

# **AMC Pilot Proposal**

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## AMC Pilot Proposal

1. **Advance Market Commitments are an innovative concept with the potential to save millions of lives by accelerating access to vaccines that would not otherwise be available for many years. A pilot has been designed that would demonstrate both the feasibility of the AMC mechanism and its impact on accelerating vaccine development, production scale-up and introduction.** AMCs have been thoroughly analyzed and vetted by experts and stakeholders. Vaccine development public-private partnerships have confirmed that current market failures inhibiting rapid product development and access could be addressed through an AMC. Vaccine and biotechnology firms have reviewed the concept and the proposal and agree that it has the potential to influence their investment decisions to ensure earlier access to sustainable supply of priority vaccines. Technical, legal and economic experts have concluded that AMCs are a powerful, practical and cost-effective mechanism. After careful review of all the data, an independent Expert Committee has recommended the disease most suitable for a pilot AMC. Heads of State and G8 Ministers of Finance have expressed strong support for the AMC proposal and called for a pilot launch by the end of 2006.

### *Rationale for an AMC*

2. Every year, diseases like malaria, Pneumococcal disease, HIV/AIDS, TB, rotavirus and HPV (Human Papilloma Virus) kill several million people, almost all of them in poor countries. Success in tackling these diseases demands a combination of prevention and treatment interventions. In all cases, the most valuable tool will be the availability of effective and affordable vaccines. However, the global resources invested in finding vaccines against these diseases are inadequate to meet the scale of the challenge, with most resources currently invested in diseases principally affecting developed countries.
3. **The risks and costs of investment in vaccine development are normally justified by future revenues once the vaccine is available on the market. Developing country markets, however, are perceived as both low value and risky and thus unpromising commercial markets for vaccines.** Vaccines no longer cost pennies per dose but are routinely introduced into industrial countries at \$50-100/dose. Introducing new vaccines into developing countries at tiered prices of \$4-\$8 per dose would be very low compared to industrial country markets and would still allow industry to recoup incremental investment costs. However, these prices would be unaffordable to the poorest developing countries. Industry's reluctance to invest in products to serve the developing country market is exacerbated by the fears, based on past experience, that actual purchases will be far less than forecasted need, and that firms, having made considerable R&D investment, may be pressured to provide a vaccine free or at very low prices.
4. **AMCs offer a powerful and cost-effective market-based mechanism to overcome these hurdles and accelerate the development and availability of priority new vaccines for developing countries.** An AMC for vaccines is a financial commitment to subsidize the future purchase of a vaccine not yet available, *if* an appropriate vaccine is developed and *if* it is demanded by developing countries. Early, guaranteed commitments encourage potential

vaccine suppliers to invest in R&D and production capacity to serve developing countries, secure in the knowledge that there will be a viable market if they supply products that eligible countries want to buy.<sup>1</sup> By creating markets for vaccines for developing nations comparable to markets in wealthier countries, AMC is a bold step towards erasing the health inequities between rich and poor.

5. **An AMC works by reducing risks – to industry, donors and developing country governments.** An AMC is a specific commitment that defines the target product standards (effectiveness, public health impact), the total AMC market size, the contract price, and the predicted demand. Firms are assured of a subsidized price if they develop a product demanded by countries and agree to abide by affordable prices after the AMC is depleted. Donors are assured that funds will only be used if a highly valuable product is developed, that a competitive market is established for firms and that their up-front investment results in sustainable supply after the AMC is depleted. Finally, and most importantly, developing country governments have early access to priority life-saving vaccines with assurances of sustainable and affordable supply in the future.
6. **The impact of this market commitment is measured in the potential for millions of lives to be saved through the accelerated access of poorest people to priority vaccines – lives that would otherwise be lost to preventable communicable diseases.** Through up-front, legally binding commitments, the AMC provides a mechanism to change industry behavior, resulting in accelerated development, scale-up and supply of priority vaccines. This efficient reduction of market risks is also designed to have long-term positive impact, since it also ensures a sustainable affordable supply of priority vaccines continuing to save lives beyond the duration of the AMC contract period.

#### *Global Experts Agree on the Value and Structure of the AMC pilot*

7. **Following the request of specific governments for analytical support and independent consultation and review of the AMC mechanism, the World Bank and the GAVI secretariat organized an extensive work program to engage global health stakeholders and experts.** A formal Advisory Group was established to provide input on the consultative process as well as insight into the optimal structure for the AMC mechanism and pilot. This group comprised of stakeholders and experts in the global health community, including the product development partnerships for the candidate diseases, global health partnerships, multilateral institutions, developing countries, the academic community and industry, has played a pivotal role in the development of the AMC pilot proposal.
8. **Special consultations were held with key stakeholders including developing country governments, biotechnology and pharmaceutical firms and technical partners such as WHO.** Health policy makers, pediatricians, researchers, immunization managers and other developing country experts have participated in the Advisory Group and Expert Committee. A broader consultation process is underway, including engagement with the Africa Union

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<sup>1</sup> Recent efforts by GAVI to assure long term predictable funding to purchase vaccines for the developing world has been shown to influence industry behavior, particularly emerging suppliers – giving further confidence in the AMC concept.

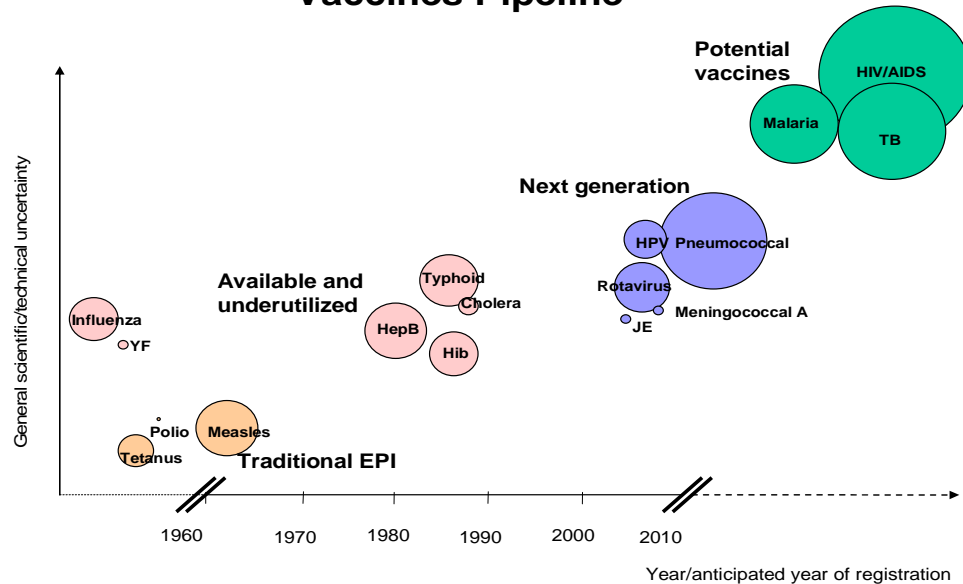
and its NEPAD program and the 2006 WHO African Regional Meeting. The AMC concept and its potential to accelerate priority technologies have been presented in several fora, including a meeting of Ministers during the World Health Assembly and the Abuja Financing for Development Conference (21-22 May). Focused consultations were held with pharmaceutical and biotechnology firms to update them on the progress of AMC thinking and to discuss outstanding issues. Companies have expressed their strong interest in AMCs and have provided very useful input on how firms will evaluate the AMC and how the AMC might be structured to maximize its impact on private sector decision making. Finally, detailed consultations with various technical partners (e.g. WHO) were conducted to explore both the optimal structure and processes for the Independent Assessment Committee and the institutional placement of the AMC pilot.

9. **As an innovative concept, a pilot AMC is needed to demonstrate both the feasibility of the AMC mechanism and its impact on accelerating vaccine development and production.** A successful pilot will demonstrate an AMC's ability to influence the decisions of private sector firms to make vaccine investments that will accelerate access in the poorest countries. A pilot will also spur the establishment of the necessary secretariat to implement an AMC for additional vaccines. Ultimately, potential donors may be interested in AMCs as a demonstrated mechanism to accelerate the development of, and access to, any priority technologies in which there is under-investment. An AMC can have an impact on investment decisions at various stages of vaccine research, development and production.
10. **The choice of disease(s) for an initial AMC pilot is clearly of critical importance. Considerable care was therefore devoted to the selection and terms of reference of an Independent Expert Committee to inform that judgment. The Expert Committee provided an evidence-based recommendation to governments on the vaccine(s) most suitable for the AMC pilot.** Based on suggestions from numerous bodies including governments, UN agencies, public-private partnerships and foundations, experts without conflicts of interest were identified in the areas of public health, epidemiology, industry economics, vaccine development and law. The Expert Committee was chaired by Dr H. Ntaba, Minister of Health of Malawi. Most of the experts were from developing countries, and their participation was complemented by developed country experts, for example from industry. The Committee carefully and extensively reviewed all six diseases initially proposed in Minister of Economy and Finance Tremonti's paper: HIV/AIDS, malaria, rotavirus (diarrheal disease), tuberculosis, pneumococcus (pneumonia and meningitis) and human papilloma virus (cervical cancer).

## *AMC Pilots*

- 11. The Expert Committee carefully assessed six candidate diseases to identify the candidates most likely to provide a measurable and timely indication of AMCs impact on industry decisions.** The Committee concluded that while all six are large public health threats in need of vaccines, the selected diseases were much more suitable to pilot the concept than others. The Committee's conclusions and recommendations were unanimous.
  
- 12. The Expert Committee recommended pneumococcal disease as the most suitable candidate for an AMC pilot.** Pneumococcal disease would rapidly demonstrate the impact of AMCs on industry decisions because access to pneumococcal vaccines depends on private investments in their development and production capacity. In addition to reducing the 1.6 million deaths occurring annually from pneumococcal disease, these vaccines have growing importance: there is increasing antibiotic resistance to treatment of pneumococcal infections, and vaccines will contribute to pandemic influenza preparedness by preventing pneumococcal pneumonia - a frequent and severe consequence of influenza infection. Based on historical experience, in the absence of an AMC or other financial effort, no pneumococcal vaccines will reach the world's poorest countries before about 2023. The recommended donor contribution to the AMC is US\$1.5 billion in nominal terms (US\$ 860 million in 2006 dollars). The price per dose is to be determined but is estimated to be within the range of US\$5-7/dose with developing countries responsible for an affordable co-payment per dose. The first payments are anticipated to begin in 2010 and last for 9-10 years. With its long term, sustainable impact, the AMC would prevent between 500,000-700,000 deaths during the AMC itself and roughly 5.4 million deaths by 2030. The AMC would provide incentives for firms to invest in the accelerated development and production scale-up of any of the 20 or so vaccine candidates. The AMC is sized to support the scenario of three products successfully reaching the market but is robust to variations of number of suppliers, country demand and product timing. Once the AMC is depleted, each participating firm will continue to supply the vaccine at a pre-determined low price for an established period. (More detailed information is available in Annex 1.)

## Vaccines Pipeline



13. **The Expert Committee recommended that a second demonstration AMC for a malaria vaccine be explored to stimulate early R&D investment and to pilot the impact of the AMC on early stage vaccines.** The Expert Committee recognized there was a strong case for both malaria and tuberculosis AMCs. After careful consideration, the Committee recommended malaria for the pilot because the vaccines are at more advanced stages and are more likely to yield a timely and measurable response to the AMC. The recommended donor contribution to the AMC is US\$ 2.3 billion in nominal terms (\$955 million in 2006 dollars)<sup>2</sup>. The price is estimated to be within the range of US\$6-8 per dose with developing countries responsible for an affordable co-payment per dose. The first payments are anticipated to begin in 2016 and last for 11 years. With its long term, sustainable impact, AMC would prevent between 0.9-1.3 million deaths and drastically reduce the disabilities and indirect burden caused by malaria during the AMC itself and prevent roughly 2 million deaths by 2030. The AMC would provide incentives for firms to invest in taking forward the most promising of the 100 candidates in the pipeline, it may also motivate firms to develop new, more promising candidates. Typically, most of these candidates will fail at some stage of the development process and so will never reach the market. The AMC is sized to support two products successfully meeting the AMC standards. Successful development of this early stage vaccine will build on and complement existing research funding from bodies such as the government research entities and the Gates Foundation. Once the AMC is depleted, each

<sup>2</sup> A 5% rate of discount per year has been applied.

participating firm will continue to supply the vaccine at a pre-determined low price for an established period. (More detailed information is available in Annex 2.)

<i>Pathogen</i>	<i>Streptococcus pneumoniae</i> ( <i>Pneumococcus</i> )	<i>Plasmodium</i> ( <i>Malaria</i> )
<b>Disease specifics</b>		
Organism	Bacterium	Protozoa
Disease	'Pneumococcal disease': - bacterial pneumonia (leading cause) - middle ear infections (leading cause) - bacterial meningitis (leading cause in adults) - sepsis	Malaria (intermittent fever, potentially organ failure, delirium, impaired consciousness and generalized convulsions)
Annual deaths	1.6 million (90% in poor countries)	1 million (leading cause of under-5 mortality)
Treatment options	Antibiotics with differing effectiveness depending on type and severity of infection  <i>NB increasing antibiotic resistance</i>	Anti-malaria drugs  <i>NB ineffective and expensive; increasing drug resistance</i>
Vaccines	20 candidates in the pipeline	100 candidates in the pipeline
Organization	PneumoADIP	Malaria Vaccine Initiative
<b>AMC specifics</b>		
Recommended size of AMC	US\$1.5 billion	US\$ 2.3 billion (serving 42 malaria-endemic countries)
Payment period	2010 – 2020	2016 – 2028
Estimated donor subsidy per dose	US\$5-7	US\$6-8
Impact – direct (during AMC)	70 – 100 million infants immunized 500,000-700,000 deaths prevented	0.9-1.3 million deaths prevented
Impact – long term	5.4 million deaths by 2030	2 million deaths by 2030

### ***AMC Implementation***

**14. An AMC will be put in place using a framework agreement that will establish its key terms, including legal obligations of donors and the implementation details for the structure.** The framework agreement will specify the market size of the AMC, and the price and requirements for the targeted vaccine. It will set out the underlying financial commitments, and the obligation to enter into a guarantee and supply agreement with any qualifying manufacturer whose vaccine meets the requirements. It will delineate the responsibilities and processes of the Independent Assessment Committee, as well as ongoing

responsibilities after the AMC funding is exhausted.

- 15. The success of AMCs will hinge on the credibility and strength of future financing commitments made by donors.** Domestic authorization and appropriation laws and processes differ. In addition, the budgetary systems for many donors do not lend themselves to making legally binding financial commitments that are contingent on a future event, such as the production of a vaccine meeting the required TPP. As a result, individual donors are likely to provide their commitments in different forms and with differing legal foundations. The financing arrangements will have to be sufficiently flexible to support these necessary variations.
- 16. To ensure that the AMC financial commitments are clear and credible to industry, donor commitments should be bundled together by a financial intermediary such as the World Bank into a single financial instrument. Given political and budgetary realities, as well as uncertainty over the timing of future AMC payments, donor commitments will not be viewed by industry as entirely riskless.** Payment risks could be managed by third-party assurance provided by a commercial entity, or possibly an international financial institution. Intermediary “bundling” of donor commitments will provide the necessary assurance to manufacturers, so that they do not have to independently assess the legal and financial credibility, and payment and timing risks, for each underlying donor commitment.
- 17. The financing structure will be sufficiently flexible to allow donors to choose their preferred payment profiles.** Nevertheless, for the pneumococcus pilot AMC, where the future commitment is relatively well-defined, donors may find that the most appropriate approach is up-front commitment to the whole AMC amount with the stream of payments made on an ‘annuity’ basis from the time of AMC establishment. By contrast, for an early-stage vaccine like malaria, it might be better to arrange for up-front commitment to the whole AMC amount but with payments starting only when a product has qualified.



18. **The secretariat to support the AMC should be hosted in GAVI with specific functions housed in the World Bank and GAVI (as outlined below), drawing on the differing capabilities of the two entities and building on the existing strong working relationship between the two organizations. The functions will vary over time, and require different institutional expertise and administrative commitment.** A detailed review of six candidate “host” institutions<sup>3</sup> identified GAVI and the World Bank as able to provide the necessary support for the AMC over the different phases of the AMC’s life. GAVI, with its immunization mandate, would be the programmatic leader on AMCs, ensuring technical support to developing countries and providing linkages with immunization stakeholders. This would include hosting the AMC Secretariat, linking with countries to assess demand, managing the procurement process and supporting the establishment and the on-going processes of the Independent Assessment Committee. The World Bank would complement GAVI by drawing on its established credibility and financial experience to manage the financial and fiduciary functions of the AMC. This would include working with donors to structure the financial commitments, and managing and disbursing funds to match vaccine payment schedules. GAVI and the Bank would share tasks such as receiving initial donor contributions, negotiating the framework and guarantee agreements and reporting on the AMC. The costs of the implementing the AMC are expected to be low, with GAVI and the World Bank building on existing capacity and requiring relatively modest support.
19. **The implementation of the AMC pilot has several distinct phases, each of which draws on a different mix of partner skills.**
- An initial setting-up phase will be needed to put in place the arrangements underpinning the AMC including negotiations, establishing the IAC, obtaining secure donor commitments, and finalizing the framework agreement.
  - Once the framework agreement is signed, an interim monitoring period would follow in which the key institutional requirement would be to monitor progress toward the AMC goals and to trigger the AMC once a product meets the required performance standards.
  - Once a guarantee and supply agreement is signed with a specific manufacturer, the implementation transactions associated with the procurement and delivery of vaccines to countries and the payment to industry must be supported. Institutional responsibilities will include efficient and timely management of these transactions, including procurement, disbursement and collection of country co-pays.
  - The credibility of the AMC pilot and transparency of its results will depend in part on good monitoring and reporting.
20. **The Independent Assessment Committee (IAC) has a critical expert role in establishing the vaccine performance and determining when vaccines meet these standards and are eligible for AMC funding.** While GAVI would provide Secretariat support to the AMC, the IAC will oversee certain expert tasks such as establishing Target Product Profiles (TPPs) for candidate vaccines, ascertaining whether they are met and monitoring progress. The recommended structure builds on existing processes and entities,

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<sup>3</sup> Six organizations were considered to host, or play a role in hosting, an AMC pilot: the Global Alliance for Vaccines and Immunization (GAVI), the Bill & Melinda Gates Foundation (Gates Foundation), the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), UNICEF, the World Bank, and the World Health Organization (WHO).

particularly WHO, to assure consistency and avoid duplication with existing regulatory bodies and UN vaccine qualification processes. Comprising seven to ten members with no vested interest in the specific products under consideration, IAC expertise would include public health, health economics, vaccine business development, contract law, clinical performance and delivery systems. Following transparent processes, the IAC will oversee the following functions:

- A TPP is the performance standard a specific vaccine would have to meet to be eligible for AMC funding. The IAC will establish the TPP based on recommendations from an expert group convened, at IAC request, by WHO. The work of this expert group will be evidence-based and conducted in a transparent manner within guidelines agreed by AMC donors.
- The IAC would review and accept progress reports prepared by the AMC Secretariat on the scientific and technical progress toward an AMC eligible vaccine.
- In the rare event that the IAC needs to revise TPPs or AMC prices, it will request expert groups be convened by WHO, in the case of the TPP, and the AMC Secretariat, in the case of pricing. Its decision will be based on the recommendations of these groups.
- The IAC will determine if a product is eligible for AMC funding based a report from WHO on whether an AMC submitted vaccine meets the TPP and other prequalification requirements such as the product having been licensed by a recognized regulatory authority and being manufactured to required standards.
- In the event of issues relating to processes overseen by the IAC, such as those delegated to other groups, the IAC would institute a dispute resolution process.

### *Conclusion*

21. **The extensive analytical and consultative work completed over the last year has resulted in development of a compelling AMC proposal. A pilot AMC for pneumococcal vaccines would not only save lives but, by demonstrating the impact and feasibility of this mechanism, would build confidence and help accelerate earlier access to other priority vaccines and health technologies. An AMC for a malaria vaccine would pilot the AMC mechanism for early stage vaccines by demonstrating capacity to stimulate additional early R&D investment.**

## Annex 1: Pneumococcal as an AMC pilot

**Pneumococcal vaccines were recommended as the most suitable candidate for an AMC pilot.** Pneumococcal vaccines are the best choice for a pilot for several reasons:

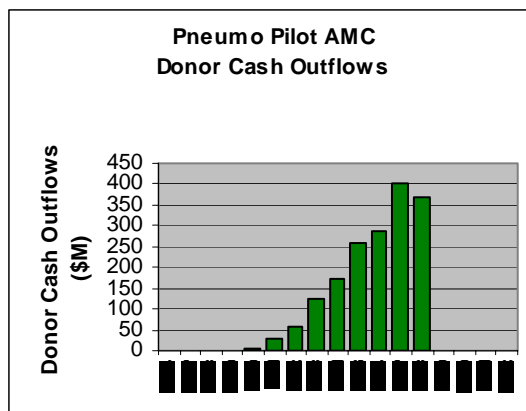
- A demonstration AMC for pneumococcal vaccines provides the ability to rapidly measure the effectiveness of the AMC concept in influencing industry behaviour and to establish effective AMC implementation mechanisms;
- There is a robust pipeline that can deliver at least two and possibly three vaccines suitable for the target countries, but testing and production capacity for these vaccines will be inadequate unless there is an AMC;
- There is a high disease burden and concern about growing antibiotic resistance
- Pneumococcal vaccine contributes to pandemic influenza preparedness by preventing pneumococcal pneumonia - a frequent and severe consequence of influenza infection;
- Pneumococcal vaccines fit into the existing delivery systems and so can be cost-effectively introduced.

**Pneumococcal vaccines have a proven ability to improve child survival in the communities where the burden of disease is greatest and are cost-effective and easily delivered through existing delivery systems.** Every year, *Streptococcus pneumoniae* kills more than 1.6 million people, including 700,000 - 1 million children under age 5 years. Although children everywhere are affected, more than 90% of pneumococcal deaths occur in poor countries. The HIV/AIDS epidemic is increasing the rate of infections and antibiotic resistance is making pneumococcal disease difficult and expensive to treat. A pneumo vaccine trial in Africa showed a 16% reduction in all-cause mortality in vaccinated children - in other words, *7 child deaths were prevented for every 1000 vaccinated children*. If there is a herd immunity effect or if second generation vaccines prevent more pneumococcal disease, the impact will be even larger. Cost-effectiveness analyses indicate that pneumococcal conjugate vaccines meet internationally recognized benchmarks for “good investment” in health. Recent analyses from Harvard University show that, conservatively, for a pneumococcal vaccine priced at \$5 per dose, the cost per DALY saved is about \$100 in target countries.

**Pneumococcal vaccines are in late stage development, but without an AMC, it is unlikely that manufacturers will invest to test or produce pneumococcal vaccines for the poorest developing countries.** Based on historical experience, in the absence of an AMC or other financial effort, no pneumococcal vaccines will reach the world’s poorest countries before about 2023. Investments to develop and produce pneumococcal vaccines have been stimulated to date, by large potential markets (\$5-6 billion) in high and middle income countries. Serving low-income countries requires additional investments in late-stage development and production capacity. The pneumococcal vaccine pipeline includes one licensed product and more than 20 candidate vaccines in varying stages of development. The licensed vaccine has safely and effectively vaccinated more than 30 million children in industrial countries. Capacity is, however, inadequate and the vaccine is not being considered for wide spread introduction in developing countries. Two vaccines that extend protection for populations in both developing and industrial countries by adding more serotypes may be licensed by 2010. Other vaccines may come to the market in the following 5-10 years.

**There is significant evidence of demand for an improved pneumococcal vaccine if the price is affordable and supply terms are reliable.**

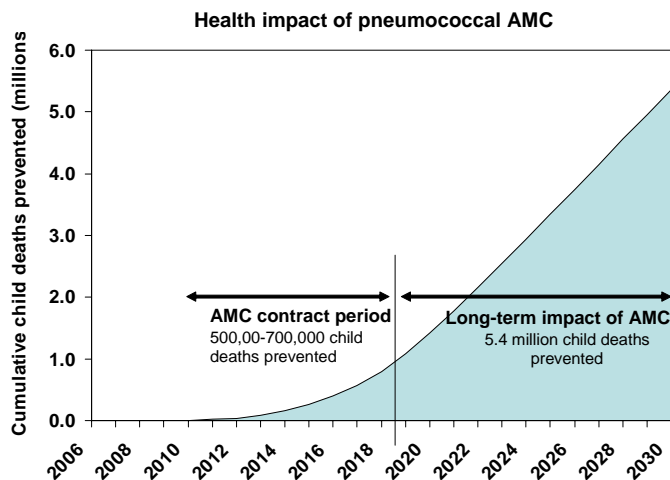
The expected demand for the vaccine is based on high recognition of the burden of pneumonia and meningitis disease. Preliminary discussions with governments in Africa and Asia have confirmed interest in introducing an affordable pneumococcal vaccine. Forecast demanded is based on the assumption that GAVI and its partners will continue to support efforts that enable governments to make evidence-based decisions on vaccine introduction. The most important, disease surveillance gives important data on the occurrence of pneumococcal disease locally and is the focus of a current \$30 million GAVI project.



**The recommended size of the AMC is \$1.5 billion in nominal terms with an NPV cost of \$860 million. The price per dose is to be determined but is estimated to be within the range of \$5-7 per dose with developing countries responsible for an affordable co-payment per dose.** The size of the AMC was calculated using a model estimating the risk-adjusted return to firms based on the specifics of the pneumococcal market, demand forecast, product pipeline and the amount of incremental private sector investments required to serve the developing world. Sensitivity analyses were run on key inputs to identify the AMC size most likely to result in a successful pilot. It assumes country co-payment of roughly \$1/dose will further contribute to the market. The anticipated AMC payment profile is illustrated; actual payments will depend on country demand. The first payments are anticipated to begin in 2010 and last for 9-10 years. Once the AMC is depleted each participating firm will continue to supply the vaccine at a pre-determined low price for an established period. The success of the AMC does not depend on this exact ‘business case’: it is robust to variations of number of suppliers, country demand and product timing.

**The impact of the pneumococcal AMC will be measured in terms of public health outcomes and industry investments. It has the potential to prevent hundreds of thousands of deaths initially and millions of deaths over time and to accelerate development and supply of pneumococcal vaccines.**

Overall the AMC will result in 70-100 million immunized infants over the life of the AMC. This will prevent between 500,000-700,000 deaths during the AMC itself. However, the impact of the AMC goes beyond the contract



period as it assures a long-term sustainable supply and price. Based on historical experience, in the absence of an AMC or other financial effort, no pneumococcal vaccines will reach the world's poorest countries before about 2023. By 2030, the AMC will have contributed to the prevention of 5.4 million deaths. This public health impact results from early access to the vaccine. The AMC would provide incentives for firms to invest in the accelerated development and production scale-up of any of the 20 or so vaccine candidates. The AMC is sized to support the scenario of three firms (two multi-national and one emerging market manufacturer) successfully producing a qualifying product. As a commercial solution to a market failure, the AMC would motivate firms to undertake the necessary late stage trials to prove efficacy in developing countries, invest in plant capacity to supply poorest countries, resurrect 'discontinued' vaccine development programs, develop second generation technologies (e.g., protein vaccines), and provide long-term, sustainable and predictable prices. Success can be defined by industry's commitment to invest in the trials and manufacturing capacity that would not otherwise have been built.

## Annex 2: Malaria as an AMC pilot

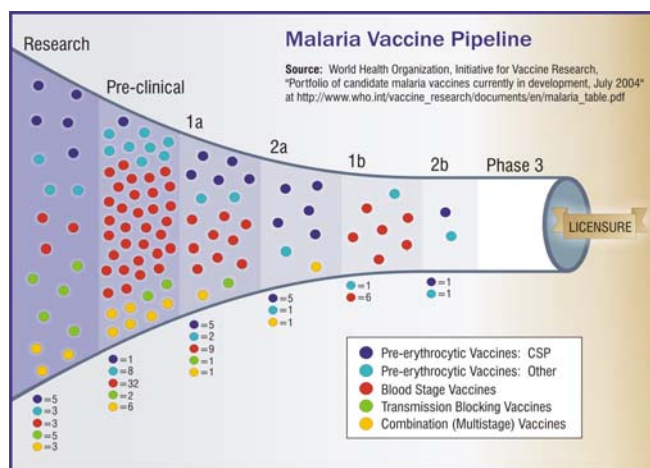
**The Expert Committee recommended that a second AMC pilot for malaria vaccine be explored to stimulate early development investment and to pilot the impact of the AMC in early stage vaccines.** While vaccines against HIV/AIDS, malaria and tuberculosis are all critically important, the Expert Committee concluded that given the state of the science for HIV/AIDS vaccines, increased levels of push funding would be more appropriate than an AMC at this time. The Expert Committee recognized there was a strong case for both malaria and tuberculosis AMCs. After careful consideration, the Committee recommended malaria for the pilot because the vaccines are at more advanced stages and are more likely to yield a timely and measurable response to the AMC.

**Malaria is the largest single killer of children under five in Africa<sup>4</sup>, kills over 1 million people a year globally and places 3.2 billion people living in malarial areas at risk. Given the health and economic costs of malaria, there is significant demand for a vaccine.**

Malaria not only threatens and takes lives but also indirectly contributes to at least another million deaths and lowers the quality of life in the developing world, by draining precious human and financial resources from the very societies and economies that can least afford it. Taking into account initial poverty, economic policy, tropical location, and life expectancy among other factors, malaria slowed growth in Africa countries by as much as by 1.3% per year, and countries who reduced their malaria burden by 10% witnessed a 0.3% higher growth per year.<sup>5</sup> Malaria is estimated to account for up to 40% of public health expenditures and 50% of outpatient visits in some African countries.<sup>6</sup> Based on extensive discussions with African governments, a model estimating likely vaccine demand in public and private markets over a 15-year period was developed. This tool, has been widely vetted as part of the collective effort of over 250 stakeholders, including scientists, donors, and public health leaders, representing more than 35 countries and 100 organizations, to set a shared vision for malaria vaccines: the “Malaria Vaccine Technology Roadmap”.

**To deliver the biggest potential impact on the disease, it is essential that earlier stage products in the global malaria vaccine pipeline are advanced.** There is a promising pipeline of early-stage malaria vaccine candidates, and an advanced candidate now entering final Phase 2 trials, with Phase 3 licensure trials being planned and registration possible as early as 2011.

Though partially efficacious, this vaccine could have a significant public health impact if deployed, and as a first generation malaria vaccine, laying the groundwork for improved



<sup>4</sup> 2005 World Health Report, WHO

<sup>5</sup> "The Economic Burden of Malaria," Sachs & Gallup, Center for International Development at Harvard, 1998

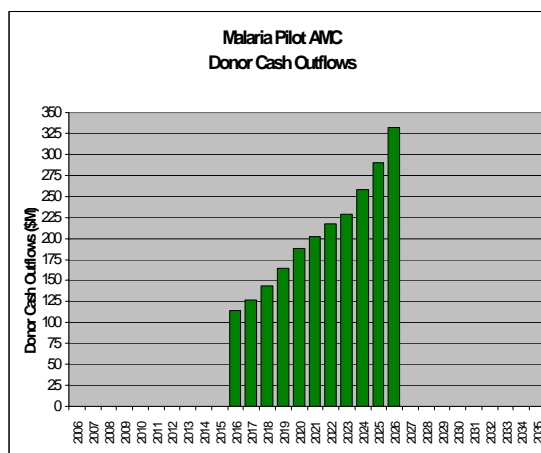
<sup>6</sup> "Economic Costs of Malaria," Roll Back Malaria Information Sheet, WHO.

[http://www.rbm.who.int/cmc\\_upload/0/000/015/363/RBMInfosheet\\_10.htm](http://www.rbm.who.int/cmc_upload/0/000/015/363/RBMInfosheet_10.htm)

malaria vaccines. However, other candidates in the pipeline have potential to be more efficacious products, and there is still a risk that the front runner may not prove successful in further clinical development. According to WHO, as of mid-2005, almost 70 out of more than 100 vaccine candidates are in research or have not yet entered clinical trials, 18 candidates are in the earliest Phase 1 trials and nine have entered Phase 2 trials. While these numbers may seem high, many ‘candidates’ are actually vaccine constructs, or pieces of vaccines, and moreover largely represent the work of academic and research institutions (and a relatively small number of private sector groups supported with public sector research money). These efforts, given current levels of public funding and industry investment, will be insufficient to push promising vaccines candidates to licensure. With an effective combination of push and pull funding to attract industry, a high-efficacy, second generation malaria vaccine could be available as early as 2016-18.

**The recommended donor investment in the AMC for a malaria pilot is \$955 million (\$2.3 billion in nominal terms). The price is to be determined but is estimated to be in the range of \$6-8 per dose with developing countries responsible for an affordable co-payment per dose.**

The market size is based on serving 42 of the poorest malaria-endemic countries (not including India) and assumes that a first generation vaccine while not likely to qualify for AMC funding, is available in 2011, and begins to experience uptake in certain countries. The size of the AMC was calculated using a model estimating the risk-adjusted return to firms based on the specifics of the malaria market, demand forecast, product pipeline and the amount of incremental private sector investments (complementing existing grant funding) required to serve the developing world. Sensitivity analyses were



run on all the key inputs to identify the optimal AMC size most likely to result in a successful pilot. It assumes country co-payments will be additional to donor contributions to the AMC. The anticipated AMC payment profile is illustrated but of course will depend on actual country demand. The first payments are anticipated to begin in 2016 and last for 12 years. Once the AMC is depleted each participating firm will continue to supply the vaccine at a pre-determined low price for an established period.

**The impact of an AMC for malaria vaccines will be measured in terms of accelerated industry investment and roughly 1 million deaths prevented.** Through the AMC, roughly 150-200 million children would be immunized, preventing roughly 0.9-1.3 million deaths. However, the actual impact of the AMC is for much longer as it assures a long-term sustainable supply and price. This means, by 2030, the AMC will have contributed to the prevention of 2 million deaths. The AMC would provide incentives for firms to invest in taking forward the most promising of the 100 candidates in the pipeline, it may also motivate firms to develop new, more promising candidates. Typically, most of these candidates will fail at some stage of the development process and so will never reach the market. The AMC is sized to support two

products successfully meeting the AMC standards beginning as early as 2016 but its success does not depend on this precise scenario. In complement to continued grants for R&D from government research bodies and foundations such as the Bill & Melinda Gates Foundation, the AMC would motivate private investment in early and late stage development activities and the production capacity to serve the poorest countries and the establishment of sustainable and predictable prices. Success can be defined by the number of new industry players engaged in malaria vaccine development, the number of candidates moving through the pipeline toward later stage development and investments in facilities sized to supply the poorest countries.

