manufacturer participation at different price levels given the uncertainties involved, and what returns manufacturers would realize in practice under different input assumptions.

Because the majority of manufacturer returns from this AMC come from tail purchases, the following analysis is focused on the tail price ceiling. While the top-up subsidy level is also important, it only represents 21% of returns (albeit front-loaded) and would require a relatively larger change in the top-up structure to have a similar effect on supplier incentives.

Two key cost inputs are manufacturers' marginal cost of goods sold (COGS) – assumed to range from $1.00-$.300, based on the IWG report analysis – and the initial expenditures in capital costs and clinical trials they would make to supply under the Pilot ($50-400 million, also from the IWG report). Because of the absence of more detailed data, the model makes the simplifying assumption that the initial investments of multinational manufacturers will be evenly spread over seven years, through 2013.[xxxv] The model also considers a range of potential values for the fraction of this AMC's total long-term demand forecast that is actually realized (75-100%); the low end of this is based on analysis in consultation with GAVI regarding the degree to which India and other graduating countries will continue to purchase doses through the end of the Pilot.[xxxvi]

As discussed in the implementation section of this evaluation, the model assumes that a third supplier will enter the PCV market in 2017, at which point approximately 29% of AMC doses will remain to be contracted (Figure 14, below). From 2017 onward, it is assumed that any new suppliers will capture 80% of the doses remaining under this AMC.

For simplicity, it is assumed that the small fraction of post-2017 contracts awarded to the two initial suppliers would continue to be priced at $3.50 a dose. Because these contracts represent so few doses, at such a relatively late stage, the impact of this assumption is relatively minimal: even a 30% price drop would only reduce their total returns by 1-2%. However, if GAVI is able to also obtain pricing reductions on existing contracts, manufacturer returns would be correspondingly reduced. Further details about the assumptions of the model are provided in Appendix III.

In the following sections, we use this pricing model to answer the following questions:

1. Given what was known at the time, was this AMC's tail price ceiling set to a reasonable level to attract the two existing manufacturers?
2. Given what we know today, what can we say about the returns suppliers are earning?

[xxxv] In principle, the model could be quite sensitive to this assumption, particularly at extreme values. Investments in early years could count for 50-150% depending on the IRR.

[xxxvi] 75% realization of the AMC Strategic Demand Forecast 5.0 translates to a long-term rate of 162 million doses a year by 2021. As a reference point, this is just below the 168 million doses of pentavalent that UNICEF procured in 2011. Additionally, demand is expected to grow further in the next decade as more Indian states roll out pentavalent programs.

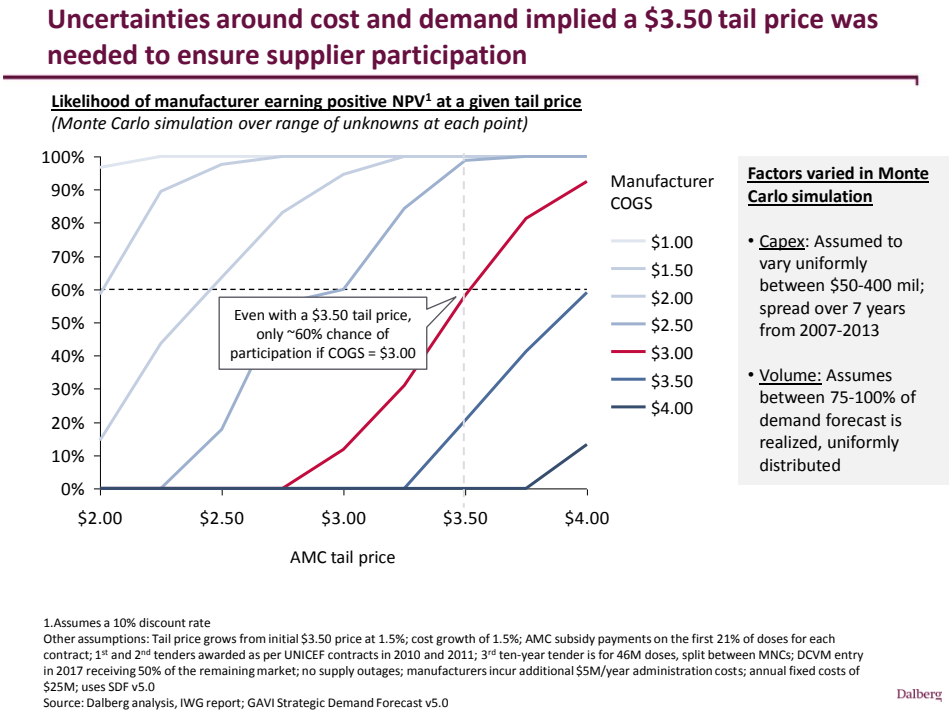
3. Under what conditions would companies have competed in the GAVI market[xxxvii] without receiving AMC top-up subsidies?
4. If future tender rounds lead to tail price drops below the ceiling, will this lead to significant cost-savings?

Given what was known at the time, was this AMC's tail price ceiling set to a reasonable level to attract the two existing manufacturers?

As noted in the previous section, when setting the price for the Pilot, the IWG and donor group faced a challenging situation. Obtaining the participation of both existing manufacturers was considered an absolute priority; the cost of under-pricing the vaccine was therefore seen as far higher than that of overpricing it. Compounding this challenge, the committee members had limited data regarding manufacturers' costs.

Below, we model how manufacturers with different cost structures would have responded to different tail price ceilings. At each combination of tail price ceiling and COGS, we run a Monte Carlo simulation over the potential combinations of capital expenditures required and percent of the GAVI Alliance demand forecast eventually be realized; we assume each value for these inputs within the ranges stated above is equally likely. Like the IWG, we assume that an individual manufacturer's decision to participate in the Pilot at each test point was exclusively based on whether the net present value (NPV) of its expenses and sales at a 10% discount rate exceeded zero.

Figure 14: Likelihood of a manufacturer earning positive NPV at a given tail price ceiling



[xxxvii] "GAVI market" refers to the market created by the combination of the following elements: demand and purchase orders from GAVI-supported countries, procurement management by UNICEF, and AMC funding by donors.

Under this model, at the Pilot's tail price ceiling of $3.50, there was only a 60% chance that a manufacturer with $3.00 COGS would participate. Manufacturers with costs of $2.50 or below would almost certainly participate; those with costs of $3.50 or above would not. This analysis suggests that, given the goal of maximizing the chance that two manufacturers would participate, and the constraint of having a single opportunity to propose this AMC's tail price ceiling, the price ceiling was set appropriately.

Given what we know today, what can we say about the returns that suppliers are earning?

In the time since the original signing of the Pneumococcal AMC, additional information has come to light regarding the investments multinationals have made in expanding their production capacity to address GAVI markets.

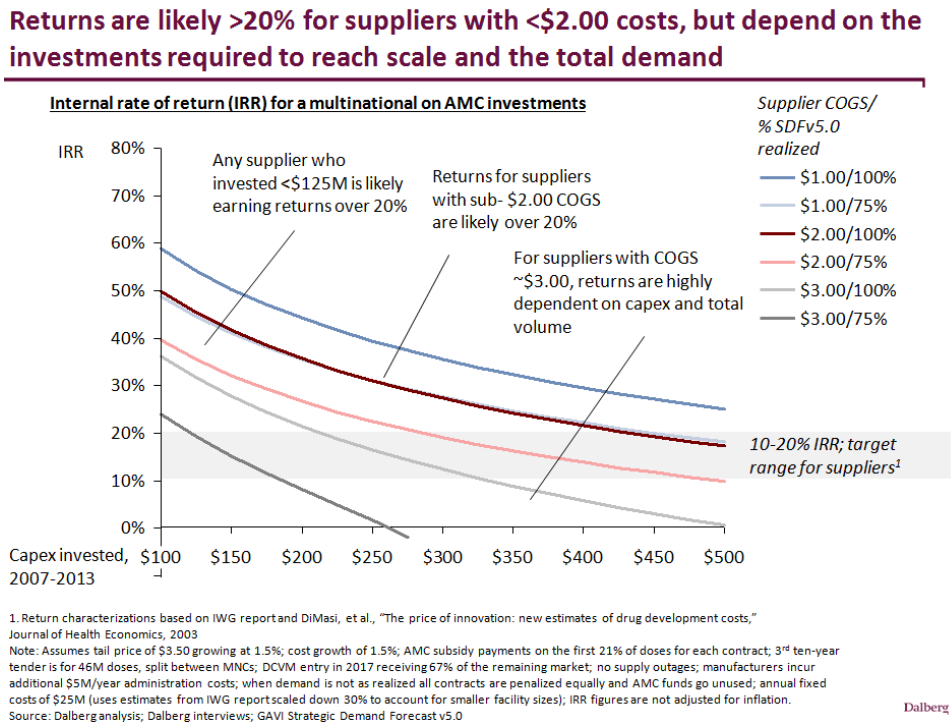
- **Pfizer.** In written communication, a spokesperson from Pfizer has stated that the company's AMC-related investments are, "in excess of the $100 million mark".

- **GlaxoSmithKline**. GSK has indicated that they have invested approximately $500-600 million in expanding their PCV capacity through a new bulk plant in Singapore, as well as approximately $100 million in other investments throughout their supply chain.[90] However, the degree to which these costs can be credited directly to this AMC and GAVI is unclear. The plant in Singapore, in particular, is shared across multiple different vaccine lines. GSK has also indicated that the plant is theoretically capable of producing 200-300 million doses of PCV per year, while the model described assumes that GSK's demand from GAVI markets never tops 85 million doses annually. Whether the remainder of this potential capacity would go unutilized, be applied to other markets, or be used to produce adult doses, significantly complicates estimating the proper cost-attribution to GAVI markets. Based on these figures, we assume that the total investment from GSK attributable to this AMC falls within the $300-500 million range.

No new information has come to light regarding individual manufacturers' COGS. Similarly, we have little insight today into another key driver of returns—namely the number of doses demanded over the long term. The Pilot was developed based on a projected forecast of 200 million doses or more, but if graduating countries and India do not take up or maintain their PCV programs in the long term, total demand could come out considerably lower.

In the graph below, we apply the model to analyze the returns of AMC-related investments for a range of COGS, demand volumes (expressed as the percentage of the GAVI Strategic Demand Forecast achieved), and capital expenditure (capex) investments.

Figure 15: Internal Rate of Return for a multinational manufacturer on AMC-related investments



Though these results depend heavily on the value of these variables and other assumptions, they suggest several scenarios where manufacturers would be earning returns above the 10-20% band. Such scenarios occur for manufacturers with COGS of $3.00 or below and capital investments below $100 million, with COGS below $2.00 and investments below $200 million, and with COGS below $1.00 and capital investments under $350 million. In nearly all scenarios tested, and in every scenario tested for manufacturers with COGS below $3.00, suppliers earn returns above both their WACCs and the IWG's 10% target rate.

Though GSK and Pfizer have provided public statements regarding their investments, ultimately whether their returns fall within the target range still depend on two unknowns: their individual COGS and the degree to which the long-term Strategic Demand Forecast will be realized (in other words, whether annual demand exceeds 200 million doses by 2019).

- **Pfizer will likely earn returns above the 20% threshold provided the long-term demand forecast is realized.** This is driven by the relatively low $100-150 million investment the firm will have made in expanding capacity for GAVI markets; even if the firm approximately breaks even on each individual dose on tail pricing, it will have received AMC subsidy payments of more than $500 million. (However, because the last of these subsidies may be paid out over a decade after Pfizer's initial AMC-related investment, the company's annualized return will be less than what such a quick calculation may suggest.) Under a scenario where demand only reaches 75% of the current Strategic Demand Forecast, and Pfizer's COGS are $3.00 or above, their returns will likely be in the 10-20% band.

- **Depending on assumptions of unit costs and total demand, GlaxoSmithKline's returns could either be above or in the 10-20% range.** As discussed above, GSK's allocated investments for this AMC will likely fall in the $300-500 million range. Consequently, while there are scenarios where the company's returns are greater than 20% (in particular, when its COGS are below $2.00 and the current Strategic Demand Forecast is fully realized), there are also several where its returns fall within the 10-20% range, particularly if demand is not fully realized.

- **Additional analysis (not shown) indicates that participating DCVMs will likely earn lower returns from this AMC than multinationals.** This is driven by a combination of several factors: DCVMs will likely receive a much smaller share of the actual AMC subsidy; their development efforts will likely take longer; and there is a credible chance that the tail price will decline once a DCVM enters the market. Though the specific returns a DCVM will earn from its AMC-related contracts are highly dependent on the actual value of these assumptions, it is will likely earn IRRs in the 10-20% target range. However, DCVMs may bear lower risk profiles, as they will be entering an already established market, and many are benefitting from grant funding from donors such as the Gates Foundation and PATH.[91]

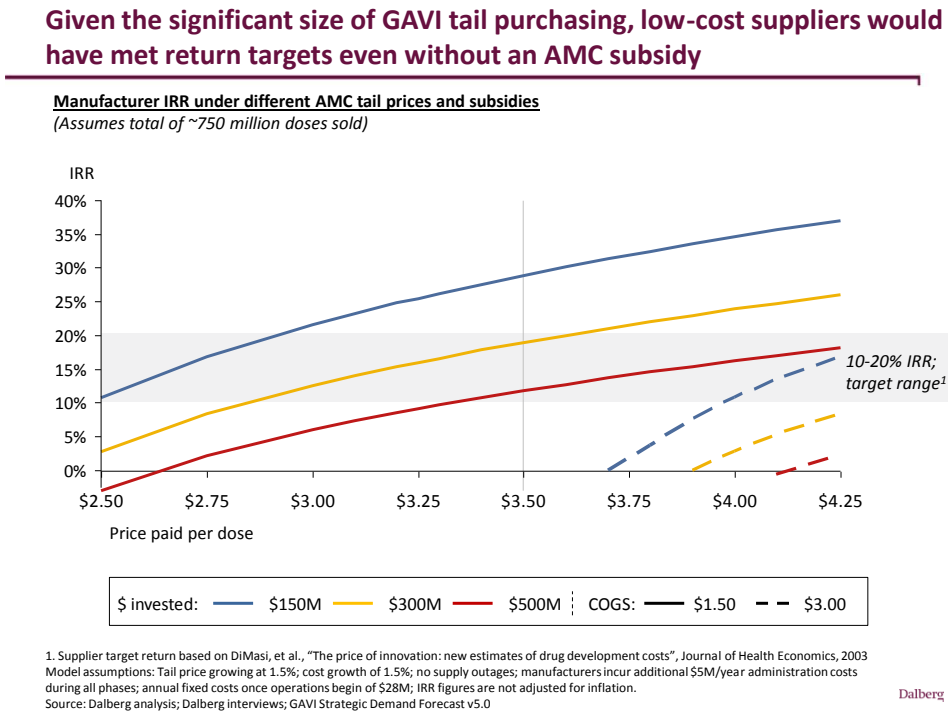
  Returns for non-DCVM third-entrant manufacturers, i.e. other multinationals, are not modeled.

The only scenario modeled where GSK's COGS fall below the target range is when its unit costs are above $3.00. Under no scenario modeled do Pfizer's returns fall below the 10% threshold.

Under what conditions would companies have competed in the GAVI market without receiving AMC top-up $1.5 billion subsidies?

The above analysis raises the question of whether manufacturers would have supplied PCV to GAVI markets independent of this AMC, and under what scenarios. To answer this, we have modeled below the returns of a hypothetical manufacturer only earning the Pilot's tail price ceiling, without the benefit of the Pilot's top-up subsidy. We assume that this manufacturer would sell slightly more than 750 million doses to GAVI, equivalent to receiving an even share of the AMC's first three contracts in a 100% demand scenario. These volumes could also be reached – even with demand not fully realized – if the manufacturer was able to earn a larger market share relative to its competitors (an extreme version of this hypothetical would be a monopoly supply situation). For clarity, we consider below the hypothetical case of manufacturers with $1.50 and $3.00 COGS as "low-cost" and "high-cost" suppliers.

Figure 16: Manufacturer IRR under different tail prices and AMC subsidies



The model's results indicate that a hypothetical multinational manufacturer with unit costs of $1.50 would have earned returns in the target range, even allowing for a wide range of investment costs, if it sold its doses at $3.50 or above.[xxxviii] However, a manufacturer with costs of $3.00 or above would have had returns in the target range only if it was able to sell its doses for $4.00 and its initial investment costs were $150 million or less.

The substantial revenue potential of the GAVI market may have therefore been enough to attract low-cost manufacturers without additional subsidies. For multinationals with higher COGS, some form of extra funding or higher pricing would have been required, though the exact amount would depend on their actual cost structures. Additionally, extra funding or specialized structures may have been required in both cases to offset the risk of full demand not materializing.

The Pneumococcal AMC could have been structured in many alternative ways. Possible alternative scenarios include an AMC with more front-loaded payments, or with a smaller pool of total funding, or the use of purchase commitments/firm orders without any top-up funds. This evaluation does not attempt to explore the range of possible permutations. However, many of these scenarios will fall in between the scenarios tested in the above graph and previous sections.

[xxxviii] A manufacturer with $1.50 COGS would earn roughly $1.5 billion over 750 million doses sold at $3.50 apiece, sufficient to compensate for a $500 million investment made 5-15 years earlier as well as any fixed annual operating costs.

If competition in future tender rounds results in tail price reductions, will this lead to significant cost savings?

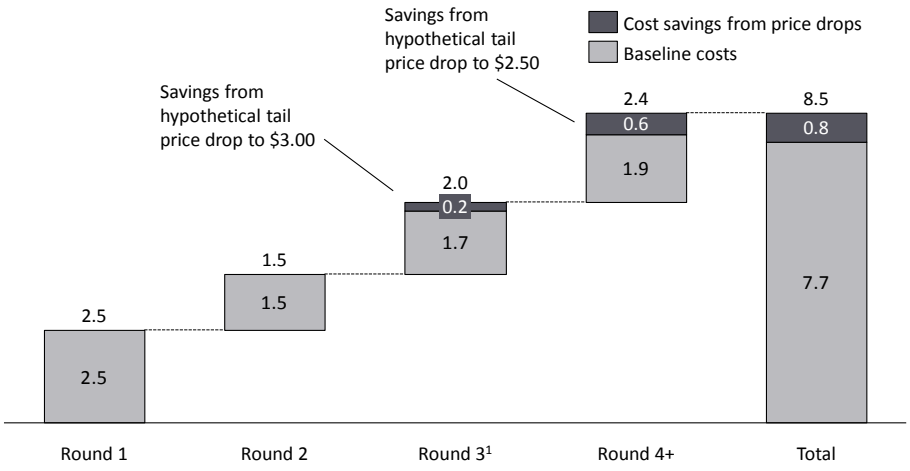
This AMC's tail price was not set at a fixed level, but rather as a ceiling under which manufacturers would be free to compete. However, in both contracting rounds to date GSK and Pfizer bid at the $3.50 cap. Some members of the EEG and IWG have indicated in interviews that this was expected, and that at the time of the Pilot's design it was believed that price drops would only occur when a third manufacturer added competition to the market.

However, because 48% of doses have already been contracted at the ceiling price, the impact of any such reduction is likely to be minimal. Because by default any price drops would only apply to new contracts, even if the weighted average price across all manufacturers was to fall to $3.00 in the third tender round (currently being conducted), and to $2.50 thereafter, the overall cost of this AMC would only be 10% lower.

Figure 17: Analysis of the effect of tail price reductions in future tender rounds on total AMC-associated spending

Tail price reductions in future AMC tender rounds are unlikely to lead to significant overall savings

AMC spending (top-up subsidy and tail purchasing) under hypothetical tail price scenarios
(In $USD billions)



1. Assumes Round 3 award of approximately 50 million per year, enough to meet SDFv5.0 demand until 2017, the presumed year of DCVM entry.
Sources: AMC SDFv5.0; Dalberg analysis

Dalberg

This AMC's implementers may be able to leverage the non-guaranteed nature of its contracts to benefit from lower price offers in the future. However, this would depend on the ability of later suppliers to scale capacity quickly. Because of the structure of its procurement contracts, this AMC's implementers may decline to purchase doses if they can source supply at lower price levels. They could also potentially use the threat of such a move to obtain more favorable pricing on existing contracts. However, the degree to which this AMC could benefit from such a move would be constrained by the

capacity of the new entrant. Assuming that the third contracting round, currently being conducted, is for 50 million doses a year, 42 million and 59 million doses in 2018 and 2019 would still remain free for later rounds.[xxxix] Only if the capacity of later-entrant manufacturers exceeds these figures would implementers be able to decline doses from earlier contracts in favor of lower-cost suppliers, or make a credible threat to do so. Additionally, as discussed above, it is not clear whether such an action would fit within the original spirit of these provisions.

Additional design elements

This section examines the role of the design elements that designers viewed as most critical to the AMC concept: legally binding contracts on donor funding, purchase guarantees, and the Target Product Profile. The section answers the questions of whether or not these three elements were both feasible to develop and effective for this particular AMC. It also addresses a question that arose during interviews for this evaluation: whether the AMC should have included explicit caps on the amount of doses any individual manufacturer or set of manufacturers could receive.

Legally binding contracts on donor pledges

Relevant TOR Questions addressed in this section:

- **Question 1:** Given the AMC's objectives, to what extent do the binding legal agreements provide a clear incentive to industry to accelerate the development of vaccines meeting the Target Product Profile and bring forward their availability?

[xxxix] Strategic Demand Forecast v5.0. assumes a total of 96 million doses a year from tender rounds 1 and 2.

Key Findings:

Legally binding commitments on donor pledges were a key element of the Pilot.

Designers and implementers have indicated that such commitments were seen as essential, both for providing tangible guarantees to manufacturers and, more broadly, building momentum with countries, donors, and suppliers around the initiative. Three of the four registered manufacturers interviewed concurred, though each expressed a strong preference for firmer commitments in the future through agreements such as guaranteed purchase contracts.

From a purely financial and legal perspective, this AMC's guarantees were relatively weak, because funding was dependent on both demand materializing and, more importantly, tail funding. In particular, the uncertainty of GAVI's 2011 replenishment round created risk for suppliers. However, interviewees have emphasized that the momentum created by the legally binding commitments meant that both the funding round was more likely to succeed, and that PCV would have been given priority in the event of budget cuts.

Evidence from manufacturer preferences and behavior is ambiguous. GSK appears to have begun planning for a large-scale production plant in Singapore, targeted at low-income markets, before the discussions around this AMC began. However, it is unclear how the evolution of the Pilot affected their subsequent investment decisions. Because Panacea, Pfizer, and Serum each appears to have made their decisions to invest in research or capacity for GAVI markets after the announcement of this AMC, we have no evidence from their revealed preferences or actual behavior how they would have acted in the absence of the initiative.

AMC designers placed heavy emphasis on securing commitments that legally bound donors to provide the funds they had pledged if demand materialized as forecasted. When this AMC was first conceived, its creators were concerned that manufacturers would not view donor pledges of future funding as credible. By design, this AMC's funding would come years in the future, and in the intervening years, any number of economic, political or other factors could cause such promised funding not to materialize. This view was buttressed by suppliers, who cited previous negative experiences in the seasonal flu vaccine space, where the U.S. government had failed to live up to its stated purchase intentions, and in previous efforts to develop thermostable polio vaccines for the developing world.[92] To counteract these concerns, AMC designers ensured that legal guarantees would be placed on the balance sheet of the World Bank, a challenging and unprecedented measure.

In the following analysis we evaluate the extent to which these legally binding agreements have contributed to accelerating the production and development of vaccines to meet low-income country needs. Because of the absence of an unambiguous counterfactual case – i.e. a scenario equivalent to the Pilot except without such agreements – we develop our conclusions by weighing inputs from several

different sources. Because the perceptions of market actors are largely the measure of a guarantee's effectiveness, we heavily weight information from interviews with donors, designers, and manufacturers. We have also used three other data sources: the direct financial role of the pledges in securing manufacturer returns, manufacturer behavior before and after the start of this AMC, and an imperfect but potentially insightful example in the form of the GAVI pentavalent market, which developed roughly in parallel with this AMC.

Interviews confirm that stakeholders across this AMC's spectrum saw legally binding commitments on donor funding as essential. Donors and implementers emphasized in interviews how the Pilot's nature as an untested new initiative made it essential that their pledges come with legal backing; simple promises would not incentivize manufacturers. It was not simply the pledges themselves that were viewed as important, but the effort required and the momentum they created. More than one interviewee cited the value of donors putting at least some "skin in the game" to convince manufacturers that interest in the Pilot was deep and credible.

Three of four manufacturers interviewed cited the binding legal agreements as a key element driving their participation in this AMC. As a senior executive at Pfizer states, "Because the AMC was a novel financing mechanism, having binding legal agreements was very important, and has contributed to the early successes of the program we've seen so far." Similarly, a senior executive at Panacea comments, "It definitely helps to have such guaranteed money upfront. It gives you confidence, clarity, and assurance at the start of your investment."[93] A spokesperson for GSK states, "Legally binding commitments are an essential element for GSK in the context of the huge financial risks that GSK has committed upfront." Serum was the only dissenter, indicating that they had begun their research program independent of this AMC and that therefore the commitments had no effect on them. It is also worth noting that each of the four manufacturers interviewed was careful to caveat these statements by commenting that the confidence stemming from these agreements did not extend to their own individual revenues, and that they would have strongly preferred an approach that provided them with specific purchase guarantees.

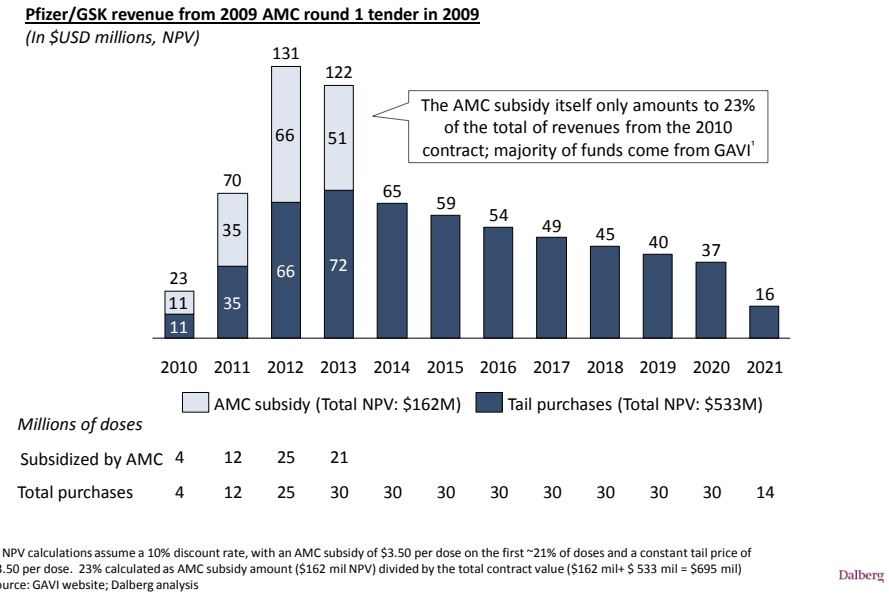
Interviewees have also emphasized that the presence of the pledges generated momentum during the AMC design process among donors, countries, and within the GAVI Alliance. The commitments helped ensure that, rather than being viewed as simply one among many global health initiatives, this AMC was able to gain a unique impetus and legitimacy in the eyes of its participants. Interviewees describe the commitments as leading to a self-reinforcing feedback loop: the guarantees built momentum around the Pilot, creating further buy-in from countries and donors, which in turn reinforced the strength and credibility of the commitments themselves. Additionally, the process's visibility fostered PCV awareness within ministries of health, which helped ensure that product demand would meet growth forecasts. The commitments also created substantial momentum within the GAVI Alliance to support PCV, which helped the program persist through difficult funding times. The binding legal commitments were thus viewed as not simply providing an improved incentive to manufacturers, but as helping forge a stronger AMC coalition overall.

From a purely financial and legal perspective this AMC's guarantees were relatively weak. Of the roughly $7.5-8.5 billion in revenues that manufacturers may expect to earn from Pneumococcal AMC-

related sales (i.e. the 2,000 doses covered under the Pilot), only $1.5 billion will come from the top-up subsidy revenues guaranteed under its binding legal commitments. The rest are due to come from tail purchases, whose funding comes from GAVI's general fund and is not guaranteed. It is true that the top-up payments are somewhat front-loaded (i.e. came in the earlier years of contracts); however, under a NPV basis using the IWG's 10% discount rate, they still only represent 23% of revenue.

Figure 18: The NPV of legally binding contracts

Legally binding contracts: The portion of AMC-related sales covered under binding contracts represents only 23% of AMC-related spending



1. NPV calculations assume a 10% discount rate, with an AMC subsidy of $3.50 per dose on the first ~21% of doses and a constant tail price of $3.50 per dose. 23% calculated as AMC subsidy amount ($162 mil NPV) divided by the total contract value ($162 mil+ $ 533 mil = $695 mil)
Source: GAVI website; Dalberg analysis

Dalberg

As one manufacturer specifically noted, until the successful GAVI pledging conference in June 2011, it was uncertain whether the Alliance would have the funds to support these PCV tail purchases[94]. It is unclear what would have happened had the funding round been unsuccessful. There was a possibility that future PCV tender rounds would have been small, and that the purchase options under existing contracts would have been declined. From a strict financial perspective, the pledge commitments under this AMC therefore provided only limited certainty of funding to manufacturers.

However, several interviewees emphasized that having legal commitments on AMC funds made the funding round more likely to succeed by exerting political pressure on donors to provide the rest of the needed funds. These interviewees also argued that, had the fundraising round only partially succeeded and cutbacks been required, PCV would likely have been given extremely high priority. In other words, from a fundraising and program continuity perspective, the donor guarantees may have helped GAVI's PCV effort, despite its nascent state, to gain the status of the well-established pentavalent program.

Evidence from manufacturer preferences and behavior is ambiguous. Press releases indicate that GSK's corporate planning for its Tuas, Singapore, vaccine facility began in 2004—well before this AMC's development and therefore without its clear guarantees of funding.[95] In written communications for

this evaluation, a spokesperson at the firm states that, "The decision to invest in additional capacity in Singapore was taken before AMC implementation and took into consideration price levels in line with current average price composed of the AMC tail price and AMC subsidy," adding, "Significant volumes for GAVI countries were always part of our core assumptions when deciding to build the Singapore site and related secondary investments."

However, the precise sequence of events remains unclear: in particular, GSK's statements do not specifically state the timeline by which the company chose to apply much of the Singapore plant's facilities to PCV production, relative to other potential uses, other than that this decision came before the final AMC price was settled. Moreover, even if GSK had made such an initial decision relatively early, the Pilot's funding commitments may have played a significant role in incentivizing the firm to build further capacity and accelerate its expansion efforts.

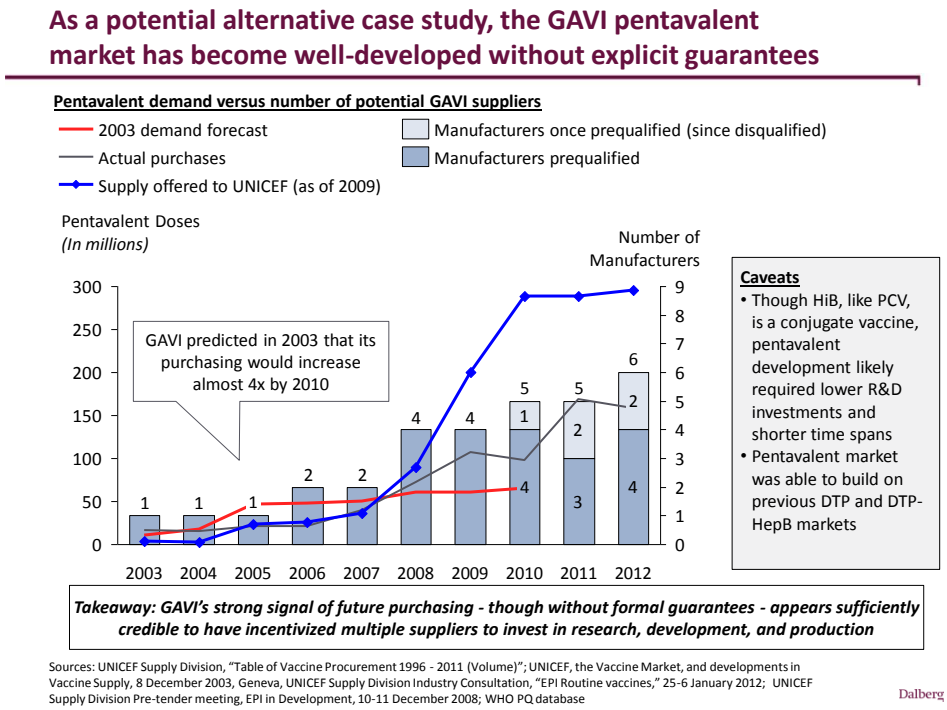
While Serum has indicated that it viewed this AMC, and thus its binding legal commitments, as irrelevant to its planning, Pfizer and Panacea have emphasized the importance of the AMC to their decision-making. However, because each of these manufacturers appears to have made their decisions to invest in research or capacity for GAVI markets after the announcement of this AMC, we have no evidence from their revealed preferences or actual behavior how they would have acted in the absence of the initiative. In addition, several next-generation suppliers, including Serum, are receiving grant funding from donors,[96] which implies that this AMC is not the only support mechanism bringing them to market.

As an imperfect but potentially alternative example, the GAVI market for pentavalent grew substantially from 2003-2011 without explicit guarantees to manufacturers. In 2003, when the GAVI Alliance was still nascent, the pentavalent market for low-income countries was relatively small. Only one supplier, the multinational GSK, provided doses to UNICEF, and total purchasing amounted to only 16 million doses. However, the GAVI Alliance, backed by funding from governments and the Gates Foundation, forecasted that its purchasing would reach 65 million doses by 2010.[97] This forecast had no legal backing behind it, simply the credibility of GAVI and its donors.[xl]

Since then, pentavalent has become a focus vaccine for the GAVI Alliance, amounting to more than half of the organization's budget.[98] The earlier procurement forecast was exceeded by a factor of three: in the UNICEF tender round in 2009 for 2011 need, 170 million doses were purchased, amounting to nearly two-thirds of the total 288 million offered. This market has also become relatively competitive: six manufacturers – two multinationals and four Indian companies – built research programs and achieved WHO prequalification (though two have since had their certifications suspended, leading to supply constraints in 2011 and 2012).

[xl] However, while GAVI provided no specific commitment to purchase pentavalent, overall GAVI funding was supported by donor grant commitments to the International Finance Facility for Immunisation (IFFIm). As of 5 September 2012, 39% of GAVI's 2000-2030 funding is expected to come from IFFIm. Source: GAVI Alliance.

Figure 19: Pentavalent demand versus number of potential GAVI suppliers



The pentavalent market appears to have grown without formal legal commitments because of the reputation the GAVI Alliance built as a trusted manager of international vaccine programs over the last decade. A senior manager at UNICEF comments that, "There are many things that have changed compared to when GAVI initially embarked on vaccine funding in the early 2000s – there was just no experience with the GAVI model. Now we've had this positive experience with pentavalent, where we've shown that demand will come and that GAVI will provide funds." A senior manager at one developing country manufacturer agrees, stating, "GAVI's credibility has been there in our mind for quite some time; with pentavalent we had no concern that the funding would not be there."[99]

Many factors that aided the development of the pentavalent market were not applicable in the PCV case. HiB is a simpler vaccine than PCV, and therefore required lower R&D investments on the part of new manufacturers. Some suppliers were able to license technology from existing providers. The UNICEF/GAVI pentavalent market was able to build on a preexisting market for DTP and, later, DTP-Hepatitis B (though the value of UNICEF DTP procurement never exceeded $15 million, and four of the six manufacturers of pentavalent had not previously supplied DTP to UNICEF/GAVI[100]). Additionally, competition in middle-income and high-income markets for HiB was spread over multiple manufacturers, unlike the PCV market, which to date remains a duopoly. Finally, it is important to note that while the pentavalent market did indeed develop competitively over the course of a decade, the overall ramp-up of supply has been considerably slower than that of PCV, and prices took several years to drop. To date, GAVI continues to face challenges in matching supply and demand, particularly because of the suspended prequalification of two manufacturers.

In the future, another potential counterfactual to the PCV market under this AMC will be the market for rotavirus vaccine. As noted in the next section, in 2011 an agreement was reached with GSK to purchase rotavirus for GAVI markets through a set of strong purchase guarantees. However, it is currently too soon to evaluate the effect of this agreement on the long-term competitive dynamics of the market.

Overall, what appears to matter most to manufacturers looking to enter a market, as the crafters of this AMC recognized, is the credibility of promised purchasing. Binding legal agreements on donor pledges is an important potential source of this credibility, not only because of the effort and moral commitment they signal, but also because they may be the only source of credibility for markets without established funding programs. However, future financing initiatives for late-stage vaccines may be able to leverage the credibility that the GAVI Alliance has built since the Pilot's conception.

Purchase guarantees

Relevant TOR Questions addressed in this section:

- **Question 2:** To what extent do specific AMC design elements contribute to the AMC objectives:
  - 3-year purchase guarantee (deescalating % of committed doses)

Key findings:

Whether the Pilot's long-term tender contracts should be firm purchase guarantees, as opposed to purchase options on the part of UNICEF/GAVI, was strongly debated during this AMC's design. Ultimately, only 6% of the value of its contracts (on an NPV basis) was guaranteed to producers. Both GSK and Pfizer have indicated that, while they believe purchase guarantees can play an important role in reducing risks and costs, the relatively small size of the Pilot's commitments meant they were largely irrelevant to their decision-making. However, recent experiences with purchase guarantees for other vaccines, such as the rotavirus vaccine, indicate that under the right circumstances large-scale commitments can be extremely powerful levers for donors to gain better pricing.

As part of its long-term contracting structure, the Pilot included a set of limited purchase guarantees. Procurement guarantees are similar to this AMC's legally binding commitments in that they involve donors pledging to provide future funding. However, in the case of this AMC's commitments, funding is contingent on demand materializing, and no individual manufacturer is assured of what fraction of the market they will receive. With procurement guarantees, donors commit to purchasing a fixed number of doses from an individual supplier over a long-term time horizon. Such agreements can be well-suited for vaccine production, where high upfront and fixed costs mean that suppliers risk considerable losses if they are unable to sell their product, which in turn leads them to charge correspondingly high risk premiums.

As part of the design process, the EEG and donors considered providing purchase guarantees to manufacturers. However, after much internal debate, they ultimately settled on a *de minimis* set of commitments: each actual contract would be 20% guaranteed in the first year, 15% in the second, and 10% in the third, for a total of 6% of the value of each contract.

The two manufacturers currently providing doses under this AMC have characterized these guarantees insufficient. A spokesperson from Pfizer stated, "The partial guarantees have not had an influence in our decision making… The fact that there are effectively no volume commitments [in the AMC] is a limitation that perhaps we should address." A spokesperson from GSK concurred, stating that future AMCs should "include solid volume guarantees. Without such guarantees, manufacturers may no longer decide to invest as much in capacity building."

The Pilot's tender awards mean that manufacturers bear nearly all the risk if demand or funding does not materialize. This is a potentially inefficient construct. As Snyder, et al, (2011) notes, "economic logic suggests that the party with the most control over an uncertain situation should insure other parties against risk, because the insurer will then exercise its control to mitigate the risk and reduce its costs." However, as they point out, while donors and GAVI may be able to subsidize or otherwise assist countries in developing their vaccine programs, "manufacturer[s] can do little to affect demand."[101]

Today, the concept of strong purchase guarantees is gaining traction in the vaccine community. In 2012, the Gates Foundation, the GAVI Alliance, UNICEF, and the Clinton Health Access Initiative negotiated a series of purchase guarantee agreements with GSK to provide the rotavirus vaccine to GAVI at significantly reduced rates. Historically, UNICEF and GAVI Alliance have also employed firm contracts of up to three years to bolster the development of various markets and obtain better prices.[xli] A senior program officer at a major foundation argues that the benefits of this approach can be significant, stating, "In general, given what we've learned over the past couple of years, the sentiment here is shifting to the belief that these bilateral mechanisms may be more efficient… In a volume guarantee [to individual manufacturers] context, you're often dealing with late-stage or licensed products, which makes the equation more knowable for everyone."[102]

Such strong purchase guarantees are not appropriate in all situations. In particular, they work best when manufacturers already have near-market or existing products and thus predictable costs. More fundamentally, these guarantees essentially work by passing risk on to donors: if demand does not materialize, donors must commit to paying the political and economic costs of purchasing unneeded doses. Donors must also carefully structure their contracts to leave the market open to competition still, instead of shutting out newcomers or creating a monopolistic supply situation. These guarantees can be challenging to set up, because they require donors to commit actual funds years in advance, and may be limited in size and duration because of the stress they place on donors' balance sheets. Finally, because contracts are negotiated with individual manufacturers, donors will be vulnerable to accusations of bias or favoritism.

[xli] For instance, GAVI negotiated firm purchases for pentavalent and DTP-Hep B in 2004-2006 and for pentavalent in 2007-2009. Source: Feedback from AMC stakeholders.

Target Product Profile

Relevant TOR Questions addressed in this section:

- **Question 2:** To what extent do specific AMC design elements contribute to the AMC objectives:
  - Target Product Profile
- **Question 3:** To what extent is the Target Product Profile used for the Pilot AMC an appropriate standard for product development?

Key Findings:

Overall, the public health experts and industry representatives interviewed agreed that the Pilot's Target Product Profile (TPP) forms an appropriate standard for PCV products targeted at low-income countries. Several interviewees praised the TPP for striking an appropriate balance between setting a high bar to ensure vaccine effectiveness and still allowing low-cost producers to compete. The experience of the AMC TPP suggests several lessons for future AMCs.

While the TPP has not played a significant role in shaping GSK and Pfizer's products, other suppliers indicate it has provided them with useful guidance for product development. However, they also indicate that for competitive reasons they will aim to outperform the minimum threshold set by the TPP. Though it is impossible to evaluate the counterfactual, manufacturer interviews also suggest that the TPP's serotype requirements have not restricted competition in the PCV market for low-income countries.

The TPP faced a significant issue regarding the use of multi-dose vials without preservatives, a new presentation for which field practice was not well-established. This caused delays and frustration. The case of pneumococcal protein vaccines also demonstrates the potential challenges faced by developers of TPPs for earlier-stage products, particularly when understanding of the underlying science is being developed in parallel with the product itself.

The concept of a target product profile (TPP) that would establish a minimum standard for qualifying existing products and provide guidance for new vaccine developers was another key feature by the original "Making Markets for Vaccines" paper. The TPP for the Pneumococcal AMC comprised thirteen mandatory elements, including serotype coverage, immunogenicity, product presentation, and labeling. These requirements were approved by both the WHO's Strategic Advisory Group of Experts (SAGE) and the Independent Assessment Committee (IAC) convened specifically for this AMC.

Overall, both public health experts and industry representatives interviewed agree that the TPP forms an appropriate standard for PCV products targeted at low-income countries. Interviewees within the public health community cite the importance of the TPP in building on the work of the Global Serotype Project at Johns Hopkins and establishing a clear benchmark for serotype coverage.[103] The TPP ensured that vaccines sold to GAVI would include not just strains prevalent in high-income markets but also

those common in low-income countries.[xlii] Several interviewees praised the TPP for striking an appropriate balance between setting a high bar to ensure vaccine effectiveness and still allowing newer, low-cost producers to compete.

Manufacturers interviewed were similarly positive about the role of the TPP. A senior executive at Panacea Biotech comments that "The TPP was very elaborate. It was designed considering which countries, geographies, and strains needed to be covered – it's very well done." A senior executive at Serum Institute concurs, stating that "the Target Product Profile helps us decide which strains we need to target in our development."[104]

The TPP also proved useful in inspiring and supporting similar guidance for other vaccines. In interviews, experts noted that the experience of developing the TPP has helped sharpen the WHO's approach to setting performance metrics for prospective vaccines for diseases such as malaria. The experience has also helped the WHO's broader program improve how it assesses the programmatic suitability of vaccines in conjunction with its prequalification process.[105]

From a new product development perspective, however, several elements of the TPP may represent redundant standards for DCVMs and multinational manufacturers alike. Seven of its 13 required elements overlapped with existing requirements for product prequalification. In practice, these elements have been entirely managed through the WHO, and suppliers have not experienced any extra regulatory burden.

More importantly, the presence of existing products provided new manufacturers with clear benchmarks. At a minimum, argues a senior executive from one DCVM, these rendered many of the requirements of the TPP unnecessary: "For all the vaccines we've developed – PCV, pentavalent, and others – we've always know what profile we should aim for. From that perspective the TPP has not changed anything."[106] Another DCVM executive takes a stronger position, that the TPP established too low of a bar and that his company will try to outperform it, "Because countries have the same co-pay for each product, they naturally prefer [vaccines] with more serotypes. So while we use it as a guide, we try to outperform the TPP to make sure countries demand our product in the long run."[107]

The TPP did not have a significant role in guiding the product development of multinational manufacturers. Both GSK and Pfizer had set their product characteristics, including the specific serotypes, well in advance of the SAGE approval of the TPP in 2007. Records from the United States Food and Drug Administration's clinical trials databases indicate that GSK had begun conducting Phase III trials for PCV10 in 2005, and Pfizer had begun Phase I/II trials for PCV13 in 2004. Both products also easily exceed the TPP's other requirements.[108]

The development of the pentavalent market also provides a useful case study against which to compare this AMC. Even without a target product profile, manufacturers who were beginning research programs in the early 2000's had a clear target because existing products from multinationals such as GSK had

[xlii] In particular, the TPP ensured that Prevnar-7, which did not include two of the three most common serotypes in Africa, 1 and 5, would not be considered sufficient for the AMC Pilot.

already paved the way. This experience suggests that detailed TPPs may be less necessary for any future AMC where reference products that meet low-income country needs already exist; in these cases, a simpler non-inferiority standard could be used.

The biggest challenge faced by the TPP has been the controversy regarding the suitability of an unanticipated product presentation, GSK's 2-dose vial without preservatives. The TPP required that "Low multi-dose presentations should be formulated in compliance with multi-dose vial policy (*The use of opened multi-dose vials of vaccine in subsequent immunization sessions*, WHO/V&B/00.09)," which mandated that presentations without preservatives be thrown away at the end of each session. However, while GSK's product met the technical requirements of the TPP, policymakers at the WHO became concerned that its new form would confuse field staff: previous multi-dose presentations without preservatives had only come in lyophilized form, allowing for an easy visual distinction from preservative-containing vials. The WHO asked GSK to conduct a year-long field survey in Kenya to ensure proper practices would be followed. Partially as a consequence of this, PCV10 introductions in other countries were delayed by nearly a year.[109]

This delay was a source of frustration for many. As one senior doctor at the WHO commented, the experience "represented an inconsistency in the process, which I think is regrettable."[110] In written statements, a spokesperson from GSK expressed similar dissatisfaction with the experience, stating that, "Discussions with WHO on Synflorix 2 doses started in 2007, six months before file submission for prequalification in January 2008 [, but] no clear position was obtained from WHO before Q2 2009… Predictability of regulatory decisions affecting development or time to market is an important factor in long term commitments." Another interviewee argues that the TPP should have established requirements for multi-dose vials with preservatives from the start, which would have helped drive the development of presentations best suited to the cold chain needs of developing countries.

While the TPP was designed to allow vaccines focused on specific global regions, some critics have charged that the profile shuts out regional producers by mandating that products include serotypes 1, 5, and 14.[111] **Though it is impossible to evaluate the counterfactual, manufacturer interviews suggest that the requirement has not restricted competition in the PCV market for low-income countries.** Plahte (2012) states that "Butantan's concerns were that the serotype 5 required by the TPP would be an unnecessary complication of a vaccine intended for the Brazilian market."[112] However, a spokesperson for Butantan indicates that because of shifting serotype prevalence in its home market, it has changed its focus from developing a three-valent PCV vaccine for the Brazilian market to one targeted at the African market. This vaccine will include the three serotypes mandated by this AMC, coupled to pneumococcal proteins. Similarly, both Indian producers interviewed have also made clear that they view the entire GAVI market as their target; it is therefore unlikely that they have been deterred by this requirement.

More broadly, it is difficult to discern whether regional producers in Brazil, China, and elsewhere would have been able to deliver PCV to market within the next ten years even without this requirement, and thus, whether it has reduced competition and innovation. In addition, GAVI could have received considerable public criticism had it supplied what might have been perceived as "substandard" vaccines to countries in other regions.

The case of pneumococcal protein vaccines also demonstrates the potential challenges faced by developers of TPPs for earlier-stage products. Conjugate vaccines (PCVs) work by joining (conjugating) polysaccharides expressed on the surface of pneumococcal bacteria to carrier proteins. However, this process is complex, expensive, and must be performed for each individual serotype. There is some chance pneumococcal common protein vaccines (PPVs) that work across nearly all variations of the bacteria, albeit at likely lower efficacy, will be developed in the next decade.

However, developing a TPP to cover PPVs in advance will be challenging. Although these new products may be only a few years away, the technical procedures to certify their immunogenicity and efficacy are still in development; standardized assays must be defined and their correlates of protection must be established.[113] In turn, this makes it difficult for the experts to write formal TPPs with the necessary detail in advance; by the time the science is fully established, the essential characteristics of various manufacturers' vaccines may have already been set. This experience also indicates that such detailed TPPs may be unnecessary to spur development of vaccines that target both low-income and high-income markets, as several manufacturers, including GSK, Sanofi and Intercell, have PPV research programs in place without a preexisting product profile.[114]

The experience of the AMC TPP suggests several lessons for future AMCs. While all future AMCs will need to include minimum standards for qualifying products, the detail that designers may need or be able to include may vary across products. Detailed TPPs may be less essential to drive development in several cases: where manufacturers are already researching products that would apply to both high-income and low-income markets; where the WHO prequalification process or other regulatory processes already cover most of the requirements; and where "reference" products exist that manufacturers can use as a target to meet or exceed. However, research may still be needed to establish whether products designed for high-income markets are appropriate for low-income countries, such as the work conducted by the Global Serotype Project for PCV. Additionally, specifying detailed TPPs for future products in advance may prove difficult, because the necessary science may not have been developed yet and because unforeseen borderline cases may prove unavoidable. Future AMC designers may want to consider instituting pre-review processes that provide manufacturers with guidance on open issues and questions before they invest in expensive development or design programs.

Capping individual manufacturers' share of the AMC

Relevant TOR Questions addressed in this section:

- **Question 2:** To what extent do specific AMC design elements contribute to the AMC objectives (including but not necessarily limited to those listed below):
  - Lack of explicit cap on manufacturer quantities (additional element)

Key Findings:

Some interviewees suggested that the AMC design should have considered explicit caps on manufacturers to ensure that third manufacturers were not shut out of the market. However, the original AMC designers decided against including such explicit caps because of concerns they would restrict competition by limiting the market share that aggressive suppliers can gain. For instance, a third supplier would have less incentive to challenge the multinationals on price, since it would have access to AMC funding they did not. No new evidence has come to light regarding how this dynamic will play out in practice.

Based on the AMC's currently signed contracts and expectations regarding future tender rounds, GSK and Pfizer will likely receive 70-80% of the AMC funds. As discussed previously, these levels are likely sufficient to ensure manufacturers are incentivized to supply under the Pilot. However, should a third manufacturer not come to market in 2017, the two existing suppliers may be able to collect additional AMC funding.

Some interviewees suggested that the AMC design should have considered explicit caps on manufacturers to ensure that third manufacturers were not shut out of the market. Under such a system, GSK and Pfizer would still be able to provide doses to GAVI after they hit their caps by charging a tail price greater than their unit costs; however, they would not have access to the AMC top-up subsidy.

However, the original AMC designers decided against including such explicit caps because of concerns that this would restrict competition by limiting the market share that aggressive suppliers can gain. This is especially true in a duopoly scenario, where the second supplier is essentially guaranteed the remainder, but also holds true in more competitive markets as well. For instance, in the scenario above, the third supplier would have less incentive to challenge the multinationals on price, since it would have access to AMC funding they did not. However, no new evidence has come to light regarding how this dynamic will play out in practice.

8. Lessons and considerations for future AMCs

This was the first AMC implemented, and designers had to navigate many unknowns during its development. Translating the AMC concept into a Pilot yielded many insights for future reference. Designers of future AMCs should first determine the type of market mechanism and solution that fits the problem they seek to address. If they decide that an AMC is appropriate, designers should then apply the below lessons to guide their design. Several of these steps are discussed and expanded upon in GAVI's *Vaccine Supply and Procurement Strategy 2011-2015,*[115] but are equally applicable to AMCs outside the specific vaccine space.

To determine what type of program is appropriate, follow these steps:

1. <u>Evaluate the current market context and challenges.</u>

Future program designers should begin by identifying the level of market maturity and type of market failure. Market failures can exist in many forms and across many points of a product lifecycle. Below are a few examples:

- New product development: Nascent markets where a product has not yet been developed and research and development is required
- Product launch: Late-stage markets where a product has been developed or nearly developed, but has not launched in desired markets or capacity is lacking
- Secondary supplier entry: Developed markets where additional suppliers should be incentivized to enter an existing market with a revised or improved product offering
- Lack of product uptake: Markets in which a product exists but has not been utilized effectively or demand has not materialized on a large scale

2. <u>Determine the best approach for addressing the market challenge.</u>

The "Making Markets for Vaccines" report from the CGD working group outlined two separate conceptions of an AMC: early-stage programs for products that require intensive R&D, and late-stage initiatives for products much closer to market. The two scenarios require very different approaches to pricing and structure. In many cases, particularly those where products are very near to market, an AMC as originally conceived may not be the approach best suited to the particular market failure.[xliii] In these cases, program designers should feel free to deviate from the original AMC concept and borrow approaches from other forms of market-shaping mechanisms. For instance, manufacturers have stressed their preference for individual purchase guarantees to offset the risks they run in making large upfront investments; though these may not be suitable in all contexts, intermediate approaches that improve the situation for all sides may be possible. Designers of future programs should, from the start, take into account the pragmatic realities of a market and design tailored, nuanced solutions accordingly.

If an AMC is appropriate, apply the following guiding principles:

[xliii] The GAVI alliance has agreed with stakeholders not to roll out a 2nd AMC until the design of roadmaps specific to each vaccine is completed for this very reason.

The following principles apply to AMCs of all types. However, while the Pneumococcal AMC allowed designers to test the feasibility of many technical aspects of an AMC, it did not test how these elements would contribute to the success of early-stage AMCs such as those for HIV or malaria vaccines. Such initiatives would face several new challenges: they would require the commitment of donors willing to invest in a 10-year or longer time horizon; they would face uncertainties in setting prices appropriately with no cost or supplier data; and they might face challenges developing a detailed TPP based on limited existing medical knowledge, among other obstacles.

Should designers decide that an AMC would be appropriate for the particular market failure, the following steps could facilitate its creation.

A. Find strong project advocates.

One of the greatest successes of the Pneumococcal AMC was translating an academic concept into reality. Moving forward, future innovative programs must find strong champions to drive them from conception to launch. In this Pilot, highly committed project champions took ownership of the initiative early on. In particular, Italy assumed an early leadership role in 2005, contributing nearly 50% of the AMC subsidy funds while reaching out to finance ministers in other countries to bring in new donors.

B. Plan to develop AMCs in an iterative fashion, rather than a fixed, sequential manner.

By their very nature, AMCs aim to create new markets. Markets, however, are complex and highly interrelated systems with dynamic feedback loops. The Pilot illustrated that each decision – price, sequencing of payments, TPP guidelines – can have a significant impact on the ultimate market created. Because each manufacturer's decisions are affected by those of other suppliers, even small design choices can have complicated second- and third-order effects.

Future AMCs should intentionally build flexibility and space for iteration into the design and implementation processes. One approach would be to include specific predetermined checks (e.g., price estimates topping a fixed amount, country co-pays falling below a certain value, or a set number of manufacturers indicating interest or lack of interest) that would trigger more fundamental reevaluations of basic parameters. This approach may help ensure that when key baseline assumptions change, designers are not locked into older approaches.

C. Decide and make clear who will bear which risks.

Participation in billion-dollar vaccine markets involves risks for both buyers and sellers. Future AMC designers should start by identifying the risks that prospective manufacturers face and deciding which risks the public sector or funders will mitigate. Such an explicit framework will help shape discussions and expectations and lead to more productive engagements.

Suppliers investing in new vaccines, particularly for the developing world, face a broad spectrum of risks: their R&D efforts may not bear fruit; their facilities may suffer unexpected outages; demand may develop slowly or not at all; donor funding may not materialize; competitors may take away market share. In some sense, the main advantage of the Pneumococcal AMC is that it eliminates one of these risks by ensuring that donor funding will be provided and mitigates another by stimulating country demand. However, many other risks are left to the suppliers.

Shifting risk from the private to the public sector is an attractive way to promote development efforts for two reasons. First, public sector actors may be able to bear more risk than private sector counterparts because of their large budgets, longer-term outlooks, desire to deliver public goods, and greater ability to influence demand.[xliv] Secondly, risk shifting, if correctly achieved, can end up being effectively costless. For instance, donors can use volume guarantees to drive down prices, which in turn can stimulate demand. This could lead to the fulfillment of the purchase commitments at no extra cost.

Donors could also use several other approaches to mitigate the risk individual suppliers face. Simply providing high-quality, trusted demand forecasts and other forms of market intelligence can play a large role in inducing suppliers to enter new markets. In-country support to increase the predictability of uptake would also be beneficial. Donors could also use mechanisms to mitigate only the most extreme downside cases, such as providing subsidized insurance to manufacturers to offset certain key risks.

D. Take into account the challenges of growing supply and demand simultaneously.

AMCs aim to develop new markets where a market failure exists. As they attempt to create both new supply and new demand, AMC implementers must be able to react to unforeseen market challenges. Because supply and demand will not necessarily develop at the same rate, it is critical to provide implementers with flexibility. Through its sequential tendering approach and capacity development period concept, the Pilot was able to successfully manage the procurement of doses and allocate funding as the manufacturers ramped up supply and the market situation evolved.

This flexibility can come at the cost of providing predictability for manufacturers, so building in the right types of flexibility is important. Future AMC designers should establish clear objectives and decision-making frameworks upfront to provide transparency to countries, donors and suppliers. They should also aim to understand what issues are most important to suppliers and establish predictable, straightforward policies in those areas. Other areas can be left open for adaptation as programs evolve.

E. Recognize that pricing the award is one of the most challenging aspects of designing an AMC, and plan accordingly.

Setting prices is one of the most difficult aspects of AMC design and the area likely to receive the most criticism. For early-stage products, actual production costs may be unknown to all involved. AMCs for late-stage products have a somewhat different challenge: suppliers know their costs but purchasers do not. In the case of the former, it may be sufficient to set the price at a level where the cost-effectiveness would be relatively high compared to other interventions; however, for the latter, designers run the risk of being criticized for providing companies with excess profits using public funds. This will be an especially complex challenge when designers intend to attract multiple manufacturers, who may have extremely different cost structures.

Designers of AMCs for late-stage products should thus explore ways to tailor their pricing structure to the context they face. For instance, AMCs for late-stage products may benefit from using direct negotiations to gain information regarding manufacturers' positions and preferences. Additionally, such negotiations would allow contracts to be fitted to suppliers' specific cost structures. Even if designers

[xliv] As a countervailing force, government actors do run the political risk of public criticism if initiatives fail to deliver on their promises.

cannot access cost data, they should explicitly design their procurement structures to drive price reductions in the long term.

F. Identify and leverage partners and stakeholders.

Leverage existing organizations and events to move the process forward. Designers should anticipate the time delays caused by the involvement of multiple stakeholders and take advantage of external institutions or events. The Pneumococcal AMC benefited by leveraging major decision-making events, such as the 2009 G8 summit, to build in a sense of urgency and move the project forward.

Communicate as needed with both civil society organizations and the broader public. Unlike more conventional procurement mechanisms, AMCs are explicitly designed to provide private sector actors with profits—profits high enough to convince them to enter markets they otherwise would not have found commercially viable. Civil society and public groups will hold such initiatives to a high standard, as an advisor at Oxfam explains: "Given that the AMC uses taxpayer funds and donor funds, we think that their role is not only to get the lowest price, but to have a transformative effect on the market."[116] This scrutiny will likely be particularly intense for (a) AMCs dealing with highly concentrated industries like pharmaceuticals, and (b) AMCs for late-stage products with greater information asymmetries. Providing clear communication of program goals and the reasons behind design and pricing decisions will be especially important for initiatives that, like the Pilot, are the first of their kind or leverage billions of dollars of public funds.

G. Set targets and track progress.

Establishing a clear monitoring and evaluation (M&E) framework with specific indicators and targets in future AMCs will allow for clear tracking of progress and the ability to adjust the program over time. Most AMCs will likely encounter difficulty in proving that their impact on markets came from funding or their unique structures. Having clear M&E metrics can help address concerns and critics as the program evolves. Because setting such metrics upfront may be difficult, especially when dealing with markets that do not yet exist, program designers should consider instituting regular review processes for updating targets and setting new ones as milestones are reached and information becomes available.

Endnotes

[1] Kremer, M., "Creating Markets for New Vaccines Part I: Rationale," NBER Working Paper w7716, Cambridge, MA, National Bureau of Economic Research, 2000.
[2] Kremer, M., "Creating Markets for New Vaccines Part II: Design Issues," NBER Working Paper w7717, Cambridge, MA, National Bureau of Economic Research, 2000.
[3] Levine, R. et al., "Making Markets for Vaccines: Ideas to Action," Center for Global Development, Washington DC, 2005. The report, financed by the Bill and Melinda Gates Foundation, was developed through an 18-month process involving consultations with economists, vaccine industry and public health experts, donors, and lawyers with experience in vaccines and contract law.
[4] GAVI Alliance Request for Proposal Number RFP- AMCPVPDE08022012.
[5] Kremer, M., "Creating Markets for New Vaccines Part I: Rationale," NBER Working Paper w7716, Cambridge, MA, National Bureau of Economic Research, 2000.
[6] Kremer, M., "Creating Markets for New Vaccines Part II: Design Issues," NBER Working Paper w7717, Cambridge, MA, National Bureau of Economic Research, 2000.
[7] Levine, R. et al., "Making Markets for Vaccines: Ideas to Action," Center for Global Development, Washington DC, 2005. The report, financed by the Bill and Melinda Gates Foundation, was developed through an 18-month process involving consultations with economists, vaccine industry and public health experts, donors, and lawyers with experience in vaccines and contract law.
[8] GAVI Alliance, http://www.gavialliance.org/support/nvs/pneumococcal/, accessed 25 October 2012.
[9] Liu et al., "Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000," pp. 2151-2161, *The Lancet* 379(9832), 2012.
[10] FDA approval year: 2000. Food and Drug Administration, Vaccines: Approved Products, "Prevnar," http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm180017.htm, last updated 24 February 2011; EMA approval year: 2001. Gomes, H. D. C., "Use of Seven-Valent Pneumococcal Conjugate Vaccine in Europe, 2001-2007," *Eurosurveillance*, Vol. 14, Issue 12, http://www.eurosurveillance.org/viewarticle.aspx?articleid=19159, 26 March 2009, accessed 20 October 2012.
[11] Request for Proposal Number RFP- AMCPVPDE08022012.
[12] Light, D., "Advance Market Commitments: Current Realities and Alternate Approaches," Health Action International, 2009.
[13] Light, D., "Saving the Pneumococcal AMC and GAVI," *Human Vaccines & Immunotherapies* (2011), 7:2.
[14] IFFIm, "Origins of IFFIm," http://www.iffim.org/, accessed on 1 October, 2012.
[15] IFC and London School of Hygiene and Tropical Medicine, "Independent Evaluation of the Affordable Medicines Facility - malaria (AMFm) Phase 1," 28 September 2012.
[16] GAVI Alliance, "Pneumococcal AMC Timeline," http://www.gavialliance.org/funding/pneumococcal-amc/, accessed on 1 October 2012.
[17] Center for Global Development, "UNITAID, background paper prepared for the Working Group on Value for Money," October 2012.
[18] Dalberg interviews, November 2012.
[19] Literature review including IFFIm annual financial statements, 2006.
[20] Dalberg interviews, November 2012.
[21] Dalberg interviews, October 2012.
[22] Ibid.
[23] Government of Canada, "Statement by G7 Finance Ministers and Central Bank Governors, London, 2-3 Dec 2005" http://www.canadainternational.gc.ca, accessed on 2 October, 2012.
[24] Dalberg interviews, October 2012.
[25] GAVI Alliance, "Key figures: donor contributions & pledges," http://www.gavialliance.org/funding/donor-contributions-pledges/, accessed on 2 October 2012.
[26] Dalberg interviews, October 2012.
[27] Ibid.
[28] Ibid.
[29] Expert Committee, "AMC Vaccine Candidate Summary Table," February 2006.
[30] Articles and publications from civil society groups.
[31] Dalberg interviews, November 2012.
[32] Advance Market Commitment for Pneumococcal Vaccines, "Consultation & Advisory Process," 20 April 2009.
[33] Letter from Italian HM Treasury to Julian Lob-Levy, subject: "Follow up to Advance Market Commitments for Vaccines," 9 January 2006.
[34] Timeline presented in Donor Committee meeting in Rome 8 March, 2007.
[35] Advance Market Commitment for Pneumococcal Vaccines, "Expert Group Terms of Reference," 27 June, 2007.

[36] Advance Market Commitment for Pneumococcal Vaccines, "Expert Group Report," 1 April, 2008.
[37] Advance Market Commitment for Pneumococcal Vaccines, "Terms of Reference for AMC Expert Group Report on Options for Modifications to AMC," 28 January, 2008.
[38] Dalberg interviews, November 2012.
[39] Written documentation and historical memos.
[40] Advance Market Commitment for Pneumococcal Vaccines, "Consultation & Advisory Process," 20 April, 2009.
[41] Advance Market Commitment for Pneumococcal Vaccines, "Expert Group Terms of Reference," Draft from 2 May, 2007 presented at Donor Committee meeting in May 2007.
[42] The World Bank and GAVI, "Framework Document: Pilot AMC for Pneumococcal Vaccines," 9 November, 2006.
[43] Advance Market Commitment for Pneumococcal Vaccines, "Implementation Working Group Report," 10 July 2008.
[44] Usher, Ann Danaiya, "GAVI takes steps to address funding woes," pp. 453, The Lancet, 377(9764), 2012.
[45] Dalberg Interviews, October 2012.
[46] Advance Market Commitment for Pneumococcal Vaccines, "Consultation & Advisory Process," 20 April 2009.
[47] Dalberg Interviews, October 2012.
[48] UNICEF Shipments Data, http://www.unicef.org/supply/index_gavi.html, 2012.
[49] AMC Stakeholder Meeting, December 2012.
[50] Source: WHO/UNICEF coverage estimates for 1980-2012, updated December 2012.
[51] Source: WHO/UNICEF coverage estimates for 1980-2011, updated July 2012.
[52] UNICEF, December 2012.
[53] Dalberg Interviews, December 2012.
[54] Ibid.
[55] GAVI Secretariat, "Doc 08 – Next Steps on the Pneumococcal AMC," Paper prepared for GAVI Alliance Board Meeting on 16-17 June 2010.
[56] GAVI Secretariat, "Doc 08 – Next Steps on the Pneumococcal AMC," Paper prepared for GAVI Alliance Board Meeting on 16-17 June 2010.
[57] "Independent Assessment Committee Charter and Bylaws," March 2011.
[58] Net Resources International, "GlaxoSmithKline Vaccine Manufacturing Facility, Tuas, Singapore." http://www.pharmaceutical-technology.com/projects/gsksingapore/; accessed 24 October 2012.
[59] Pfizer, "World Health Organization Grants Expansion To The Prequalification For Prevenar 13 To Include Adults 50 Years Of Age And Older," 11 September 2012.
[60] Dalberg Interviews, October 2012.
[61] Ibid.
[62] Plahte, Jens, "Is the pneumococcal vaccine Advance Market Commitment motivating innovation and increasing manufacturing capacity? Some preliminary answers," pp. 2462-2466, *Vaccine* 30, 2012.
[63] Source: GAVI Alliance, Stephano Malvolti and Jon Pearman, "Update on Pneumo Introductions," AMC Stakeholders' Meeting, 3 December 2012.
[64] Dalberg interviews, October to December, 2012.
[65] Dalberg interviews, October to December, 2012.
[66] UNICEF Supply Division, 2012.
[67] Dalberg Interviews, October to December, 2012.
[68] Cernuschi, T. et al, "Pneumococcal Advance Market Commitment: Lessons Learnt on Disease and Design Choices and Processes," GAVI Alliance, 2011.
[69] For examples, see Cernuschi, T., "The pneumococcal Advance Market Commitment (AMC): innovative finance to help the poor," pp. 142-146, Global Forum Update on Research for Health, Vol 6 , 2009: "Only a limited purchase guarantee is offered, equivalent to 45% of one year's committed supply. Final purchase of AMC vaccines is for the most part dependent on demand.", and Pearman, J. and Fihman, J., "The Pilot Advance Market Commitment Concept and Development", 10 March 2011: "[Mitigation of] Demand risk: … Opt-out provision if demand absent."
[70] Levine, O. et al., "The future of immunisation policy, implementation, and financing", *The Lancet*, DOI:10.1016/S0140-6736(11)60406-6, 2011.
[71] Nguyen, A. et al, "Market shaping: Strategic considerations for a healthy vaccine marketplace," *GAVI Alliance*, 2001; GAVI Alliance, "GAVI Alliance secures lower price for rotavirus vaccine," 10 April 2012.
[72] Jack, Andrew, "Flexible pricing pays off for drugs groups," *Financial Times,* 21 January 2010.
[73] Bloomberg Finance LP, accessed 7 November 7 2012.
[74] DiMasi et al., "The price of innovation: new estimates of drug development costs," Journal of Health Economics, 2003.
[75] U.S. Center for Disease Control, "Vaccines for Children Program," http://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html, accessed October 24, 2012. Prices taken from annual July quotes.

[76] "Making Markets for Vaccines," p. 30.
[77] "Making Markets for Vaccines," pp. 32, 51.
[78] Dalberg interviews, October and November 2012.
[79] Dalberg interviews, October and November 2012.
[80] Cernuschi, T. et al, "Pneumococcal Advance Market Commitment: Lessons Learnt on Disease and Design Choices and Processes", GAVI Alliance, 2011.
[81] Dalberg interviews, October 2012.
[82] Dalberg interviews, October 2012.
[83] UNICEF Supply Division, "Vaccine Security," http://www.unicef.org/supply/index_vaccine_security.html, accessed October 26, 2012.
[84] Dalberg interviews, September 2012.
[85] Dalberg interviews, November 2012
[86] Dalberg Interviews, December 2012.
[87] Implementation Working Group Report, pp. 38, 10 July 2008.
[88] Ibid.
[89] Usher, Ann Danaiya, "Dispute over pneumococcal vaccine initiative," The Lancet, 5 December 2009.
[90] GlaxoSmithKline, "World Health Organization Grants Prequalification for Global Use to GSK's 10-Valent Synflorix™ Vaccine," http://us.gsk.com/html/media-news/pressreleases/2009/2009_pressrelease_10125.htm, accessed 19 December 2012; Dalberg interviews, November 2012.
[91] "Gates Foundation to fund two cos for vaccine research," The Economic Times, http://m.economictimes.com/PDAET/articleshow/7784192.cms, 25 Mar 2011; Levin, O. "Progress on uptake of pneumococcal vaccines in developing countries," 2003.
[92] Dalberg interviews, October 2012.
[93] Dalberg interviews, October 2012.
[94] Dalberg interviews, October 2012.
[95] Net Resources International, "GlaxoSmithKline Vaccine Manufacturing Facility, Tuas, Singapore." http://www.pharmaceutical-technology.com/projects/gsksingapore/, accessed 28 November 2012.
[96] PATH, "Projects and Partners," http://www.path.org/projects/pneumococcal_protein_vaccine_project_partners.php, accessed 5 November 2012.
[97] UNICEF Supply Division, "UNICEF, the Vaccine Market, and developments in Vaccine Supply," 8 December 2003.
[98] Lob-Lebyt, Jacob, "GAVI update," Presentation to the Global Immunization Meeting, Geneva, 1 February 2010.
[99] Dalberg interviews, October 2012.
[100] UNICEF Supply Division, "Table of Vaccine Procurement 1996-2011 (Value)," http://www.unicef.org/supply/files/Table_Total_Doses__of_Vaccines_bought_1996-2011_table.pdf, accessed 4 December 2012.
[101] Snyder, C. et al., "Economic Perspectives on the Advance Market Commitment for Pneumococcal Vaccines," pp. 1508-1517, *Health Affairs:* 30(8), 2012.
[102] Dalberg interviews, October 2012.
[103] Dalberg Interviews, October and November 2012.
[104] Dalberg interviews, October 2012.
[105] Ibid.
[106] Ibid.
[107] Ibid.
[108] Dalberg Interviews, October 2012.
[109] Dalberg interviews, November 2012.
[110] Dalberg Interviews, October 2012.
[111] Light, Donald, "Advance Market Commitments: Current Realities and Alternate Approaches," Health Action International, 2009.
[112] Plahte, Jens, "Is the pneumococcal vaccine Advance Market Commitment motivating innovation and increasing manufacturing capacity? Some preliminary answers," pp. 2462-2466, *Vaccine*: 30, 2012.
[113] Ginsburg, A. et al., "Issues and Challenges in the Development of Pneumococcal Protein Vaccines," *Expert Rev. Vaccines*: 11(3), 2012.
[114] Ibid.
[115] GAVI Alliance, *Vaccine Supply and Procurement Strategy 2011-2015, Approved 17 November 2011*
[116] Dalberg Interviews, October 2012.