Advance Market Commitments: A Policy to Stimulate Investment in Vaccines for Neglected Diseases

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Malaria, tuberculosis, and the strains of HIV common in Africa kill five million people each year, almost all of them in poor countries. Vaccines arguably offer the best hope for tackling these and other so-called “neglected” diseases concentrated in poor countries, yet, relative to the social need, there is a dearth of research and development (R&D) on such vaccines.

In this article, we outline the economic rationale for an “Advance Market Commitment” proposal, which the G8 Finance Ministers have decided to pilot in 2006. Under the proposal, donors would commit to help finance the purchase of vaccines against neglected diseases, if and when such vaccines are developed.

We first summarize the value of vaccines in addressing diseases in poor countries, and then outline two market failures which limit private sector investment in vaccines against neglected diseases. We argue that Advance Market Commitments could accelerate the development of new vaccines for neglected diseases by addressing each of these market failures, and describe how such commitments can be designed to facilitate widespread access to these vaccines if they are developed. Finally, we discuss evidence suggesting Advance Market Commitments would be a cost-effective way for donors to save more lives than would be saved by virtually any comparable health expenditure.

The Value of Vaccines in Poor Countries

Vaccines are perhaps the quintessential example of a cheap, easy-to-use technology that can have tremendous health impacts even in very poor countries with weak health-care infrastructures. Compared to drug treatments, vaccines require little training or expensive equipment for delivery, do not require diagnosis, can be taken in a few doses instead of needing longer-term regimens, and rarely have major side effects.

Despite the challenges facing health systems in many poor countries, three-quarters of the world’s children already receive a standard package of childhood vaccines through the
Expanded Programme on Immunization (EPI). The EPI vaccines save an estimated 3 million lives annually—almost 10,000 lives a day—and protect millions more from illness and permanent disability (Kim-Farley et al. 1992).

An expanded version of the standard EPI vaccine package is among the most cost-effective health interventions for poor countries—costing an estimated $16 to $22 per life-year gained in poor countries (World Bank 1993a, adjusted to 2005 prices).

At this cost per life-year saved, immunization is an extremely cost-effective intervention by any measure. In the US (Neumann et al. 2000) and the UK (Towse 2002), medical interventions are considered cost-effective at $50,000 or $100,000 per life-year saved. In poor countries, health interventions are generally considered extremely cost-effective if the cost per life-year saved is either less than $100 (World Bank 1993b) or less than a country’s annual per capita income (GAVI 2004). Vaccination is also highly cost-effective compared with other health interventions for poor countries; for example, anti-retroviral drug treatments for HIV cost a great deal more than $100 per life-year saved (Creese et al. 2002). As we shall see, vaccines purchased under an Advance Market Commitment are estimated to cost as little as $15-$30 per life-year saved.

**Market Failures for Vaccines for Neglected Diseases**

Poor countries have benefited enormously from the EPI vaccines, but these vaccines were developed largely in response to the prospect of valuable sales in rich-country markets. In the case of neglected diseases, there are no such market incentives, and so, as argued by Michael Kremer and Rachel Glennerster in their recent book *Strong Medicine*, private firms lack incentives to undertake R&D on these diseases. One indicator of this lack of investment is that of the 1,233 drugs licensed worldwide between 1975 and 1997, only four were developed by commercial pharmaceutical firms specifically for tropical diseases of humans (Pécoul et al. 1999).

One reason for the lack of incentives for R&D on vaccines for neglected diseases is that the potential consumers of these vaccines (that is, individuals and their governments) are poor. In a technical sense, this is not a market failure. But there are two key market failures that limit R&D on vaccines needed primarily in poor countries.

First, governments and other purchasers of vaccines face *time-inconsistent incentives*. Before a vaccine is developed, governments want vaccine producers to invest in R&D and to establish large-scale production facilities. But once a vaccine has been developed, governments want the vaccine to be sold at the lowest possible price, to allow limited budgets to purchase the vaccine for as many individuals as possible. Governments are the main purchasers of vaccines, and vaccines used in poor countries are purchased through a small number of international agencies (such as UNICEF). These institutions can use their dominant purchasing power and regulatory control (as well as the power of public opinion) to drive prices down, once vaccines have been developed—thus making it difficult for firms to recoup their R&D investments. Private firms anticipate this time-inconsistent

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1 “Life-years,” throughout this paper, refer to disability-adjusted life-years (DALYs).
behavior, which thus reduces incentives for firms to make the necessary R&D investments in the first place.

Second, R&D in new medicines is a global public good. Because the benefits of scientific advances on (for example) an HIV vaccine would spill over to many countries, none of the many small countries that would benefit from such a vaccine has an incentive to unilaterally encourage the development of a vaccine. While intellectual property rights create incentives for innovation, granting private firms temporary market exclusivity increases dynamic benefits (that is, creates incentives for innovation) at the cost of static welfare (in the form of reduced access to medicines).

The goals of creating incentives for R&D on new medicines (which requires high prices) and ensuring wide access to medicines once developed (where low prices enable limited budgets to go further) are often pitted against each other. However, as we will explain, Advance Market Commitments can de-couple these goals and promote both effectively.

**Advance Market Commitments: Addressing Market Failures and Facilitating Access to New Vaccines**

One proposal which seeks to address both of these market failures is an Advance Market Commitment. A Working Group convened by the Center for Global Development, with financial support from the Bill & Melinda Gates Foundation, explored the details of how this proposal could be implemented (Barder et al. 2005).

Under an Advance Market Committee, sponsors would make a legally-binding commitment to fully or partially finance the purchase of qualifying vaccines for poor countries, at a pre-specified price, up to a fixed number of individuals immunized. Poor countries would decide whether to purchase a vaccine, and they (or donors, on their behalf) would pay a low price (say, $1) per person immunized. Sponsors would then top up this low price to a higher, subsidized price (say, $15 per person immunized), which would provide market returns to the vaccine developer comparable to those of other, average-revenue pharmaceutical products. Once the pre-determined number of treatments (say, 200 million persons immunized) had been purchased at the high price, manufacturers would then be contractually obliged either to sell further treatments at a low, affordable price in the long-term, or to license their technology to other manufacturers. If no vaccine were to be developed, no donor funds would be spent.

This Advance Market Commitment approach addresses the two market failures identified above:

- First, it addresses the time inconsistency market failure by pre-committing governments and other vaccine purchasers not to negotiate down the price once a vaccine has been developed and productive capacity has been built.
- Second, it addresses the public good market failure by remunerating investment in R&D without restricting access to the product. The producer receives a high price that enables recovery of its R&D investment, while the purchaser pays an affordable price that reflects the low marginal cost of producing vaccines.
For diseases prevalent in rich countries, public and philanthropic resources fund basic scientific and clinical research on new medicines, while the prospect of profits in rich country markets provides incentives for private sector firms to transfer basic research into useable products. In the case of neglected diseases, the second half of this pipeline is currently missing. Advance Market Commitments, complementing public investment in R&D, would replicate, for neglected diseases, the mixture of public and private financing which exists for diseases prevalent in rich countries.

A key issue from the perspective of improving public health in developing countries is that policies should not only provide incentives for innovation, but also link these incentives to access to products once they are developed. In recent years, there have been long delays in introducing new vaccines on a broad scale in poor countries; for example, even as much as fourteen years after the introduction of the *Haemophilus influenzae* B (Hib) vaccine in the US and Europe, less than ten percent of infants in the world’s poorest seventy-five countries were routinely receiving this the vaccine (Levine et al. 2004). As a result of these delays, more than two million individuals in poor countries die annually from vaccine-preventable diseases (www.vaccinealliance.org, quoting 2005 WHO estimates).

A key advantage of advance purchase commitments is that they can be structured to ensure that vaccines—once developed—are made available quickly and affordably to individuals in poor countries. In the short-term, access to the vaccine in countries that need it most is facilitated through donor purchasers at the higher, pre-specified purchase price per person immunized. In the long-term, financially sustainable access to these technologies is facilitated by the contractual requirement on developers to, after the high-price purchases have been made, either drop the price to a low level (close to marginal cost), or to license their technology to other manufacturers.

**COST-EFFECTIVENESS OF AN ADVANCE MARKET COMMITMENT**

Under an Advance Market Commitment, donor funds are spent only if desired products are developed. In this section we discuss how, if desired vaccines are indeed developed, an Advance Market Commitment would be an extremely cost-effective expenditure from a public health perspective.

The specified price and quantity of vaccine that would be purchased at the higher, subsidized price together determine what size of market would be generated under an Advance Market Commitment. One reasonable way of setting this market size is to examine the realized revenues of drugs and vaccines that have, in the past, been developed by private firms — under the rationale that the expected market sizes of these medicines must have been sufficient, in the past, to spur private sector innovation.

A recent study by Ernst Berndt and colleagues (2005) calculate that the mean revenues for a sample of new drugs developed during the 1990s, adjusted down for lower marketing expenditures, had a net present value of approximately $3.1 billion in 2004 prices. Berndt and colleagues outline how this estimate can be combined with estimates of likely revenues from private markets—such
as travelers, the military, and middle income countries—to determine the size of the donor commitment that would provide an overall market size comparable to the realized revenues of existing medicines.

Based on the cost per life-year saved as a result of vaccines purchased under the Advance Market Commitment, the Commitment would be extremely cost-effective. Berndt and colleagues estimate that creating a $3.1 billion market for a malaria, HIV, or tuberculosis vaccine would cost approximately $15, $17, or $30 per life-year saved, respectively. These expenditures would be among the most cost-effective development interventions, and Berndt and colleagues document that Advance Market Commitments would be cost-effective within a wide range of possible commitment sizes. Smaller commitments could also be used to scale up the supply of vaccines for which the R&D is already largely complete—such as pneumococcal or rotavirus.

### Conclusion

Though vaccines for diseases concentrated in poor countries hold enormous potential social benefits, two key market failures reduce incentives for R&D on such vaccines. Advance Market Commitments, of the sort now being considered by the G8 Finance Ministers, could accelerate the development of new vaccines for neglected diseases by addressing both market failures, and can be designed so as to facilitate widespread access to these vaccines, if they are developed. Such commitments would provide a highly cost-effective, market-led, results-based way for donors to save more lives than would be possible with virtually any comparable health expenditure.

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### References and Further Reading


