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Pneumococcal Advance Market Commitment:

Lessons Learnt on Disease and Design Choices and Processes

By: ***Tania Cernuschi, Eliane Furrer, Susan McAdams, Andrew Jones, Johanna Fihman, Nina Schwalbe***

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Markets for life-saving vaccines often do not generate the most desired outcomes from a public health perspective in terms of product quantity, quality, affordability, programmatic suitability and/or sustainability for use in the lowest income countries. The perceived risks and uncertainties about sustainably funded demand from developing countries often leads to underinvestment in development and manufacturing of appropriate products. The pilot Advance Market Commitment (AMC) for pneumococcal vaccines (Pneumo AMC), launched in 2009, aims to remove some of these market risks by providing a legally binding forward commitment to purchase vaccines according to predetermined terms. To date, 14 countries have already introduced pneumococcal vaccines into their national immunisation programmes through the AMC with a further 39 countries expected to introduce before the end of 2013.

Due to its innovative nature, the Pneumo AMC inevitably carries risks and will require careful independent evaluations of its design, processes and impact. While evaluations are scheduled from the third year of implementation onwards, this document is a first attempt to take stock of the experience to date and to encourage a constructive debate about the Pneumococcal AMC. It provides a starting point to inform discussions about the potential applications of the AMC concept to other vaccines or health interventions and helps to advance considerations of AMCs in alternative fields, such as agriculture or clean energy. Indeed, testing the concept and its feasibility is one of the key objectives of the pilot AMC.

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Abbreviations

ADIP	Accelerated Development and Introduction Plan
AMC	Advance Market Commitment
AVI	Accelerated Vaccine Introduction
CGD	Center for Global Development
CSO	Civil society organisation
DFID	Department for International Development (United Kingdom)
EEG	Economic Expert Group
EMEA	European Medicines Agencies
EPI	Expanded Programme on Immunization
G7	Group of seven industrialized nations
GAVI	The GAVI Alliance
GNI	Gross National Income
GSK	GlaxoSmithKline
HPV	Human papillomavirus
IAC	Independent Assessment Committee
IEC	Independent Expert Committee
IRC	Independent Review Committee
IWG	Implementation Working Group
M&E	Monitoring and evaluation
MDG	Millennium Development Goal
NGO	Non-governmental organisation
PAHO	Pan American Health Organization
PCV	Pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
PDP	Product development partnership
PneumoADIP	Pneumococcal Vaccine Accelerated Development and Introduction Plan
R&D	Research and development
SAGE	Strategic Advisory Group of Experts
SDF	Strategic demand forecast
TPP	Target product profile
UK	United Kingdom
UN	United Nations
UNICEF	United Nations Children's Fund
US$	United States dollar
WB	World Bank
WHO	World Health Organization

A. Background

A.1 Design and Early Implementation Process

An Advance Market Commitment (AMC) for vaccines aims to stimulate the development and manufacture of vaccines needed in low income countries. By making a legally binding forward commitment to subsidize the purchase of needed vaccines at predetermined terms, donors make the market for vaccines in developing countries more viable and thereby encourage the vaccine industry to increase investments in these products. An AMC for vaccines gained public attention with the publication of a report by the Center for Global Development in April 2005 entitled, "Making Markets for Vaccines: Ideas to Action".[1] The Government of Italy, with the support of the World Bank, presented a report (the "Tremonti Report")[2] to the G7 Finance Ministers proposing ways to move forward with a pilot AMC for vaccines and identifying six potential target diseases for the pilot - HIV/AIDS, malaria, tuberculosis, rotavirus (diarrhoeal disease), pneumococcal disease (pneumonia and meningitis) and cervical cancer (caused by human papillomavirus, HPV).

Following a supportive statement from the G7 Finance Ministers, the World Bank and the GAVI Alliance were asked to co-lead the design of a pilot AMC. An Advisory Group comprising key partners provided insight into the technical and structural options for the pilot, and determined criteria based on which a target disease should be chosen among the six identified candidate diseases.[3] An Independent Expert Committee (IEC) was then tasked with evaluating the diseases against the agreed criteria and to provide a recommendation on the most suitable option for the initial AMC pilot.[4] In February 2006, the IEC unanimously concluded that while vaccines for all six diseases would benefit from AMCs in due course, pneumococcal vaccines

[1] Barder O., Kremer M., Levine R., Making Markets for Vaccines: Ideas to action. Working Group Report. Washington DC, Center for Global Development, 2005. Available at: http://www.cgdev.org/section/initiatives/_archive/vaccinedevelopment/chapters [accessed 13 September 2011]

[2] The report is named after Giulio Tremonti, Italian Minister of the Economy and Finance at the time of the G7 Finance Ministers Meeting in London in December 2005.

Background papers to Advanced Market Commitments for vaccines. A new tool in the fight against disease and poverty. Report to the G8 Finance Ministers. London, Ministry of Economy and Finance of Italy, 2005. Available at: http://www.gavialliance.org/library/documents/amc/tremonti-report-to-the-g8-finance-ministers/ [accessed 13 September 2011]

[3] The Advisory Group was co-chaired by the World Bank and GAVI and included representatives from WHO, UNICEF, the Bill & Melinda Gates Foundation, public -private partnerships (IAVI, pneumo ADIP, MVI, Aeras, etc), members from the Center for Global Development (CDG) task force working on AMC, BIO Ventures for Global Health, as well as designated industry and donor representatives.

[4] The IEC was convened from a long list of possible members suggested by governments, UN agencies, public-private partnerships and foundations. The final committee was composed of 13 internationally recognized experts without conflict of interest in the areas of public health, epidemiology, industry economics, vaccine development and law.

were the most suitable candidate for a demonstration AMC, *"because of both their ability to rapidly demonstrate that the AMC concept works and because of their potential impact on the health of the target populations."* [5] An AMC for late-stage vaccines was thus chosen, i.e. for vaccines in late stages of clinical trials or under regulatory approval. It should be noted that the Independent Expert Committee also recommended a second demonstration AMC targeting malaria vaccines to test the impact of the AMC mechanism on early-stage vaccines (i.e. those in pre-clinical testing and early clinical development phases).

An independent evaluation of possible institutions to host the Pneumococcal AMC[6] concluded in 2006 that the optimal arrangement for an AMC would draw on the capacities of both GAVI and the World Bank, with GAVI providing the programmatic functions and hosting the AMC Secretariat, while the World Bank would provide financial and fiduciary functions. In the second half of 2006, a Technical Working Group composed of representatives from 15 potential donor countries, a range of other institutions (the European Commission, the World Bank, GAVI, the Bill & Melinda Gates Foundation and the World Health Organization) and vaccine industry representatives, met to review the technical, institutional and financial aspects of a pilot AMC for pneumococcal vaccines.

In February 2007, as a result of the preparatory work of the various committees, the Government of Canada made the first pledge to fund a pilot AMC for pneumococcal vaccines, followed by five other donors. Joint pledges totalling US$ 1.5 billion came from the Governments of Italy, the United Kingdom, Canada, Russia, Norway and the Bill & Melinda Gates Foundation.

Following the launch, GAVI and the World Bank continued to lead efforts to set out the detailed terms of the AMC pilot. A Target Product Profile (TPP) for AMC pneumococcal vaccines was established to guide companies in developing and producing vaccines which would be particularly suitable for use in developing countries. The TPP for pneumococcal vaccines was developed by an ad-hoc group set up in April 2007 by the World Health Organization (WHO) and it was approved in December 2007 by the WHO Director-General after endorsement by the WHO Strategic Advisory Group of Experts (SAGE). The TPP defines vaccine specifications related to the public health impact and suitability of the product, covering measures of vaccine

[5] Independent Expert Committee Recommendations for AMC Pilot, Executive Summary, February 2006. Available at: http://www.gavialliance.org/library/documents/amc/independent-expert-committee-recommendation-for-amc-pilot/ [accessed 13 September 2011]

[6] Considered institutions included the Bill & Melinda Gates Foundation, WHO, UNICEF, The Global Fund to Fight AIDS, Tuberculosis and Malaria, GAVI and The World Bank.

efficacy, safety, dose-scheduling, presentation and packaging. It is the threshold standard a vaccine needs to meet in order to be eligible for AMC financial support.[7],[8]

In mid 2007, an Economic Expert Group (EEG) was convened as an independent advisory body to the AMC donors. The mandate of the EEG was to examine and review key AMC design features (such as incentive and tail prices, supply obligations, currency provisions) and provide recommendations to the donor group on how to finalize these terms. The work of the EEG was informed by a series of industry consultations, analytical work conducted by external consultants and extensive modelling exercises to assess the likely industry behaviour in the face of different AMC structures. In April 2008, the Expert Group delivered its final report to the AMC Donor Committee.[9]

While endorsing many of the options recommended by the EEG, the AMC Donor Committee decided to create an Implementation Working Group (IWG) with the task of elaborating on the selected options and completing relevant analytical work in order to provide the necessary detail on the final terms, pricing and parameters for the pilot AMC.[10] The IWG published its final report in July 2008.[11]

In parallel, the AMC Stakeholders[12] negotiated the suite of legal agreements that actually establish the AMC. These include the AMC's core legal and technical terms and conditions, governance and procedural structures, the roles of the GAVI Secretariat, the Independent Assessment Committee (IAC), the AMC donors, the World Bank, and UNICEF. Finally, a monitoring and evaluation plan was established for the programme. The legal agreements,

[7] Target Product Profile (TPP) for the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (Part 1), Master Table. Geneva: World Health Organization; 2008. Available at: http://www.gavialliance.org/library/documents/amc/tpp-master-table/ [accessed 13 September 2011]

[8] Target Product Profile (TPP) for the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (Part 2), Supplementary Information. Geneva: World Health Organization; 2008. Available at: http://www.gavialliance.org/library/documents/amc/tpp-supplementary-information/ [accessed 13 September 2011]

[9] Advance Market Commitment for Pneumococcal Vaccines. Expert Group Report presented to the Donor Committee. April 2008. Available at: http://www.gavialliance.org/library/documents/amc/economic-expert-group-(eeg)-report/ [accessed 13 September 2011]

[10] Response of the AMC Donor Committee to the Interim Report of the Economic Expert Group: Summary. 2008. Available at: www.gavialliance.org/library/documents/amc/eeg-donor-response/ [accessed 13 September 2011]

[11] Advance Market Commitment for Pneumococcal Vaccines. Implementation Working Group Report presented to the Donor Committee. July 2008. Available at: http://www.gavialliance.org/library/documents/amc/implementation-working-group-(iwg)-report/ [accessed 13 September 2011]

[12] The term "AMC Stakeholders" will be used in this document to refer to the GAVI Alliance, the World Bank and the six AMC donors.

reflecting the detailed recommendations of the IWG, were signed in Lecce, Italy, on 12 June 2009 on the eve of the G8 Finance Ministers meeting.[13]

During the establishment phase, consultations were undertaken with different stakeholders, including GAVI-eligible countries, civil society organisations (CSOs), and vaccine suppliers. Consultations in GAVI-eligible countries with health policy makers, paediatricians, researchers, and immunisation managers were crucial particularly during the initial phase of design. Developing country representation in the initial advisory groups, the Independent Expert Committee and the Economic Expert Group was given high priority. Later in the process, briefings were also organized by GAVI, the World Bank and AMC donors with interested CSOs (in particular, Oxfam, Médecins sans Frontières and a working group of U.S.-based NGOs), focusing on the EEG report and the final report of the IWG, as well as monitoring and evaluation plans. The United Kingdom and Norway played a crucial role in this consultative process with civil society. Industry consultations were undertaken in several rounds from 2005 through 2009 with suppliers having active or pipeline pneumococcal conjugate vaccine programmes, including the multinationals Wyeth, Merck, Sanofi Pasteur, GlaxoSmithKline Biologicals, and Novartis, and emerging market suppliers Biological Evans, Shantha Biotechnics, Serum Institute of India and Panacea (India), Chengdu Institute of Biological Products (China), and BioManguinhos/Fiocruz (Brazil).[14]

Once the AMC legal agreements were signed, suppliers were eligible to register their interest in participating in the AMC by entering into AMC Registered Manufacturer Agreements. Registration to the AMC is a prerequisite for a supply offer to be reviewed by UNICEF and indicates the supplier's formal agreement to the AMC terms and conditions while not implying any commitment to effectively participate in the AMC. While suppliers may decide to keep their registration confidential, four suppliers - GlaxoSmithKline (GSK) Biologicals, Pfizer Inc., the Serum Institute of India and Panacea Biotech Ltd - have publicly disclosed their AMC registration.[15]

[13] GAVI Partners Fulfil Promise To Fight Pneumococcal Disease. GAVI Press release on 12 June 2009. Available at: http://fr.gavialliance.org/media_centre/press_releases/2009_06_12_AMC_lecce_kick_off.php [accessed 13 September 2011]

[14] Consultation & Advisory Process: Advance Market Commitment for Pneumococcal Vaccines. 2009. Available at: http://www.gavialliance.org/library/documents/amc/consultation-and-advisory-process/ [accessed 13 September 2011]

[15] Advance Market Commitment for Pneumococcal Vaccine: Annual Progress Report 12 June 2009 -31 March 2010. Geneva, GAVI Alliance Secretariat, 2010. Available at: http://www.gavialliance.org/library/documents/amc/2010-pneumococcal-amc-annual-report/ [accessed 13 September 2011]

Following the publication of a Strategic Demand Forecast by GAVI, UNICEF Supply Division issued a first Call for Supply Offers on 4 September 2009, and received four offers.[16] On 23 March 2010, UNICEF entered into provisional supply agreements with GSK and Pfizer. Both agreements became effective shortly after as both vaccines met the target product profile and were deemed eligible for purchase, pursuant to the terms and conditions. The supply agreements provide that each manufacturer will supply 30 million doses annually for 10 years, starting in January 2012 for GSK and in January 2013 for Pfizer. The vaccines are supplied at a price of US$ 3.50 per dose. As part of the AMC Capacity Development Period, GSK and Pfizer have also committed to supply 7.2 million, 24.2 million and 20 million doses additionally for the years 2010, 2011 and 2012 respectively.[17]

In April 2011, UNICEF Supply Division and GAVI issued a new Call for Supply Offers for the procurement of additional pneumococcal vaccines to meet increasing country demand[18].

A.2 The Pneumococcal AMC Terms

An AMC is a flexible concept. The idea put forward in the Center for Global Development's report, *Making Markets for Vaccines: Ideas to Action*, evolved as the pilot was negotiated; indeed, any AMC will need to be tailored to its specific purpose and desired product and market impact. In the context of the pilot Pneumococcal AMC donors focused carefully on a clear statement of its overarching goal – to reduce morbidity and mortality from pneumococcal diseases, saving an estimated 7 million lives by 2030 – and the specific AMC objectives:

1. to accelerate the development of pneumococcal vaccines that meet developing country needs as specified in the Target Product Profile;

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

3. to accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers, including binding commitments by participating companies to supply the vaccines at low, long-term and sustainable prices; and

[16] Advance Market Commitment for Pneumococcal Vaccine: Annual Progress Report 12 June 2009 -31 March 2010. Geneva, GAVI Alliance Secretariat, 2010. Available at: http://www.gavialliance.org/library/documents/amc/2010-pneumococcal-amc-annual-report/ [accessed 13 September 2011]

[17] "AMC Capacity Development Period" means the period during which an AMC-eligible manufacturer is developing Dedicated Manufacturing Capacity as defined in the relevant Supply Agreement.

[18] Advance Market Commitment for Pneumococcal Vaccine: Annual Progress Report 1 April 2010 -31 March 2011. Geneva, GAVI Alliance Secretariat, 2011. Available from : http://www.gavialliance.org/library/documents/amc/2011-pneumococcal-amc-annual-report/ [accessed 13 September 2011]

4. to pilot the effectiveness of the AMC mechanism as an incentive for needed vaccines and to learn lessons for possible future Advance Market Commitments;

The pilot Pneumococcal AMC is intended to motivate suppliers with target vaccines[19] that are close to being licensed to bring the vaccines to market more quickly and, most importantly, increase manufacturing capacity to serve developing country demand. The Pneumococcal AMC also aims to spur the development of second generation vaccines.[20]

To achieve these objectives, the Pneumococcal AMC offers a legally binding commitment to support the market of qualifying pneumococcal vaccines with US$ 1.5 billion, the "AMC funds", for which vaccine manufacturers can compete. Interested suppliers manufacturers compete over successive tenders to supply a share of the annual forecasted demand of vaccines as it increases over time, reaching an estimated 200 million doses per year at peak. In exchange, the AMC provides a portion of the
US$ 1.5 billion directly proportional to each manufacturer's supply share. For instance, if a manufacturer enters into an agreement to supply 50 million doses of vaccines annually (i.e. 25% of the target dose amount), it could receive up to US$ 375 million of the AMC funds (i.e. 25% of the total AMC funds, see Figure 1 below). Total award to suppliers at each tender round cannot be higher than the forecasted demand five years into the future.[21, 22] Competing bids are assessed against four main criteria: ensuring supply to meet demand; country preference; price offered by the manufacturer; continued vaccine supply and multiple manufacturer participation (supply security).

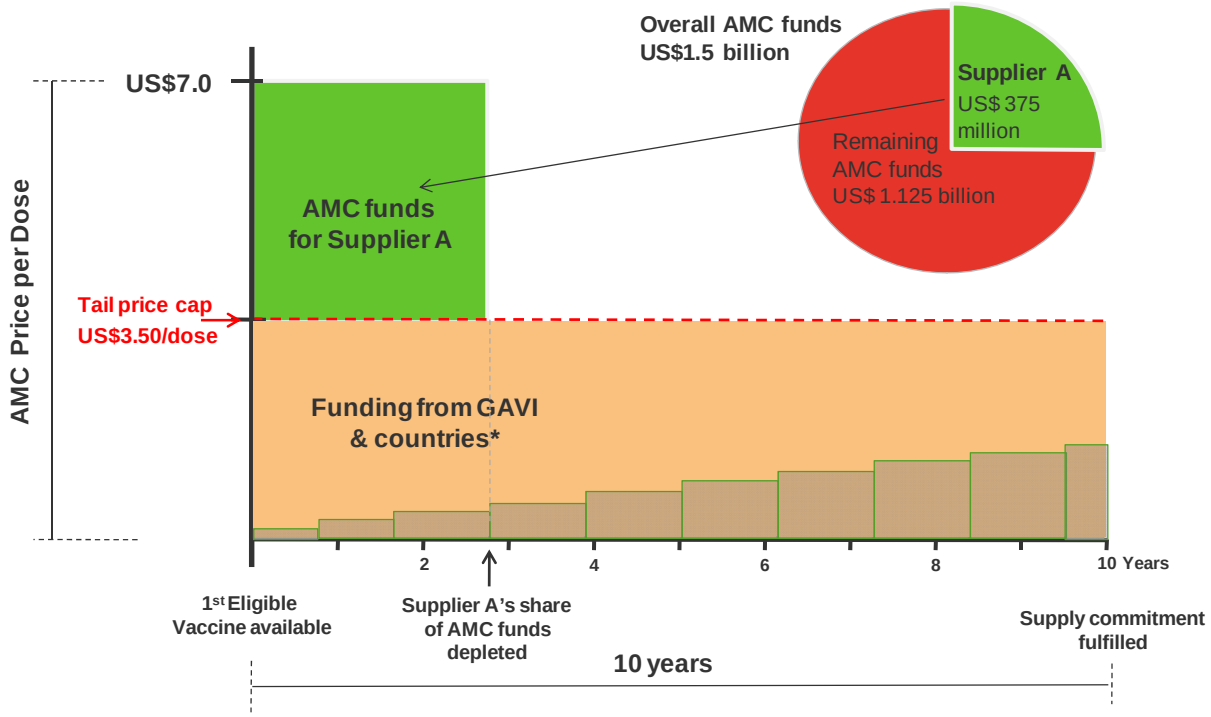
[19] At the time pneumococcus was chosen, there was a rich pipeline of potential candidate vaccines, two of which already in advanced stages of development: a 10-valent formulation in a 2-dose vial presentation by GlaxoSmithKline (GSK) and a 13-valent formulation in a 1-dose vial presentation by Pfizer Inc. GSK's PCV10 obtained WHO pre-qualification in March 2010 and Pfizer's PCV13 pre-qualified in August 2010.

[20] Independent Expert Committee Recommendations for AMC Pilot, Executive Summary, February 2006. Available at: http://www.gavialliance.org/library/documents/amc/independent-expert-committee-recommendation-for-amc-pilot/ [accessed 13 September 2011]

[21] Advance Market Commitment for Pneumococcal Vaccines. Expert Group Report presented to the Donor Committee. April 2008. Available at: http://www.gavialliance.org/library/documents/amc/economic-expert-group-(eeg)-report/ [accessed 13 September 2011]

[22] Advance Market Commitment for Pneumococcal Vaccines. Implementation Working Group Report presented to the Donor Committee. July 2008. Available at: http://www.gavialliance.org/library/documents/amc/implementation-working-group-(iwg)-report/ [accessed 13 September 2011]

Figure 1: AMC funding structure (illustrative example)



* Co-financing levels are determined in line with the applicable GAVI co-financing policy.

All manufacturers are required to enter into a standard supply agreement. Certain terms - such as contract duration, price conditions, demand guarantee, penalties, opt out options - are set up front and are identical for all participants. Each manufacturer must commit to supply its share of doses for at least ten years. The doses supplied can be priced at a maximum of US$ 3.50 per dose ("tail price cap") to be paid by GAVI and GAVI-eligible countries.[23] Each supplier's share of AMC funds is disbursed as a incentive per dose (additional to the amount paid by GAVI and countries) - bringing the total price up to the AMC price (US$ 7) for the initial 20% of vaccine doses procured from each supplier. This "AMC price" is set with the aim to enable companies to quickly recover incremental investment costs incurred to serve the GAVI market. Only a limited purchase guarantee is offered, equivalent to 45% of one year's committed supply. Final

[23] The tail price cap was set close to the estimated marginal cost of production at the time of the AMC design to encourage sustainable production and access to the vaccine. GAVI-eligible countries will contribute according to GAVI's co-financing policy. For more information on co-financing, see GAVI website: http://www.gavialliance.org/about/governance/programme-policies/co-financing/ [accessed 13 September 2011]

purchase of the remaining AMC vaccines is dependent on demand. In other words, countries must desire vaccines and must be able, jointly with GAVI, to pay their share of the final price.[24]

[24] Detailed information on the terms of the Pneumococcal AMC can be found in the AMC legal documents on the GAVI Alliance website: http://www.gavialliance.org/funding/pneumococcal-amc/amc-legal-agreements/ [accessed 13 September 2011]

B. Lessons Learnt

For analytical purposes, the experience to date with the Pneumococcal AMC can be divided into three areas: lessons learnt on i) disease selection, ii) design choices, and iii) processes.

B.1 Lessons Learnt on Disease Selection

While the CGD report presented the rationale for an AMC, the evaluation and choice of a target disease was made through an independent process led by an Independent Expert Committee (IEC). Over 60% of the Committee's 13 expert members were from developing countries. The members, with expertise in public health, epidemiology, industry economics, vaccine development and law, were identified based on suggestions from numerous bodies including governments, UN agencies, public-private partnerships and foundations.[25] The Committee's mandate was to provide an impartial technical evaluation of the six candidate diseases suggested in the Tremonti report.[26]

The exercise to prioritise the options was based on the following two main criteria: first, the value of the AMC in accelerating the availability of vaccines to reduce the mortality and morbidity from the given disease; and second, the value of the vaccine-preventable disease in testing and proving the AMC concept. The Committee's review was informed by disease specific background papers submitted by disease expert groups. These background papers followed an agreed standardized format, and provided data and information on the following main issues, as defined by the Advisory Group (see footnote 3):

1) *Background information on the vaccine-preventable disease, status of vaccine and other interventions*

   - Disease burden and rationale for a vaccine: importance of the disease burden in the poorest developing countries (e.g. GNI/capita <US$ 1000) and potential impact (deaths prevented) and cost-effectiveness of a vaccine, given expected efficacy. Readiness and feasibility for introduction with existing delivery systems.
   - Other interventions: alternative interventions available to address the disease (e.g. screening and effective treatment in developing countries, bed nets, antibiotics).

[25] The Vice President of Concessional Finance at the World Bank, the Chief Executive Officer of the GAVI Alliance, and the Head of the Immunization, Vaccines and Biologicals Department at WHO approved the list of experts who could serve as members of the group.

[26] The six candidate diseases were : HIV/AIDS, malaria, tuberculosis, rotavirus (diarrhoeal disease), pneumococcal disease (pneumonia and meningitis) and cervical cancer (caused by human papillomavirus, HPV)

- Product environment and anticipated impact on industry: supply factors such as products in the pipeline of pharmaceutical companies; potential degree of competition; product characteristics.

2) *Value of an AMC for the vaccine-preventable disease*

- Overview of investment for the disease.
- Estimated size of the AMC: required AMC envelope to stimulate market reaction needed to achieve objectives.
- Demand estimates with AMC: demand factors such as level of confidence in demand estimates, potential barriers at the local level, requirements linked to delivery systems.
- Impact in countries and impact of the AMC on the obstacles limiting progress on the vaccine: ability of the AMC to speed availability and affordability in the poorest countries. Potential impact of a market guarantee on industry decisions to serve the developing country market given the state of development, the number of interested suppliers and the investment decisions that are still open to suppliers.

3) *Value as a pilot*

- Extent to which the disease can show the efficacy and effectiveness of the AMC concept.

The IEC recommended pneumococcal vaccines as the most suitable candidate. The main reasons for choosing pneumococcal vaccines were: a) the magnitude of their potential impact on the health of the target population; b) the ability to leverage an already existing robust pipeline of efficacious vaccines, whose development and production for effective use in target countries needed to be accelerated; c) the likelihood of pneumococcal vaccines to fit into the existing delivery systems, thereby facilitating cost-effective introduction; and finally, d) as a result of the above mentioned features, the possibility to rapidly test the viability and effectiveness of the AMC

concept.[27] The IEC also recognized, as the preceding Advisory Group had, that an AMC was likely to be more easily applied to technologies closer to market (rather than technologies in the early stages of development), as it would require a smaller overall donor investment and would provide more direct incentives to manufacturers. Contextually, the Committee also clearly stated that malaria would be a very suitable candidate for an early stage AMC.

[27] Independent Expert Committee Recommendations for AMC Pilot, Executive Summary, February 2006. Available at: http://www.gavialliance.org/library/documents/amc/independent-expert-committee-recommendation-for-amc-pilot/ [accessed 13 September 2011]

The main issues and challenges faced during the disease selection process included:

- An extremely tight timeline, with donors driving a very ambitious schedule leading up to the 2006 G8 Summit, contributed to a lack of transparency in the selection of members of the Independent Expert Committee. It also led to tight timelines for submission of investment cases by disease expert groups – primarily product development partnerships (PDPs) – that were given only about four weeks to submit their case, which some of them felt limited the depth of analysis.

- Considerable attention was paid to isolating the disease selection process from political pressure. For some potential donors, interest and willingness to support an AMC depended on the selected target disease, as well as the amount of required AMC funds.[28] To ensure independence and credibility of the disease selection process, none of the AMC Stakeholders was represented in the Independent Expert Committee. Donors wanted to ensure that the selection process was credible and independent, and limited themselves to providing guidance on the desired objectives of the AMC and on its feasibility.

- The presence of a broadly representative Advisory Group in charge of mapping the technical and structural options for the pilot and providing recommendations about the level playing field and criteria to be used in assessing the candidate diseases was perceived to be helpful in ensuring independence and credibility of the process. Nevertheless, a lot of discretion was left to the Independent Expert Committee. For instance, it was left to the Independent Expert Committee's judgement to establish the hierarchy between the two selection criteria, i.e. i) accelerating vaccine availability, and ii) ability to test the AMC concept. And the IEC enjoyed a high level of discretion in weighting and ranking the various elements presented in the proposals.

- Variation in data availability across diseases: there was transparency and clarity with regard to the data and information presented in support of each candidate disease and the standardised format of these background papers facilitated comparison across the six target diseases. However, vaccines against the six diseases evaluated by the IEC were at very different stages of development. In consequence, data availability differed significantly across them and some observers think that the process was biased toward late-stage interventions because more and better data were available for these diseases/vaccines.

[28] Indeed, some donors supported the AMC concept but ultimately not the pilot due to the choice of pneumococcal disease.

- While the AMC concept is in principle applicable to both early-stage and late-stage vaccines (as indicated in the CGD report), the AMC had been primarily discussed as a mechanism to incentivize R&D investments. Since the Pneumococcal AMC primarily acts as an incentive to scaling up production capacity and as a procurement mechanism for nearly developed products rather than a R&D incentive, some felt that the Pneumococcal AMC may not have been an appropriate choice for the pilot project.[29] This suggests that communication on the potentially diverse applicability of the AMC concept was not effective.

- Similarly, some critics feared that the Pneumococcal AMC would claim attribution for bringing to market the 10- and 13-valent vaccines, whose developments were instead driven by the existence of wealthier country markets. While the Independent Expert Committee did point to the need for this AMC to accelerate development of PCV10 and PCV13, it was never the intent of the Pneumococcal AMC to take credit for early development efforts of these two products.

- As work progressed, it became clear that the AMC model, as outlined by the CGD report, was broad and required considerable work to be tailored to the specific characteristics of the target market, in this case pneumococcal vaccines. Consequently, it became evident that the Pneumo AMC would provide insights only for products presenting a similar market landscape as pneumococcal vaccine.

Lessons learnt on disease selection

- For future similar initiatives, it may be desirable to allow more time for the important step of selecting a target disease. This would facilitate the establishment of a more open process to choose committee members (a process more similar to the selection of members to the Independent Assessment Committee (IAC)[30] could be envisioned, for instance). This

[29] Wilson P. Giving developing countries the best shot: An overview of vaccine access and R&D. Joint report of Oxfam International and Médecins Sans Frontières. 2010. http://www.oxfam.org/en/policy/giving-developing-countries-best-shot-vaccine-access [accessed 13 September 2011]

[30] The Independent Assessment Committee was created as an impartial oversight body of the AMC. Its mandate is to review and approve the minimum technical requirements (i.e. the Target Product Profile) that vaccines must meet in order to be eligible for AMC funding and to determine whether a candidate vaccine fulfils these requirements. The IAC members are selected by a panel composed of representatives from vaccine industry associations, WHO, the WB and GAVI after an open call for nominations. See section on 'Governance structure' for more information on the IAC.

would also help address criticism around lack of transparency and time for the preparation of disease background papers.

- To tackle the concern of isolating the disease selection process from political pressure: a higher degree of transparency on the established decision-making framework to guide the Independent Expert Committee's choice and on the IEC's discussions and rationale for decision may be advisable.

- Impact evaluations will determine the applicability of the AMC mechanism to late stage technologies and whether the AMC did help accelerate the latest phases of development of PCV10 and PCV13. Yet, for the future, improved communication on the potential scope of an AMC and on the target objectives of a particular AMC would help prevent false expectations on the programme's potential.

- The Pneumo AMC provides insights only for products presenting a similar market landscape as pneumococcal vaccines. Thus, the pilot's ability to test the efficiency and effectiveness of the AMC concept for advancing development and production of different technologies in different markets should not be overestimated.

- The involvement of experts from developing countries in the choice of the target disease ensured that developing countries' needs and preferences were well represented. An equilibrated mix of experts from different backgrounds and a strong presence of developing country representatives should be ensured again in future initiatives of this type.

B.2 Lessons learnt on design choices

The CGD report presented the rationale for an AMC and proposed a basic design, including a Framework Agreement and Supply Agreement. Drawing upon this basic concept of an AMC, GAVI and the World Bank developed a pilot proposal for consideration by G8 members in mid-2006. Work continued on different aspects of the AMC (the legal structure, financial arrangements, Target Product Profile, programme management, Independent Assessment Committee functions, etc.). In mid-2007, the Economic Expert Group was convened to examine and review the key AMC design features. New information from industry consultations, demand forecasts, and modelling of returns to industry under various demand and price scenarios were used to arrive at a series of findings and recommendations to the donor group. Subsequently, as a result of these new suggestions, the Implementation Working Group was charged to finalise design terms. Some of the challenges and lessons learnt regarding the design framework indicated below draw upon issues identified by these two groups.[31,32]

The main issues and challenges included:

a) *The nature of an 'Advance Market Commitment'.*

The work of the EEG and IWG was subject to delays and difficulties from controversy about whether these groups should flexibly craft the AMC to maximize what the experts thought was needed to create a mechanism with the optimum chance of achieving its objectives efficiently, versus one that followed the pilot proposal worked out with donors and that reflected CGD's original AMC concept. In addition, there was no uniform agreement on what could be defined as an "AMC".

b) *Ensuring a competitive market and adequate supply*

Another challenge was presented by the trade-offs among multiple objectives of the Pneumococcal AMC and the need for a clear prioritization from the outset. The overarching goal, emphasised over and over by donors, was saving lives. In addition, the pilot AMC targeted two objectives simultaneously: i) motivating first generation suppliers - with nearly licensed vaccines - to increase manufacturing capacity and
ii) spurring development of new vaccines by second generation suppliers, hence fostering

[31] Advance Market Commitment for Pneumococcal Vaccines. Expert Group Report presented to the Donor Committee. April 2008. Available at: http://www.gavialliance.org/library/documents/amc/economic-expert-group-(eeg)-report/ [accessed 13 September 2011]

[32] Advance Market Commitment for Pneumococcal Vaccines. Implementation Working Group Report presented to the Donor Committee. July 2008. Available at: http://www.gavialliance.org/library/documents/amc/implementation-working-group-(iwg)-report/ [accessed 13 September 2011]

competition in the long term. Yet, since both generations of suppliers compete for AMC funds on equal terms, second generation suppliers may have little incentive to participate as they will require more time to enter the market and AMC funds may be depleted by the time they do. The main rationale for this design was to ensure adequate early supply capacity to serve imminent demand - allowing countries to introduce these life-saving vaccines as fast as possible. In addition, setting equal conditions for all manufacturers was a way to minimize concerns of preferential treatment. In part the lack of clarity around the relative emphasis in AMC objectives from the outset and in part the potential disadvantage of emerging suppliers in the AMC led to criticism, particularly from Civil Society Organisations and manufacturers from emerging economies. One of the main points of criticism is that this design may reinforce a too narrow industry structure instead of promoting a broad base for innovation in the long-term.[33] Indeed, the AMC pneumo market is currently dominated by two companies, GSK and Pfizer, and the market will be truly competitive when and if additional manufacturers enter the market.

c) *Establishing a 'level playing field'*

The choice of pneumococcal disease meant that two first generation suppliers would potentially be able to participate in the programme at an early stage. Engagement by both suppliers was considered highly desirable to ensure sufficient and secure supply in the early years of the programme. Consequently, the terms of the AMC offer (in particular the tail price cap) were equal for all manufacturers, which ensured that both suppliers were sufficiently encouraged to participate. As incumbents had different production technologies and thus different production costs, and different strategic objectives, 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.

d) *Coordinating push and pull funding*

Global health has diverse and significant "push" funding sources supporting R&D directly to vaccine researchers (for early-stage research) or through product development partnerships (which are often used in sharing costs with the vaccine industry). Coordination between push and pull funding mechanisms is important to ensure that the development of a promising product is encouraged without the product being over-subsidised. This implies that, firstly, availability of push funding must be taken into account to determine the efficient level of required AMC funds prior to establishment of an AMC. While this was less relevant in the case of pneumococcal vaccine – as push funding was limited – it is more important in cases such as

[33] Wilson P. Giving developing countries the best shot: An overview of vaccine access and R&D. Joint report of Oxfam International and Médecins Sans Frontières. 2010. http://www.oxfam.org/en/policy/giving-developing-countries-best-shot-vaccine-access [accessed 13 September 2011]

malaria, tuberculosis or HIV. Secondly, availability of AMC funding must be factored in to subsequently established push funding contracts. In the case of the pilot, following the announcement of a Pneumococcal AMC, two partnerships were created between PATH and the China National Biotechnology Group (CNBG) and PATH and the Serum Institute of India to accelerate the development of a pneumococcal vaccine responding to the AMC target product profile. It will be important to understand how these partnerships have been structured to ensure different incentives are complementing each other and synergies are exploited.

e) Determining the size of incentives

One of the most time-consuming challenges faced during the design of the Pneumococcal AMC was determining the required AMC incentive size and, more generally, the required set of incentives for manufacturers (e.g. AMC price, tail price cap, demand guarantee) that would pull industry's investment towards the expected outcomes, while making most efficient use of scarce public resources. Two related analytic tools were developed for this purpose:

1) Applied Strategies Consulting, a life-sciences strategy consulting firm, was commissioned to develop a Financial Implications and Risk Model – known as the AMC-FIRM model.
2) A subgroup of the AMC Economic Expert Group undertook a series of new calculation exercises, using a spreadsheet-based tool.

Given the sensitivities related to the use of public funds for the AMC, estimates of the required AMC incentive have been subject to criticism from civil society organizations mainly. Criticism was directed to i) inherent uncertainties in some of the underlying assumptions, such as investment and production costs and, ii) lack of public availability of the data used to inform the decision (because of confidentially on cost of goods analysis for respective manufacturers). While the AMC-FIRM model was reviewed and discussed in detail by the Advisory Group and was provided to industry during consultations, further peer review or external validation of the models used to determine the size of the AMC might have helped build transparency.

f) Long-term forward commitment

One of the intrinsic difficulties of the AMC is to establish a long-term, credible commitment in a changing and unpredictable environment. Some issues leading to potential uncertainties for manufacturers (such as inflation) were taken into account during the design phase. An inflation provision was recommended by the EEG and IWG and incorporated into the legal agreements,

allowing prices to increase if deemed necessary by the Independent Assessment Committee.[34] Other issues were more difficult to address. These include, as outlined below, the uncertainty around long-term demand and uncertainty around evolution of the pneumococcal bacteria and of vaccine technologies.

i. Demand uncertainties

Considerable time and effort was spent on addressing demand uncertainty. The developing country market for vaccines has been perceived by industry to be risky and unpredictable, and the international public health community is perceived as having a poor track record in estimating vaccine uptake. For the pilot AMC, demand forecast was based on individual country expected demand, taking into account past vaccine introduction experience in each country, and aggregating across countries. The forecast was also informed by country consultations and government letters of interest to GAVI.

The Pneumococcal AMC is set up to encourage development of 200 million doses of annual production capacity for targeted pneumococcal vaccines. 200 million doses represented the estimated annual demand of vaccine from countries eligible for GAVI financial support at the time of the AMC design. Yet, the AMC agreements allow for demand fluctuation due to:

- Countries' willingness and ability to adopt the vaccine. The case of India is particularly important, as India represents approximately one third of the estimated pneumococcal vaccine demand from GAVI countries. Given the size of the country and the potential pressure on GAVI resources, there is a cap on the amount of financial resources that India can receive from GAVI. This implies that the Indian Government would be required to pay for the great majority of its required pneumococcal vaccines: some feel this may hamper vaccine introduction. In addition, India's willingness to adopt is proving difficult to forecast due to recent anti-vaccine campaigns in the country.

- GAVI's ability to revise its policy and change the list of eligible countries. Indeed, in order to reflect changing economic conditions of recipient countries and to ensure higher likelihood of success of vaccination programmes, the GAVI Board revised the list of eligible countries and criteria for support in November 2009.[35] This had an impact on the size of the GAVI pneumo market, reducing estimated peak demand by 17%. It should be

[34] Even in this case, industry feels that inflation risks are not adequately tackled as a high degree of discretion is left to the IAC. Industry states that higher predictability would have been preferable.

[35] The new eligibility policy includes: 1) A new gross national income (GNI) per capita threshold to define annually country eligibility (US$ 1,500 instead of US$ 1,000 (in 2003 values)) to be applied as of 2011; and 2) a new threshold of 70% DTP3 coverage to define future access to new vaccine support (NVS). Note that during its meeting on 30 November – 1 December 2010, the GAVI Board decided to suspend the November 2009 decision of the Board to raise the filter to 70% thereby re-establishing the filter to 50% for DTP3 coverage for the 2011 round of applications.

noted that in June 2010 the GAVI Board decided to allow all GAVI countries eligible at the time when the AMC deal was set up to keep procuring at AMC terms to avoid changes in the pneumococcal demand. However, graduated countries will have to fully fund the vaccine price (tail price). Many believe that despite this recent change, demand for pneumo will be reduced as the current need for graduated countries to pay for the vaccine price, previously covered by GAVI, will impact countries' ability to introduce the vaccine.

- GAVI's ability to fund applications for pneumococcal vaccines from GAVI-eligible countries over the long run as GAVI pays a considerable proportion of the vaccine price. While AMC funding (US$ 1.5 billion) has been set aside up front, GAVI's funding is contingent upon continuing substantial contributions from its donors. Consequently, the actual size of demand will heavily depend on GAVI's ability to raise sufficient resources over time.

Any reduction in peak demand due to the above factors would lead to lack of full use of the AMC. For instance, the likelihood of participation of late market entrants would be reduced, endangering the AMC's objective of broadening the supplier base. Additionally, some AMC funds would lie unutilised, as disbursement of the US$ 1.5 billion is contingent on the supply of 200 million doses annually. Any drops in demand would also create an inefficient use of AMC funds: the AMC reimburses manufacturers for capacity investment costs; in turn it requires suppliers to ensure continued supply over ten years. Decreased demand would mean the paid-for dedicated production capacity would not be fully used. From donors' perspective, their funds would not be used efficiently; while suppliers, who bear most of the demand risk, would be left with binding supply agreements but unexploited production capacity.

More generally, uncertainty of demand may reduce the power of the AMC to signal to manufacturers the size of the pneumo market and the required production capacity.

ii. Serotype replacement

Another element of potential change over the course of project implementation is related to the risk of serotype replacement.[36] The pre-defined Target Product Profile may become partially obsolete in guiding industry towards development and production of vaccines containing particular serotypes that may not remain the most prevalent in developing countries over time. Unfortunately, the extent and impact of potential replacement is difficult to predict. The IAC recognised this challenge and recommended to closely monitor for potential serotype

[36] Extensive use of pneumococcal conjugate vaccine is expected to result in some increase of disease occurrence due to serotypes not in the vaccine (referred to as "serotype replacement").

replacement in GAVI-eligible or analogous countries as the vaccine is introduced.[37] The first relevant information will be obtained in impact studies in the Gambia, Kenya, and South Africa. Should serotype replacement become an issue in future years, GAVI and the IAC may need to consider how this should be taken into account in the TPP. Common protein vaccines may provide a long-term approach to address serotype variability: in this case, a new TPP for common protein vaccines will need to be developed (see below).

iii. New technologies

Eligibility of common protein vaccines for AMC support was contemplated during the AMC design, but a specific product profile was not defined due to scientific uncertainties and little knowledge about this novel vaccine technology. This shows again the difficulty of setting long-term incentives in an environment of many unknowns.

g) Challenges outside the realm of the Pneumococcal AMC

Some challenges are not specific to the AMC mechanism but are worth mentioning. One of these concerns, brought up by industry, is the differential pricing of the same vaccine in GAVI and non-GAVI-eligible countries. The GAVI Alliance and its suppliers apply the concept of tiered pricing to AMC funded vaccines and any other GAVI supported vaccine alike. While this arrangement has been fairly well accepted in the past, it is challenged now as the new vaccines for which GAVI has started to provide support still command very high prices in high and middle income markets.[38] This challenge applies not only to the AMC, but to all GAVI supplied vaccines.

[37] Background Note, PCV Serotype Replacement Issue, prepared by Claire Broome, Chair of the Advance Market Commitment Independent Assessment Committee (IAC), approved by the IAC, September 2010. Available at: http://www.gavialliance.org/library/documents/amc/serotype-replacement-note---prepared-by-the-iac/ [accessed 13 September 2011]

[38] Wilson P. Vaccines and the developing world: Issues in pricing and R&D financing. A background paper for Oxfam, 2009. [unpublished]

Lessons learnt on design choices

- Retrospectively, it seems that the definition used in recent discussions around AMCs for low carbon technologies is useful.[39] In this context, the AMC was defined as a forward commitment by funders to make a market for a particular product more viable so as to encourage private sector investment. The Pneumococcal AMC experience illustrates that a similar broad and flexible definition would be useful as a starting point for future AMCs: it would then allow flexible crafting to define an adequate AMC contract ensuring appropriate incentives for desired goals. Crafting should be based on the analysis of a particular technology's demand and supply landscapes. A broad definition of an AMC must be accompanied by agreement on the specific programme objectives and their prioritisation and clear communication from the outset (considering there will likely be trade-offs among objectives).

- To ensure achievement of dual objectives (i.e. increasing manufacturing capacity and encouraging development of new vaccines) one could explore options of targeting early and second generation suppliers separately, perhaps with different simultaneous AMCs.[40]

- There are several possibilities for specifically enhancing participation by emerging manufactures. One potential option is the creation of targeted AMCs (see above). Another option would be to focus in future initiatives on less complex vaccines without a large developed world market which can be produced at lower costs.[41] A third option could be to make technology transfer (and granting access to patents) to emerging suppliers a condition for participation.

[39] Chatham House/DFID, Meeting Report: Advance Market Commitments for Low Carbon Technology: Creating Demand in Developing Countries. April 2010. Available at: http://www.chathamhouse.org/sites/default/files/public/Research/Energy,%20Environment%20and%20Development/0110amcs_mtgsummary..pdf [accessed 13 September 2011]

[40] Similar considerations were noted by Oxfam and MSF, although suggestion was oriented more towards issuing two subsequent offers rather than simultaneous offers. This option was discussed by donors in the fall of 2007 and was not endorsed.

[41] Wilson P. Vaccines and the developing world: Issues in pricing and R&D financing. A background paper for Oxfam., 2009. [unpublished]

- When an AMC targets late-stage vaccines for which suppliers have already been identified, entering into a tailored bilateral AMC with each supplier may lead to efficiency gains.[42],[43] While this option was discussed, it was rejected on the basis that it would not be advisable to establish what could be perceived as preferential terms for different suppliers and that tailored bilateral contracts may not test the AMC concept adequately. The potential benefits from tailored contractual terms would have to be carefully balanced against concerns regarding preferential treatment of specific suppliers and the risks of increased complexity of the deal. In contrast, tailored contractual terms would not be required in case no specific supplier was targeted (e.g. in case of a large supplier base or in case of an early-stage AMC when no supplier has yet vested interests). Under such circumstances, the terms of the deal would be set independently of cost of goods or estimated needs of specific suppliers and equal terms for all would attract exclusively the most efficient suppliers.[44]

- Participation by companies that benefitted from push funding for development of the target vaccine is on balance a positive issue, as it will likely increase participation by emerging suppliers[45] and, more generally, increase competition which may lower prices and potentially increase quality. However, it will be important to avoid the potential suboptimal use of scarce public resources as a result of uncoordinated push and pull funding mechanisms for the same product. It is therefore essential to carefully identify and assess existing push and pull funding arrangement for each potential vaccine and factor these in when designing contracts with industry (e.g. by negotiating for lower prices or reimbursement mechanisms if the same vaccine has benefitted from other public support).

[42] Barder O, Kremer M, Levine R. Making Markets for Vaccines. Ideas to action. Working Group Report. Washington DC, Center for Global Development. 2005.

[43] Cernuschi T. The Pneumococcal AMC: Innovative Finance to Help the Poor. Global Forum Update on Research for Health Volume 6: Innovating for the Health of All. 2009.

[44] Similar considerations were made in the CGD Report and the Economic Expert Group Report. Please see references above.

[45] AMC critics point out that a pure pull mechanism like the AMC inherently favours the few organisations with sufficient access to capital required to fund very expensive R&D up-front.

- Determining the right incentives for the AMC deal will remain challenging by nature. The intrinsic difficulty lies in the fact that well informed decision-making on the appropriate size of the AMC and the overall incentive structure requires access to sensitive information from industry (i.e. regarding cost of production). In providing these data, vaccine suppliers have an evident conflict of interest. Besides, suppliers might not be willing to share confidential information with the designers of an AMC if they fear that this data will be made public. Sensitive information might be shared if there is sufficient assurance that only designated parties have access to it. This concern and its implications, have to be communicated properly to the public up-front so that lack of wider information sharing on proprietary information is not always perceived as a lack of transparency but a necessary condition for receiving this type of data.

- In designing an AMC, there is a trade-off between flexibility in the terms of the deal and predictability. Both are necessary to successfully implement the initiative. Incorporating a flexible approach into the model allows for effectively handling unknown variables and adapting to a changing environment. However, too much flexibility renders the deal less predictable. The difficulty is indeed to find the right balance between the two elements. From current experience some lessons may be derived, particularly around the issue of demand predictability. Despite the inherent demand risks (which remain as a result of uncertainties at country level about vaccine uptake), the AMC could potentially have done a better job at enhancing demand predictability. Firstly, the case of India: the IWG discussed the potential risk associated with the uncertainty of India's introduction decision and considered applying a discount to the total demand value included in the AMC agreement. The final decision was to reduce the estimated peak demand by a small amount to account for part of this risk.[46] This, however, may have been a too conservative risk mitigation strategy and forecasted demand could have been reduced further to reflect uncertainties. Secondly, to increase demand stability, the AMC contracts could have fixed the list of eligible countries over the

[46] See Implementation Working Group Report Advance Market Commitment for Pneumococcal Vaccines. Implementation Working Group Report presented to the Donor Committee. July 2008. Available at: http://www.gavialliance.org/library/documents/amc/implementation-working-group-(iwg)-report/ [accessed 13 September 2011]

duration of the programme, rather than allowing for changes. Thirdly, the importance of GAVI's financial situation for the overall success of the initiative may have been underestimated (see section on Funding).

- It is important to manage expectations regarding the potential and limitations of the AMC mechanism. It must be recognised during the design phase of such an initiative that the AMC will be implemented in a complex environment which it is not necessarily able to influence. Appropriate communication of potential risks alongside the expected benefits is therefore important.

B.3 Lessons Learnt on Processes

a) *Governance Structure*

The pilot AMC, distinct from other new development initiatives, did not create a new organisation for project management. Rather, the intention has always been to leverage the comparative advantage and expertise of existing institutions (GAVI, the World Bank, UNICEF Supply Division, WHO). This is an important positive aspect as it reduces costs, avoids duplication of work, and helps to avoid vested interests and thus allows for easier reorientation to new, different instruments, in case the AMC would prove not to be the most desirable instrument for achieving its objectives. The choice of implementing the Pneumococcal AMC through existing institutions has also been valuable to keep implementation costs low as no new structures and policies had to be created. Nevertheless, it may be noted that this choice possibly has led to a lengthier and more inhibited design process as priorities, policies and internal processes of future implementing agencies had to be taken into account when setting up the initiative.

The only newly created permanent function for the implementation of the programme is the AMC's Independent Assessment Committee (IAC). This committee consists of 11 members with balanced expertise in public health, vaccinology, vaccine business economics, contract law, health economics, and finance. A group of international experts, the IAC Selection and Oversight Panel, is charged with the task of selecting and appointing IAC members as well as with reviewing claims of potential or declared conflicts of interest involving IAC members. The

IAC's role is to act as an independent, impartial, and credible oversight body with the authority to[47]:

1. Review and approve the minimum technical requirements (i.e. the Target Product Profile established by WHO) that pneumococcal vaccines must meet in order to be eligible for AMC funding.
2. Determine AMC eligibility of a vaccine submitted by a supplier (i.e. establish whether WHO pre-qualified vaccines meet the TPP and can access AMC funding).
3. Review suppliers' requests for price increases (in case of inflation or extraordinary circumstances) and authorise/deny them.
4. Monitor and report on the project's progress.

The IAC is the final decision-maker on all above mentioned issues and is called to resolve any conflict or dispute in relation to these matters. From the outset, there was a strong view that the AMC would need a credible, independent decision-making authority; indeed the most debate among stakeholders around the structure of the IAC was whether it needed legal capacity.

The main issues and challenges faced regarding the governance structure:

The IAC process was created to be separate from WHO's prequalification process for functions related to TPP setting and vaccines eligibility determination. One reason was to allow for the possibility that vaccines of sufficient quality and public health importance could be used in developing countries (hence get WHO pre-qualification), while a TPP for an AMC vaccine might require additional criteria to be met and therefore set a higher bar. The creation of two distinct standards within WHO was highlighted as a problem, and thus the IAC was designed, in part, to resolve this. Nevertheless, as the programme is being implemented, it appears that the IAC's role and contribution may be limited by: i) the role of WHO in defining or modifying the TPP; ii) the role of WHO in pre-qualification of vaccines; iii) the overlap between TPPs and WHO pre-qualification requirements.[48]

The IAC is also asked to monitor and report on the AMC's progress and its influence on the development and production of vaccines. This monitoring and reporting role was defined to ensure credibility of the process, as the IAC would guarantee an impartial judgement of the AMC's progress against target objectives. Nevertheless, the IAC's monitoring role overlaps with

[47] Independent Assessment Committee Charter and Bylaws. Final version 2009. Available at: http://www.gavialliance.org/library/documents/amc/revised-independent-assessment-committee-charter-and-bylaws/ [accessed 13 September 2011]

[48] Only a couple of TPP requirements are not identical to the WHO pre-qualification requirements and it is only on these few requirements that the IAC can pronounce itself.

the role of the GAVI Board to oversee progress of projects implemented by the Alliance and the GAVI Alliance's evaluation policy and process which provide for independent and impartial evaluation of all programmes.[49]

It is also worth highlighting that, given the high level of expertise required and the concurrent requirement of independence (avoiding conflict of interest), identification and selection of IAC members has been challenging.

Lessons learnt on the governance structure

- Ensuring credibility, independence and acceptance of the TPP and of decisions around vaccine eligibility for AMC funding is crucial. To date, the IAC has provided impartial and credible authority in these matters. At the same time, WHO has proved to be a reliable partner in establishing the TPP and determining whether vaccines meet the target profile. In particular it seems – also from consultations with industry – that WHO has the necessary technical authority and capacity to justify that some of the IAC's technical functions be transferred to WHO's prequalification team in similar future initiatives. This would streamline procedures and avoid duplication of efforts.

- Similarly, the GAVI Board may possess the necessary authority, through its established monitoring and evaluation policy and process, to monitor the progress of the AMC against target objectives, rather than requiring an IAC to carry out this task.

- Based on the above, for future similar initiatives, it may be useful to explore the possibility of narrowing the role of an IAC-type body. For instance, the IAC's role could be circumscribed to judging the potential need for a price change. The Committee's composition would then be more targeted to conduct such a specific function.

[49] For more information on the GAVI Alliance evaluation policy please refer to: http://www.gavialliance.org/about/governance/corporate-policies/evaluation/ [accessed 13 September 2011]

b) *Project Management*

The complexity and ambition of the initiative required leveraging the expertise from a wide range of different stakeholders. These included the AMC donors, the GAVI Secretariat and the World Bank, and the technical agencies engaged in implementation such as WHO and UNICEF Supply Division. This approach was driven by the innovative nature of the initiative, which required high donor involvement and the desire to implement the initiative through already existing organisations and institutions. This section on project management first describes the roles and responsibilities of different stakeholders, and then outlines some of the major challenges faced during the process to subsequently highlight key lessons learnt.

Assignment of responsibilities among key stakeholders:

- The AMC donors (Canada, Italy, Norway, Russia, the United Kingdom, and the Bill & Melinda Gates Foundation) jointly committed US$ 1.5 billion to launch the Pneumococcal AMC. Following the launch event in February 2007, a formal donor committee provided inputs into the technical design and processes for the AMC during the negotiation phase and to allow monitoring of its implementation and progress toward the AMC's objectives.

- The GAVI Alliance together with the World Bank led the analytical, legal and project design work and has subsequently become responsible for supporting the programmatic functions of the Pneumococcal AMC.

- The AMC Secretariat, hosted by GAVI, is responsible for providing operational, administrative and financial support to the Pneumococcal AMC. This role includes communication, coordination with and contracting of implementation partners, such as the World Bank, UNICEF's Supply Division and WHO, as well as supporting the IAC. The AMC Secretariat also liaises with AMC donors, and organises the annual AMC donor meetings and any special events as necessary and defined in the AMC Stakeholders' Agreement. The AMC Secretariat provides industry partners with regular updates, such as the latest demand forecasts and progress reports on implementation and also acts as the interface between vaccine suppliers and the IAC. The AMC Secretariat monitors the project environment, identifies potential risks and proposes risk mitigating measures while conducting monitoring and evaluation activities. Fund-raising activities linked to GAVI's financial participation in the Pneumococcal AMC are another aspect of the AMC Secretariat's work.

- The World Bank is responsible for supporting the financial functions of the AMC. During the design phase, the Bank negotiated bilateral grant agreements with individual AMC

donors. During implementation, the Bank provides financial and fiduciary administration of the AMC deal and manages the donor commitments and AMC disbursements.

- The World Bank also agreed to place the US$ 1.5 billion in donor-contributed AMC funds on its balance sheet, committing to pass AMC funds to GAVI for the purchase of vaccines, whether or not donors pay on schedule or default. This commitment was made at the request of donors to provide complete certainty about the AMC incentive amount.

- The World Health Organization was responsible for developing and approving the basic Target Product Profile (TPP) for pneumococcal vaccines. Moreover, WHO provides technical inputs to various design questions.

- The UNICEF Supply Division procures vaccines for GAVI under the Pneumococcal AMC (as well as for all other GAVI vaccines). As such, UNICEF issues calls for supply offers, assesses bids from suppliers and awards quantities in response to each tender. UNICEF's responsibility includes supply coordination with countries and suppliers and assurance of the safe delivery of the vaccines to the port of entry in the beneficiary country.

- GAVI-eligible countries are potential beneficiaries of the Pneumococcal AMC and obviously a key player in the initiative. The ultimate success of the AMC deal depends on the countries' willingness to adopt and co-pay the pneumococcal vaccines.

- A number of ad hoc committees and working groups were created during the design phase of the project with the aim of providing technical analysis on specific questions (see Background section). Representatives from the institutions mentioned above were often part of these groups.

Main issues and challenges faced with regard to project management:

- While Terms of Reference for a donor group were created, the extent and nature of the role of donors in the process would have benefitted from more clarity. In particular, there was some confusion around the level of authority the donors had delegated to GAVI and the World Bank and to technical donor working sub-groups.[50] Due partly to the broad mandate set out in the Terms of Reference and the absence of a clear technical design for the Pneumococcal AMC at the time of its launch (February 2007), the donor group

[50] The donor working sub-groups on different work-streams (legal, financial, economic design issues, procurement and communication) were created by the AMC stakeholders (donors, GAVI and the World Bank) to coordinate donors' technical input.

tended to become the forum for detailed discussions on AMC technical issues (e.g. serotype study, penalty clauses, inflation provisions) despite the existence of specific technical donor working sub-groups. Using donor group meetings as a forum for such discussions raised some challenges:

  - Many issues discussed were of a technical nature and required specific expertise.
  - Significant time for coordination/management was required from the GAVI Secretariat and the World Bank as donor meetings were held frequently (weekly calls and in person meetings every few months), the group was large, and membership often changed. Delays in the timeline resulted from difficulty to reach consensus on issues discussed and because some donor representatives lacked sufficient authority for decision-making as, over time, donors sent lower-seniority representatives to meetings.
  - Political considerations affected technical discussions and decisions, as donors factored in the risk of being viewed as favouring "big pharma".
  - A related challenge was the fact that GAVI was reporting on the project progress to the AMC donors rather than to its governance structure. This created an additional line of reporting and to some extent undermined the role of the GAVI Board to oversee design of projects to be implemented by the Alliance.

- At the request of the UK and Italy, the World Bank initially took the lead in managing the project. At the Bank's request, GAVI played an increasing role and by 2007, GAVI had the lead on project management and communications. The Bank focused on legal, financial structure, fiduciary administration, management of donor commitments and AMC disbursements. However, the lack of clearly agreed roles and responsibilities from the outset and the absence of a single designated decision-making body resulted in some duplication of work and other efficiency losses. Clearly agreed-upon leadership delegation and division of work could help accelerate processes and improve efficiency.

- The Economic Expert Group was convened as an independent advisory body to the AMC donors charged with reviewing the key AMC terms and working out the details of the deal. The expected output of this group was a series of concrete recommendations including the mechanism to pay out the incentive, supply obligations in the post-AMC period, recipient countries' co-pay, and most critically, the appropriate tail price.

  - The work of this group took longer than expected and led to the re-evaluation of some of the basic tenets of the AMC. As more information became available and discussions were undertaken, significant departures in design were considered to ensure the original design would be effective for pneumococcal vaccines. While these

changes were well intended and led to improvements in the overall structure, delays frustrated those who believed the project was too much advanced as to allow for major redesign. As highlighted in previous sections, it was unclear whether this group, as well as the IWG, were tasked with clear objectives and guidance on how to handle tradeoffs among them to design the most efficient and effective project. One of the challenges faced with regard to the composition of the EEG was that experts in vaccine research and development, procurement, distribution and contract law were under-represented in view of the programmatic/managerial nature of many of the recommendations requested from the EEG.

  - Coordination of high-level experts from across the globe proved challenging, despite incredible dedication of the group's members. Notably, the experts in the EEG, as well as many other high-level experts consulted over the course of the project, provided mostly unpaid services to this initiative.

- The mandate of the Implementation Working Group, set up later by the AMC donors to make the recommendations of the Economic Expert Group operational, was much more specific. This group represented a good balance of expertise and matched independent experts in various relevant areas (economics, public health and vaccine industry) with staff of implementing agencies with sector specific know-how (GAVI, World Bank and UNICEF Supply Division).

Roles of other entities and main issues and challenges faced with their involvement:

- Civil society organisations, e.g. Médecins Sans Frontières (MSF) and Oxfam, were engaged in the design process only as of 2008 and through consultations rather than as members in design or governance structures. It may have been better to engage CSOs earlier in consultations and more formally in the working committees, given their interest and expertise in some AMC-related matters.

- The Pan-American Health Organization (PAHO) is a major purchaser of vaccines for countries in Latin America and the Caribbean. PAHO was not directly involved in either strategic or technical thinking around the AMC – although WHO was involved. In light of the particular role of PAHO in procurement of vaccines in Latin America and the Caribbean through its Revolving Fund, it might have been beneficial for GAVI and UNICEF Supply Division to reach out earlier to PAHO to discuss the implications of the AMC on procurement of pneumococcal vaccines for GAVI-eligible countries in this region.

- Manufacturers from both developed countries and emerging economies have been consulted regularly at various stages of the process.[51] Efforts were made to include them from the very beginning as evidenced by their wide representation at the first high-level meeting between donors and all major suppliers in April 2005. Between June and October 2007, five multinational corporations and six emerging suppliers with past or currently active pneumococcal vaccine programmes were visited in order to explore their interest in a potential AMC offer and seek feedback and comments on key elements of the pilot AMC. An additional round of industry consultations on draft legal AMC agreements took place from December 2008 to January 2009 through the International Federation of Pharmaceutical Suppliers and Associations (IFPMA) and Developing Country Vaccine Suppliers Network (DCVMN). Companies were informed that the AMC offer would consist of standard terms and conditions that were non-negotiable with industry. This approach may not have been appropriate for manufacturers with vaccines already in late-stages of development as noted above.

Lessons learnt on project management

- The issues which came up around the role of AMC donors must be considered in the context of a ground-breaking innovative initiative. The AMC donors agreed to commit considerable funds in advance of a concrete project plan; to provide funding on schedules far longer than the usual practice; and to support a concept that always risked to be perceived as ”subsidising big pharma”. Thus, they drove the process. If the pilot has succeeded in generating the knowledge and trust in the AMC concept and process, for future similar initiatives donors may wish to consider the following approach: i) delegate responsibility to implementing agencies and, if needed, to relevant technical donor working groups; ii) meet only to guide the process; and, iii) take advantage of the legal structure and agreements put in place with the pilot AMC to minimise negotiation complexity. In addition, future initiatives of this type may benefit from using the existing governance structures and the policies of the agencies that are steering the process for reporting purposes rather

[51] Consultation & Advisory Process: Advance Market Commitment for Pneumococcal Vaccines. 2009. Available at: http://www.gavialliance.org/library/documents/amc/consultation-and-advisory-process/ [accessed 13 September 2011]

than creating an additional line of reporting to particular donors.

- Designation of a clear lead institution with decision-making authority or a shared leadership with clearly distributed roles at an early stage of the project could result in overall efficiency gains, better division of roles and responsibilities and improved guidance over the course of the project. However, this should by no means imply monopolisation of the debate by a single institution. On the contrary, such an arrangement should allow different organisations and entities with a key interest in the AMC to be included and consulted systematically according to their comparative advantage, technical expertise and/or interest.

- The lack of clearly defined AMC objectives and terms of reference for designated working groups must also be seen in the context of a novel initiative where actors were exploring different approaches as they went along in the design phase. Again, the key reflection here is that hopefully the pilot will allow testing of the suitability and effectiveness of a set of rules so that future AMCs would have at least partially chartered waters. It seems indeed likely that future AMCs would benefit from a sufficiently clear process with already established milestones and deadlines as well as a clear idea of the type of expertise needed in different stages.

- With regard to the technical agencies, the role and involvement of WHO in the design of the Target Product Profile (TPP) for the target pneumococcal vaccines was very clear and should be maintained on similar terms in future initiatives. The design would have benefited from participation by the UNICEF Supply Division in the EEG. Including UNICEF's procurement experts at an earlier stage would help to ensure that no important design features are missed and the feasibility of various options is better assessed from the very beginning.

- It is important to ensure that experts from a variety of sources and areas of expertise, including vaccine markets (public and private) and contract law are part of the relevant working groups and that all implementing agencies are involved from the beginning of the process.

- The project benefitted from generous contributions of high-level experts who worked long hours as volunteers. However, the project may have

been more appropriately supported by dedicated and appropriately financed teams with a clear mandate, timelines and the necessary trust from the relevant parties involved in the deal.

- There is a need for earlier and wider consultations with a broader group of stakeholders (e.g. PAHO, CSOs).

- Some consideration could be given to engaging differently with manufacturers that have products in late-stages of development, perhaps through bilateral negotiations (please see design section).

- Involvement of developing countries is crucial for the successful design and implementation of the pilot AMC. All along the process, emphasis was therefore put on taking into account developing countries' perspectives and needs. This was sought first, by ensuring adequate representation of experts from developing countries in the different working groups and committees, and second, the organisation of several developing country consultations and briefings especially during the initial AMC design process.[52] It might be beneficial for future initiatives to enhance interactions with developing countries during later stages of the process.

c) *Funding*

The financial architecture of the AMC is complex and involves a number of stakeholders: the six AMC donors, the World Bank, GAVI, UNICEF, GAVI-eligible countries and eligible vaccine suppliers. This section discusses two particular aspects of the AMC funding arrangement. First, the role and function of the World Bank in managing AMC donor contributions, and second, the financial implications of the AMC deal structure on the GAVI Alliance.

Main issues and challenges regarding funding architecture:

- The design of the AMC deal included extensive work on the funding structure and financial management arrangements. The World Bank presented a range of possibilities

[52] Consultation & Advisory Process: Advance Market Commitment for Pneumococcal Vaccines. 2009. Available at: http://www.gavialliance.org/library/documents/amc/consultation-and-advisory-process/ [accessed 13 September 2011]

as donors considered how they would structure their contributions, including form of contribution (cash, promissory notes, and guarantees), timing, credit enhancement, and ways to ensure that there would not be excess liquidity in the system. Final grant and payment arrangements with AMC donors vary considerably to accommodate diverse authorisation schemes and donor payment preferences. Most importantly, this flexibility helped donors structure very long-term payment arrangements that differ markedly from their usual official development assistance (ODA) commitments, and was instrumental in successfully aggregating donor contributions to a final, certain incentive amount. At the same time, it contributes to the complexity of financial management of the AMC.

- Under the current design, vaccines are purchased at a maximum price of US$ 3.50 per dose to be paid by the GAVI Alliance and the developing country governments that introduce the vaccines. For approximately 20% of the committed doses, companies will also receive an additional payment of about US$ 3.50 per dose supplied, which is paid with donor commitments. These “AMC funds” provided by the six donors cover investment costs to stimulate capacity scale-up and are meant as an incentive to suppliers to develop vaccines and to build production capacity.

- For this design to be successful, two important conditions have to be met. Firstly, participating firms need to have confidence in the ability of the GAVI Alliance and the recipient countries to pay their respective per dose contribution, as suppliers cannot access the AMC funds otherwise (drawing down the AMC funds is contingent on a corresponding amount being spent by GAVI and recipient countries). Secondly, the buyers must be in a position to purchase the vaccines sustainably on an ongoing basis, since the supply contracts are deliberately for a ten-year period. If the first condition is not met, suppliers may not invest in creating production capacity. If the second condition is not met, firms may be left with unused production capacity, public funds (AMC funds) would remain unspent (to be used for other purposes but after substantial delay), and, most importantly, many children would remain unvaccinated.[53] The analytical work focused on the appropriate size of the AMC incentive and design mechanisms to motivate industry. However, more and broader attention should have been paid early in the process on the long-term financial implications of the AMC pilot for the GAVI Alliance. One of the main reasons for this is that the original AMC design as spelled out in the “Framework Document” had set GAVI’s contribution during the early years of the

[53] In the AMC, manufacturers make legally binding commitments to supply a certain amount of doses of vaccines each year. It should be noted, though, that the Pneumococcal AMC contract does include some risk mitigation provisions for firms if demand does not materialise (fast AMC subsidy payout for early cash flow, partial demand guarantee, opt-out provision in the absence of demand). Nevertheless, as highlighted in previous sections, considerable demand risk is left on firms. See also Cernuschi T. The Pneumococcal AMC: Innovative Finance to Help the Poor. Global Forum Update on Research for Health Volume 6: Innovating for the Health of All. 2009.

AMC lower than the marginal cost of the vaccine, while also foreseeing a lower marginal cost of the vaccine (and thus a lower tail price cap).[54] In other words, initially the financial implications for GAVI were estimated to be fairly low. Over the course of the design process, and as a result of inputs from the expert groups, more informed assumptions around the marginal cost of production, the terms changed in a number of ways – most importantly, the tail price cap was increased and also GAVI's contribution to match it.

While this design is deemed to establish more efficient and sustainable levels of production, it has had major financial implications for GAVI. Also, it was decided that GAVI's own co-financing policy would apply without modifications to the AMC for policy coherence; as a result the level of country co-payment over the course of the AMC contract would increase substantially less than originally forecasted and thus the majority of the financial burden ended up with GAVI. It is estimated that between 2011 and 2015, GAVI will have to spend around US$ 1.8 billion in order to satisfy expected cumulative country demand for the pneumococcal vaccines.[55] The issue of financial sustainability highlights one of the inherent challenges of the AMC: while attempting to reassure industry of the viability of the developing country market for vaccines, the AMC still heavily depends on donor funding to GAVI to ensure long-term purchases of much needed vaccines.

- As indicated above, each AMC supply agreement includes a minimum purchase obligation equivalent to 45% of one year's committed supply, disbursed over the first three years of the supply agreement. In order to reduce any financial risks, UNICEF cannot enter into a supply agreement until funds covering these minimum purchase obligations have been received in cash into a designated procurement bank account.[56]

[54] In fact, the Framework Document, prepared by the World Bank and GAVI for the second Donor Working Group meeting in November 2006 suggested a two-step pricing structure with donors guaranteeing to pay US$ 5-7 per dose for US $ 1.5 billion worth of vaccines ("the AMC price"), and industry committing to provide vaccines at US$ 2 per dose for an agreed period thereafter ("the tail price"). Developing countries were expected to be responsible for an affordable co-payment per dose of roughly US$ 1. The Framework Document also indicated that GAVI may chose to further subsidise the country co-payments, for example, reducing the agreed co-payment of US$ 1/dose to a lower amount based on the GAVI co-financing policy. See:

Framework Document, Pilot AMC for Pneumococcal Vaccines, Document prepared by the World Bank and GAVI for the second Donor Working Group meeting on 9 November 2006 in London. Available at: http://www.gavialliance.org/library/documents/amc/second-donor-working-group----framework/ [accessed 13 September 2011]

Also see section on integrating the AMC with GAVI financing, procurement and vaccine introduction system in the Economic Expert Group Report (2008). Available at: http://www.gavialliance.org/library/documents/amc/economic-expert-group-(eeg)-report/ [accessed 13 September 2011]

[55] The above figures are based on the assumption that India adopts the pneumococcal vaccine within the expected timeframe. For more information, see document prepared for the GAVI Board meeting 16-17 June 2010, Doc08 Next steps on the Pneumococcal AMC. Available at: http://www.gavialliance.org/about/governance/gavi-board/minutes/2010/16-june/minutes/next-steps-on-the-pneumococcal-amc/ [accessed 13 September 2011]

[56] This requirement is not for AMC funds for which UNICEF has accepted a promissory note from GAVI.

This means that GAVI must transfer these funds in a designated bank account before UNICEF can enter into supply agreements with manufacturers. As the deal is structured, this cash will lie idle in a bank account for some months/years before the vaccines are effectively purchased. When negotiating the AMC agreements, involved stakeholders were probably not conscious enough of this requirement which potentially leads to a suboptimal use of GAVI funds.

Lessons learnt on funding

- Accommodating the individual preferences of donors with regard to the modalities of grant agreements is necessary and helps to pull together a substantial incentive amount, but adds to the complexity of the initiative. The need for legal and financial expertise to effectively handle these issues should not be underestimated. The World Bank was well placed to assume this role. There was a benefit in having a number of donors in the deal as some donors demonstrated flexibility in their arrangements to make up for the constraints of others.

- The inter-relationship between the economics and financial sustainability of the deal needs to be kept more closely in mind during the design of AMC-like initiatives. The sustainability of the target intervention must be kept central during design discussions.

- Likewise, fundraising efforts need to highlight both the resources required to create the necessary incentives for industry to invest in product development and manufacture (i.e. “the AMC funds”), and the additional resources required to ensure long-term funding of ongoing cost of pneumococcal vaccines. More importantly, it might be desirable to explore, for potential future AMCs, the coupling of an AMC with long-term and predictable donor commitments to GAVI’s (or any other buyer’s) budget as well as innovative, less pro-cyclical sources of funding.

- Minimum purchase guarantees ensure participating suppliers of minimal revenue even if demand does not materialise, thereby alleviating some of the risks associated with demand uncertainty. While these provisions increase the overall attractiveness of the deal and the likelihood of

industry participation, it comes at an additional cost for the project sponsor who takes on an increased share of the demand risk. When deciding to include minimum purchase guarantees in the deal structure, all practical implications must be considered as well as potential solutions to avoid having funds lying committed but not used on bank accounts for a substantial period of time.

- This first experience illustrates the need for alignment between decision-making within an initiative and other parties who may end up paying as well. GAVI's regular donors should have been engaged early on for efficient and effective deliberation and buy in. Earlier involvement may have led to addressing the considerable funding challenges.

C. Conclusion

While some analyses of the Pneumo AMC are available already[57,58] it is clearly too early to draw any firm conclusions on the pilot's efficiency and effectiveness. For now, the AMC pilot stands out for having been established as a result of successful collaboration among different partners. To date, 37countries have been approved for funding support from the GAVI Alliance and 14 countries introduced pneumococcal vaccines into their national programmes. By 2013 a total of 53 countries are expected to have introduced pneumococcal vaccines. The first of these introductions happened within approximately one year of introduction of the same products in high income countries.

Because of its innovative design, the AMC has received a tremendous amount of attention from the international community, country governments, industry, media, CSOs, academia and think tanks. This has led to increased awareness and attention to vaccines in general, and to pneumococcal disease and vaccines in specific, as a powerful prevention measure.

Moreover, experience with the Pneumo AMC so far suggests that long-term donor commitments can be made credible to industry and induce manufacturers to sign long-term binding commitments themselves to supply a fixed amount of vaccines per year at a pre-determined price. This is unprecedented, as historically, industry has entered only into good faith three years agreements with no binding obligation to supply. Since the signature of the legal agreements, four manufacturers - GSK, Pfizer Inc., the Serum Institute of India and Panacea Biotech Ltd - have publicly disclosed their formal agreement to the AMC terms and conditions. As a result of a first tender issued in September 2009, UNICEF entered into supply agreements with GSK and Pfizer under which both manufacturers supply 30 million doses annually each for ten years, starting in January 2012 for GSK and in January 2013 for Pfizer. Both manufactures have also committed to supply additional doses in 2010 and 2011 while scaling up production capacity. A second tender for additional doses is currently underway.

The supply price of US$3.50 can also be considered a significant achievement: more than a 90% reduction in price compared with the European Union and the United States, where average public prices are EUR 40 and US$96, respectively.[59] The existence of this new reference price for the lowest income countries may impact prices charged for other segments

[57] Snyder CM, Begor W, Berndt ER, Economic Perspectives on the Advance Market Commitment for Pneumococcal Vaccines, Health Affairs, August 2011 30:81508-1517

[58] Hargreaves JR et al. Making new vaccines affordable: a comparison of financing processes used to develop and deploy new meningococcal and pneumococcal conjugate vaccines. Lancet. Early Online Publication, 9 June 2011

[59] CDC vaccine price list for Pfizer's PCV-13 from July 18, 2011, available at: http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm [accessed August 2011] and internal communication from GSK (March 2010)

of the market. Some authors suggest that, given the cost structure in vaccine production, consumers in developing countries and those in high- price markets may both benefit from such a tiered pricing scheme.

A monitoring and evaluation framework was established to assess the Pneumococcal AMC from different angles. The framework is articulated around four components. First, annual monitoring to be implemented by the GAVI Secretariat; second, a ”Baseline Study” to establish the environment (industry and country situation) at the beginning of the intervention and development of counterfactuals[60]; third, an independent ”Design and Process Evaluation” (scheduled for 2012) to assess the AMC implementation process, and the efficiency and effectiveness of the AMC design; and finally, ”Impact Evaluations” every four years from the entry into the first AMC supply agreement to assess the achievements of the AMC and causality between the AMC intervention and observed outcomes.[61] All reports related to annual monitoring, baseline and evaluations are to be made public to share the results and inform potential future applications of this mechanism. In the meantime, this document is intended to serve as a starting point for a constructive debate.

Since the launch of the AMC concept, a number of alternative options for application and improvement[62] of the AMC mechanism have been suggested.[63] It was not in the scope of this document to review these ideas, but a potential future application of the AMC concept for vaccines would benefit from an assessment of recent developments and alternative options in this field.

[60] Available from : http://www.gavialliance.org/library/documents/amc/amc-baseline-study/ [accessed 13 September 2011]

[61] For more details on the evaluation framework, see Advance Market Commitments for Pneumococcal Vaccines: Report of the Monitoring and Evaluability Study. 2008. Available from : http://www.gavialliance.org/library/documents/amc/monitoring-and-evaluability-study/ [accessed 13 September 2011]

[62] A wide range of specific provisions and more general “pull mechanisms” can be considered, for example: milestone prizes, technology transfer provisions, technology transfer requirements around intellectual property rights and licensing.

[63] See for instance, the proposed application of the AMC mechanism for low-carbon development:

Advance Market Commitments for low-carbon development: an economic assessment, Final report by Vivid economics, DFID, 2009. Available from : http://www.vivideconomics.com/docs/Vivid%20Econ%20AMCs.pdf [accessed 13 September 2011]

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