

Advance Market Commitments: Helping to accelerate AIDS vaccine development

The AIDS epidemic continues to grow, killing three million people in 2004 even as five million more became infected with HIV – over 95 percent of them in developing countries. Antiretroviral therapy can extend lives and relieve suffering, but only effective prevention can halt and reverse the epidemic’s spread. A preventive AIDS vaccine remains the best hope for a decisive victory over the pandemic.

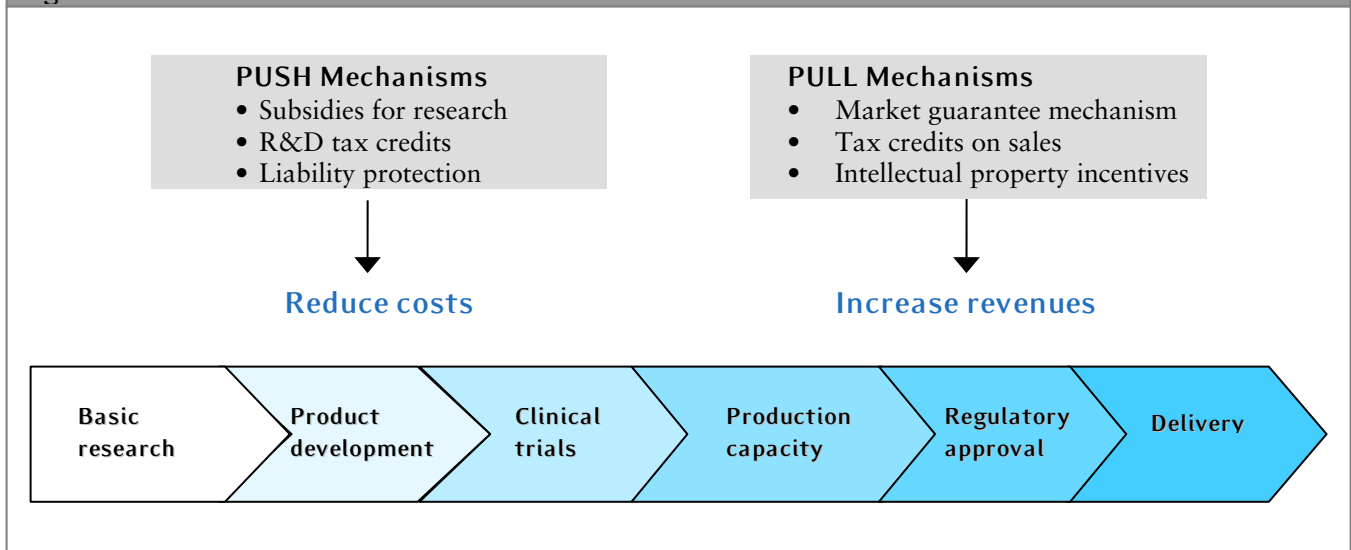
Researchers face significant challenges in developing an AIDS vaccine. Success will require significant and sustained investment in basic research, preclinical development, large-scale trials and manufacturing capacity. Bringing a vaccine to market will require the unique expertise and resources of the pharmaceutical industry. Many companies, however, currently have little or no involvement, and industry accounts for only 10% of current spending on AIDS vaccine R&D.¹ The private sector has been deterred from greater investment by scientific uncertainty but also by market risks. The need for a vaccine is greatest in the countries that are least able to pay; in addition, firms worry that political pressures would compel them to provide vaccines at a very low and unprofitable prices.

A novel incentive mechanism – an advance market commitment (AMC) – could provide additional motivation for industry to increase its R&D investments. An AMC would provide a legally-binding promise to vaccine manufacturers to pay a price for a future AIDS vaccine that would generate revenues matching those from other health products in the global marketplace. Donors would pay this price for up to a certain number of doses, after which the manufacturer would be obligated to sell to eligible countries at a lower price that is affordable for developing nations. When combined with other incentives, an AMC could speed the development and widespread uptake of an AIDS vaccine, thus helping to prevent tens of millions of HIV infections and AIDS-related deaths.

Part of a larger package

IAVI has undertaken an analysis of the feasibility of an AMC for AIDS vaccines.² Its findings suggest that an AMC should be seen as a vital component of a larger package of incentives needed to “push” and “pull” a vaccine candidate faster through research, testing and production (Figure 1).

Figure 1. Incentives for vaccines



An AMC would be a welcome addition to other “pull” mechanisms, such as patent extensions, that are currently used to stimulate investment in so-called “orphan drugs” and pediatric formulations. By increasing the rewards for success, an AMC would complement existing “push” mechanisms, notably government funding of basic research and product development by academia and industry.

To reap the full benefits of an AMC for vaccines against AIDS and other diseases found in poor countries, the global health community also needs to address bottlenecks that discourage R&D investment, such as unpredictable vaccine demand, inefficient procurement and weak vaccine delivery systems. An AMC will not solve these problems – they should be tackled in parallel with an AMC.

How an AMC would work

To launch an AMC for an AIDS vaccine, donors – most likely governments or foundations – would propose a Framework Agreement establishing the terms of the commitment. These would include technical vaccine criteria to be met or exceeded, the guaranteed price, the maximum quantity to which this price would apply, the lower price that firms would charge after the guarantee commitment is exhausted and a definition of eligible countries that could buy the vaccine using AMC funds. Interested companies would then sign on to the Framework Agreement and report annually on their AIDS vaccine R&D activities.

A company that develops a potentially qualifying AIDS vaccine would apply to an Independent Assessment Committee (IAC) comprising experts from the biopharmaceutical industry and the global public health community. The IAC would decide if the product meets the qualifying criteria and could grant waivers if a vaccine does not meet all the original standards but still brings substantial public health benefits in preventing HIV infection.

If the vaccine is approved by the IAC, the company becomes eligible to sign a Guarantee Agreement with the donors. The Guarantee Agreement would require donors to finance AIDS vaccine purchases made by developing countries. The countries themselves would make a small “co-payment” of a few dollars for each course of vaccination, with the donors topping up this payment with a substantially larger amount of money for each course of vaccine. This payment scheme would apply equally to first and later-developed vaccines, with developing countries choosing which qualifying AIDS vaccine they wish to purchase.

Once the maximum quantity of vaccines has been purchased, thereby using up the AMC's funding guarantee, the participating companies would be required to continue supplying vaccines at the agreed-upon long term price. Figure 2 provides a summary of the AMC implementation process.

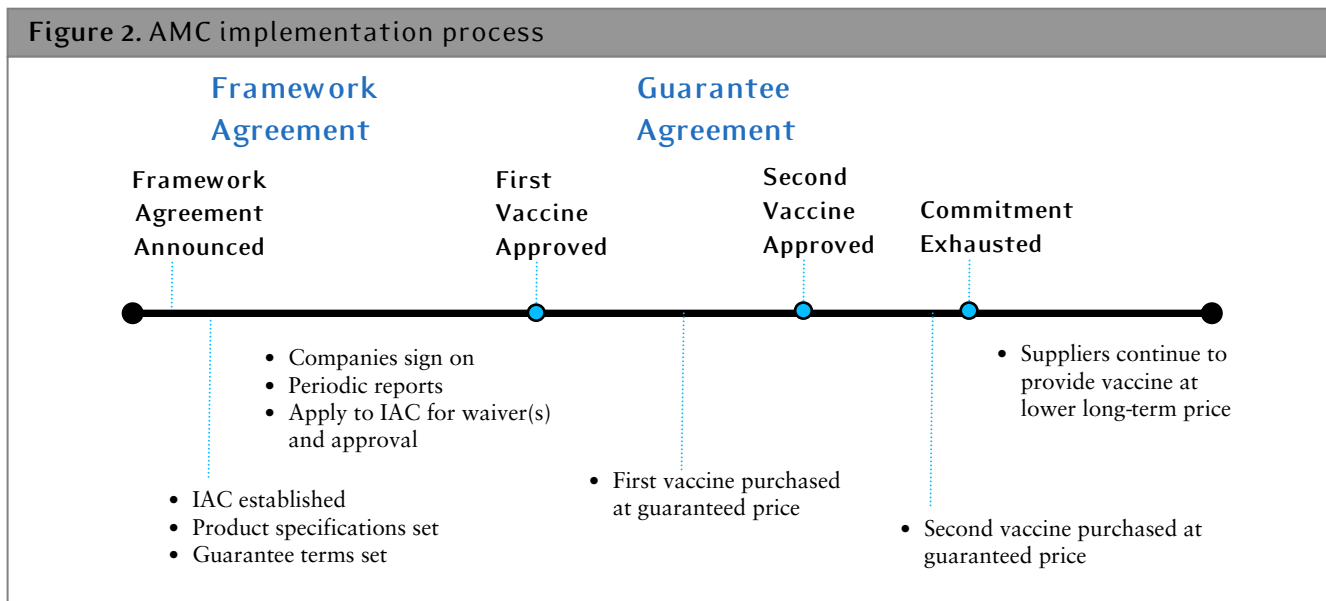
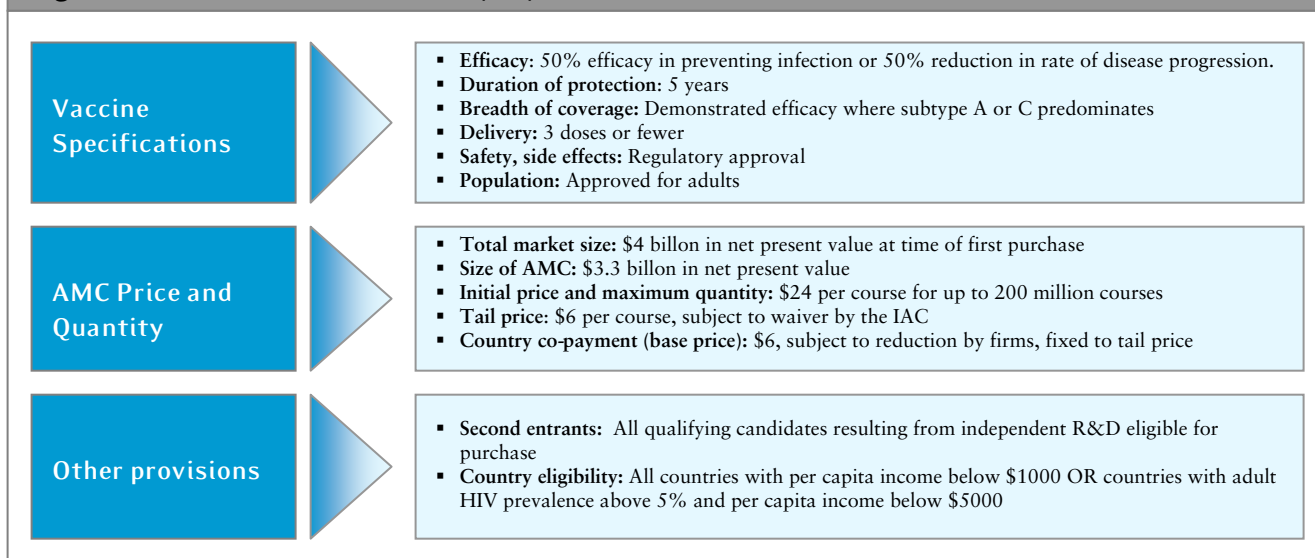


Figure 3. Overview of IAVI's draft proposal for an AIDS vaccine AMC



What an AMC for AIDS vaccines could look like

Based on analysis conducted by IAVI, an AMC program was developed for an AIDS vaccine with a range of recommended features covering: (1) the characteristics of qualifying vaccines (2) AMC market size and price; and (3) provisions for second and third vaccines and country eligibility. Several uptake scenarios were elaborated using different prices and vaccine quantities. The base scenario is shown in Figure 3.

One of the major challenges in developing an AMC is determining the market size needed to stimulate vaccine R&D. IAVI based its estimate on sales revenues from existing pharmaceutical products. This approach is well suited to AIDS vaccines since it does not rely on detailed estimates of risks and manufacturing costs which are not yet available for early-stage products. IAVI estimated that a global market for AIDS vaccines of about \$4 billion in net present value (NPV) would attract industry. Subtracting expected sales in rich country markets, this suggests that AMC market would need to have an NPV of \$3.3 billion. In one AIDS vaccine uptake scenario developed by IAVI, this corresponds to a guaranteed price of \$24 per course for 200 million people. Such a commitment would last about 10 years, long enough to stimulate the development of a second generation of improved AIDS vaccines.

An important feature of AMCs is two-tiered pricing. During the initial AMC period, firms would receive the subsidized high price (\$24 in the scenario mentioned above), including both the developing country's modest share of this price (the “co-pay”) and the larger “top up” payment by AMC donors. In this example, once the first 200 million vaccine courses had been purchased and the AMC funds had been used up, the vaccine manufacturer would be required to continue supplying the AIDS vaccine at a lower price which still covers their production costs. As long as the manufacturer abides by the terms of the commitment, it would retain all intellectual property rights and existing patent laws would apply.

The IAVI proposal suggests \$6 per course for both the country co-pay and the long-term price, consistent with the best available information on likely manufacturing costs. In the scenario where the AMC price is \$24 per course, this would mean that the AMC donors would pay the difference of \$18 per course of vaccination.

Since the production costs of future AIDS vaccines are difficult to determine now, the IAVI study proposes allowing these prices to be changed. Firms could petition the Independent Assessment Committee for a waiver to increase the long-term price if they can demonstrate that their vaccine cannot be manufactured for \$6 per course. Firms competing with other AIDS vaccine makers could

also lower the co-pay and long-term prices if they felt this would make their vaccine more attractive to developing countries. These measures would foster competition and allow countries to weigh long-term price in deciding which vaccine to buy.

Benefits of an AMC

By accelerating development and ensuring reliable and affordable supply of an AIDS vaccine, an AMC would benefit developing country governments, vaccine developers, donors and, most importantly, the billions of people across Africa, Asia, and Latin America at risk of HIV infection.

An AMC would give developing country governments the authority to select the AIDS vaccines they prefer for their national circumstances. These governments would also benefit from stable and affordable long-term prices.

An AMC would allow firms to assure investors that there would be a viable market for their vaccine and could help answer criticisms that the large biopharmaceutical companies could do more for the poor. IAVI conducted extensive consultations with vaccine companies, including both the large multinationals and smaller biotech firms, and learned that a number of them felt that an AMC could help improve the investment climate for vaccine R&D.

For donors, an AMC would ensure that an AIDS vaccine would be available in low-income countries bearing the brunt of the AIDS epidemic. Importantly, donors would only pay when a vaccine is developed, leaving them free to spend their current funds on push mechanisms and vaccine-promoting efforts.

In fact, donors would realize substantial social returns on their investment in an AMC for AIDS vaccines. IAVI estimates that purchase of an AIDS vaccine under the terms of an AMC would cost between \$21 and \$67 per disability-adjusted life year (DALY) saved. (DALYs are a measure of years of

healthy life lost to illness and premature death.) This level of cost-effectiveness compares very favorably to other HIV/AIDS interventions and health sector investments.

Conclusions

An AIDS vaccine is urgently needed to end the epidemic. A properly designed and adequately funded Advance Market Commitment, implemented in conjunction with other incentive measures, could help speed up the development and delivery of a vaccine. IAVI's analysis suggests that an AMC for AIDS vaccines would be technically sound, credible to industry, and attractive to sponsors, developing countries and industry alike.

By removing obstacles to private sector involvement in AIDS vaccine development, an AMC would increase private investment to complement public and donor funding and encourage a more efficient transition of promising science from the laboratory to industry. An AMC would also make a vaccine readily available in the poor countries where it is needed most urgently. By guaranteeing a secure, long-term supply of vaccines at an affordable price, an AMC would speed adoption and ensure sustainability. Developing and supplying an AIDS vaccine will be expensive, but the gains, measured in tens of millions of lives savedⁱⁱⁱ and billions of dollars of economic benefits, would far outweigh the costs to governments and industry.

Notes and references

ⁱ HIV Vaccines and Microbicides Resource Tracking Working Group (IAVI, AIDS Vaccine Advocacy Coalition, Alliance for Microbicide Development, and UNAIDS). Tracking Funding for Preventive HIV Vaccine Research: Estimates of Annual Investments and Expenditures, 2000 to 2005. June 2005.

ⁱⁱ An Advance Market Commitment for AIDS Vaccines: Accelerating the Response from Industry. Consultation draft, October, 2005. International AIDS Vaccine Initiative, New York.

ⁱⁱⁱ Estimating the Global Impact of an AIDS Vaccine. IAVI Policy Research Working Paper #4. October 2005. International AIDS Vaccine Initiative, New York.

About IAVI: IAVI (www.iavi.org) is a global not-for-profit organization whose mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. IAVI's financial and in-kind supporters include the Bill & Melinda Gates, Rockefeller, Alfred P. Sloan and Starr foundations; the governments of Canada, Denmark, Ireland, the Netherlands, Norway, Sweden, the United Kingdom and the United States; multilateral organizations including the European Union and the World Bank; corporations such as BD (Becton, Dickinson & Co.), Continental Airlines and DHL; leading AIDS charities such as Crusaid, Deutsche AIDS Stiftung and the Until There's A Cure Foundation; and other private donors such as the Phoebe W. Haas Charitable Trust B.