



3

A market
not a prize

Chapter at a glance

- The idea of making an advance purchase commitment has been discussed for several years, but the details of how it could be implemented have not been worked out. Our Working Group was established to determine whether a commitment could be designed that could be implemented and that would be effective and good value for money.
- We propose a framework for an advance market commitment that would bring new impetus to R&D in vaccines for diseases occurring mainly in developing countries. The arrangements are intended to create a market analogous to the market for medicines in affluent countries.
- Our proposal is for a market not a prize. There is no winner-take-all.

By underwriting the purchase of vaccines, donors create incentives for firms to compete to bring products to market quickly. Better products can compete for market share, as they can in affluent markets.

- Advance market commitments would accelerate the production and availability of late stage products (rotavirus and pneumococcus vaccines) as well as the R&D and availability of early stage products (vaccines for malaria, HIV, tuberculosis).
- We have set out a quantified example for a malaria vaccine. A market worth \$3 billion would create incentives for commercial investment to accelerate R&D, and the purchase of the vaccines at \$15 per dose for the first

200 million people would provide remarkable value for money for donors—less than \$15 per life-year saved.

- The commitment has been designed to meet the needs of all stakeholders. It would be of significant benefit to donors, industry and most of all the people in developing countries.
- An advance market commitment would fill an important gap in our arrangements for R&D for global health challenges. But our enthusiasm for it does not diminish the importance we attach to a range of other measures that we can and should take in the near term to save lives immediately and to enhance the prospect of developing new medicines that are essential for developing countries.

A practical advance market commitment

We have developed a new proposal for an advance market commitment that responds to the needs of donors, industry and the public health community. Unlike some alternative “pull” proposals, as summarized in chapter 2, this commitment does not create a prize to reward R&D.¹ Instead it creates a market, broadly reproducing the market incentives to develop medicines for affluent countries (box 3.1).

We worked with experts in public policy, law, economics, health and scientific research, and we consulted potential sponsors and firms in the pharmaceutical and biotech sectors, in developed countries

and in India. Our aim has been to determine whether it would be possible, in practice, for sponsors to make a commitment that would be effective in accelerating the development of new vaccines.

The advance market commitment proposed here aims to mimic the size and certainty of a market for medicines in affluent countries, and so create similar incentives for commercial investment in R&D. As well as accelerating the development of new vaccines, this approach would create incentives for rapid, large-scale production and provide the funds needed to buy the vaccines when they are available.

We conclude that an advance market commitment is indeed practical and that it would be effective. This chapter outlines the main features of how a commitment could work, summarizing the implications for the main stakeholders. The rest of the report considers the design of the commitment and its likely impact in more detail.

Box 3.1 The main features of the commitment

- A technical specification—in terms of outputs—required of a new vaccine.
- A minimum price guarantee, available up to a fixed number of treatments.
- Guaranteed co-payments on products meeting the specification, paid by sponsors, permitting eligible countries to buy vaccines at affordable prices, for a maximum number of treatments. (For example, the price might be fixed at \$15 per treatment, with the developing country perhaps paying \$1 and the sponsors paying \$14, for up to 200 million treatments).
- An overall market size of about \$3 billion—enough to make it worthwhile for firms with scientific opportunities to undertake research and development, but well below the social value of the vaccine.
- An independent adjudication committee to oversee the arrangements and commitments enforceable under the law.
- An obligation on the producer to produce and sell further treatments in eligible countries at a fixed, affordable price, in return for having had the advantage of sales at the initial higher price.
- Total sales of each qualifying product would depend on demand from developing countries. This in turn would depend on the effectiveness of the vaccine and the alternatives available.

Commitments for late-stage and early-stage products

The idea of an advance market commitment is this: because the potential market is made more valuable and more certain, firms will make investment decisions that accelerate the development of products for developing countries and invest in manufacturing capacity to produce larger volumes. This analysis applies both to late-stage products (those in the final stages of regulatory approval and for which manufacturing capacity is being established, such as rotavirus vaccine) and to early-stage products (those requiring scientific progress and extensive testing of candidate medicines, such as malaria or HIV vaccines).

The impact of an advance market commitment for late-stage products

The rationale for using an advance market commitment for late-stage products is that, even after a product has proven successful in clinical trials, the low and uncertain value of demand from developing countries continues to affect the firm’s investment decisions, which will determine the speed, volume and price of making the vaccine available.

The firm’s decisions that will be affected by market prospects include:

- Whether and how quickly to conduct clinical trials in developing countries.²

- Whether to make a version of the product with the specification and presentation suitable for developing countries.
- The speed of obtaining regulatory approval for developing countries.
- Whether enough production capacity is put in place for large-volume, low-unit-cost production.
- The price of the product in developing countries.

Each of these decisions is critically affected by the prospects for future demand from developing countries, by the predictability of that demand and by the price the firm expects for sales to those markets. Experience has shown that, in the absence of reliable demand for developing-country markets, firms prefer to focus first on producing new vaccines in low volumes and selling them mainly into high-value, developed-country markets. When high-value market needs have been met, and as the competition from lower cost generics producers becomes more likely, producers move toward the high-volume, low-cost production needed for the developing world.

Using an advance market commitment for late-stage products would:

- Accelerate the availability of new vaccines in large quantities and at low prices, adapted as necessary for use in developing countries, creating a virtuous circle (figure 3.1).

- Accelerate uptake of new vaccines by guaranteeing an affordable long-term price once the commitment is exhausted.
- Ensure affordable access for people who need vaccines.
- Add to the credibility of the commitment for early-stage products and so accelerate the development of new vaccines.

The impact of an advance market commitment for early-stage products

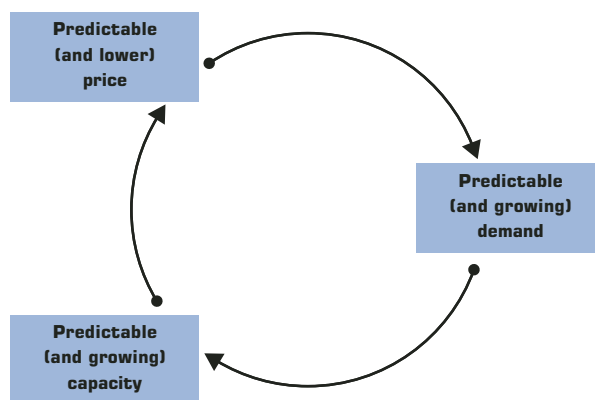
Firms cannot make substantial investments in R&D if the market for the final product is expected to be small and risky. The pharmaceutical industry has to decide where to invest its resources based on its expectation of success and its estimate of the value of the market. As long as the market for vaccines for developing countries remains small, there is little incentive for commercial investment in vaccines for diseases concentrated in developing countries.

The case for an advance market commitment for early-stage products is that it would create an expected return from developing-country markets large enough for some pharmaceutical firms to increase their investment in R&D in these products.

In practice, pharmaceutical companies invest in R&D through a combination of work in their own laboratories, contract research, licensing intellectual property from others and acquiring or entering joint ventures with other pharmaceutical and biotech companies. These investments are made by the company on the basis of the long-term expected returns from market sales of a new product. Both empirical evidence and theory tell us that commercial investment in R&D is strongly influenced by the size of the expected market. In one study an increase of 1% in the potential market size for a drug category led to a 4–6% increase in the number of new drugs in that category.³

If an advance market commitment creates incentives for pharmaceutical companies to invest in R&D, those companies will in turn create a range of more immediate incentives within the R&D community. The market value of discoveries relating to global health issues will rise. More research contracts will be signed. Venture capitalists will increase investment in biotech. In this way, the incentive created by the establishment of a final market will “reach back” to create more immediate incentives for the intermediate research outputs required. Biotech companies

Figure 3.1
A virtuous circle of demand, capacity and price



and their investors will not have to invest on the basis of returns that are likely to take 10 or more years to materialize. If they are successful, they can expect to license their products to pharmaceutical companies much faster than that. The basis for our expectation that this will work in practice is that this is precisely how collaboration on R&D on products for affluent markets works. There may be room for improvement in the way these contracts are created. But the functioning of these markets gives us good reason to believe that a healthy market for intermediate outputs would follow from a suitable advance market commitment for the end product.

In addition to creating incentives for R&D, an early-stage advance market commitment would have the same benefits as a late-stage advance market commitment in that it would create incentives for high-volume, low-unit-cost production and ensure financing for access to these vaccines.

Design differences between early-stage and late-stage commitments

The main difference between the design of an early-stage commitment and a late-stage commitment is that the contract for late-stage products would likely be with specific named suppliers while the contract for early-stage products would initially be an open framework agreement, with firms competing for the right to benefit from the guaranteed price in the second contract.

We set out below examples of how an advance market commitment could work for malaria (an early-stage product) and pneumococcus or rotavirus (late-stage products). These examples were developed to focus and discipline the thinking of the Working Group. They do not necessarily imply that these should be the diseases for which a commitment would be most appropriate.

A sample advance market commitment for malaria

We looked at malaria as an example of a specific case where advance contracting is needed to complement ongoing public and philanthropic funding efforts to accelerate development of an essential early-stage vaccine. We are particularly grateful to the staff of the Malaria Vaccine Initiative for contributions to this analysis, though they are not responsible for the analyses or the conclusions.

The need for advance contracting for malaria

The World Health Organization estimates that at least 2.3 billion people are at risk from malaria and at least 1 million people, possibly as many as 2 million, die of the disease each year.⁴ It is possible that estimates of the burden of diseases will be increased during 2005 as a result of new analysis.

More than half of all malaria deaths are among children in Sub-Saharan Africa. Though estimates of economic impact are necessarily based on imperfect information and multiple assumptions, some studies have estimated that malaria may reduce average economic growth in Africa by half a percentage point a year or more.⁵

Malaria transmission occurs through the bite of an infected anopheles mosquito. Parasites multiply in the liver and red blood cells of affected people. Symptoms include fever, headache, muscular aches and weakness, vomiting and diarrhea. The disease may result in long-term debilitation or be fatal if untreated or treated with ineffective drugs.

Malaria was almost completely eradicated from North America and Europe using insecticides and environmental management. But the same can not be achieved elsewhere, for a combination of climatic and biological reasons. Africa's temperatures, mosquito species and humidity give the continent the highest malaria burden. Africa's malaria mosquitoes almost exclusively bite humans, which enhances the chain of human-to-human transmission. The combination of high temperatures, sufficient rainfall for mosquito breeding and human-biting anopheles mosquitoes make it much more difficult to control the disease than elsewhere. In addition, there is increasingly widespread resistance to malaria drugs and insecticides. Given that childhood vaccinations already reach more than 75% of the world's children, and the immense challenge of controlling the mosquito vector, an effective malaria vaccine suitable for young children, which could be delivered through the EPI schedule, and for women of childbearing age would be a major and much needed addition to the prevention strategies such as insecticide-treated bednets and vector control.

In addition to public funding through organizations such as NIH, two initiatives provide "push" support for malaria vaccines:

- The European Malaria Vaccine Initiative, founded in 1998 by the European Union, provides a mechanism to facilitate the development of candidate molecules through

the post-validation phase of nationally and internationally funded malaria vaccine R&D—and to see candidate molecules through to limited clinical trials in close collaboration with the African Malaria Network Trust. This is intended to ensure that appropriate vaccines are developed as quickly as possible.

- The Malaria Vaccine Initiative (MVI) was founded at the Program for Appropriate Technology in Health in 1999 with funding from the Bill & Melinda Gates Foundation. It has received total funding to date of \$150 million. Of the 20 vaccine candidates MVI is supporting, 8 have entered clinical development (Phase I or Phase II clinical trials).

Malaria vaccine research has made painstaking gains over many years. With its multistage life cycle, malaria presents a unique and complex vaccine challenge. There are no vaccines on the market, but three types of vaccines are in development, targeting points in the malaria life cycle: pre-erythrocytic, blood stage and transmission stage.

In October 2004 researchers reported preliminary results from the largest vaccine efficacy trial ever conducted in Africa.⁶ This Phase II trial in Mozambique of a vaccine⁷ was supported by MVI and GSK Biologicals. The trial found vaccine efficacy of 30% against clinical malaria attacks, 45% against primary infection with *Plasmodium falciparum* and 58% against severe disease. Further progress on this candidate vaccine will depend, however, on there being sufficient investment. There may be other candidate vaccines that would be as effective or more so but for which there are not sufficient resources to conduct trials.

While collaboration between philanthropic foundations and the private sector has had a significant impact on malaria vaccine development, a complementary mechanism to enhance the market is also needed for at least two reasons, as noted in chapter 2. First, more research is needed in a wider range of candidate vaccines to identify the best opportunities and accelerate progress on those ideas. Experts are in broad agreement that the first malaria vaccine will be only partially efficacious, and efforts will be required to develop superior products as new knowledge about the immune response is obtained. The most successful vaccines are likely to be second or third generation.

Second, today's funds are not sufficient to pursue enough of the possible avenues of research. After Phase II trials, the cost of developing and testing a candidate vaccine in humans escalate,

and progress toward commercialization will require the prospect of a sufficient market to make it economically viable. Even if MVI put all its funding into a single candidate, and if that proved a success, there would not be enough money to bring that one candidate to licensure, nor into full-scale production.

Proposed contract structure for malaria

The proposed structure for an advance market contract for malaria is set out in draft contract terms sheets in appendix F (the Framework Agreement) and appendix G (the Guarantee Agreement). These drafts are annotated with rationales and explanations.

The main characteristics of the commitment are as follows:

- The sponsors will make a legally binding promise to pay \$14 of the cost of up to 200 million treatments purchased, at a guaranteed price of \$15 per treatment (adjusted for inflation).
- Recipient countries will pay \$1 per treatment. This can be subsidized by donor funding at the time.
- In return, firms will guarantee to provide further treatments (after the 200 million) at a sustainable base price, reflecting the cost of production, about \$1 per treatment.
- An Independent Adjudication Committee will be established to determine whether the technical specification of the vaccine had been met.
- If a firm develops a subsequent, superior product (as agreed by the Independent Adjudication Committee), that product will also be eligible for the price guarantee (the price guarantee would apply to the first 200 million treatments bought, shared among the eligible products according to demand).

This offer will create an expected market of some \$3 billion, approximately the average revenues for which new pharmaceuticals have been developed for affluent countries (see chapter 5). A commitment of this magnitude should attract some pharmaceutical companies to invest in R&D.

It is important to remember that the figures indicated above were developed as a working example, and we are not making specific recommendations. Further work and expert consultation would be required to set such parameters, in the event that a sponsor wished to create an advance market commitment.

Under very conservative assumptions—for example, ignoring the benefits of herd immunity, and the savings from health care

costs averted—we estimate that the cost will be about \$15 per disability-adjusted life year (DALY) saved (discounted in 2004 dollars), making vaccine purchases under the program one of the world's most cost-effective development interventions (box 3.2 and table 3.1). Once the commitment of 200 million doses has expired, the cost of the vaccine will fall to the sustainable long-run price.

Advance market commitments for rotavirus and pneumococcus

Recent developments in a vaccine for rotavirus

Rotavirus is the most common cause of severe dehydrating diarrhea among children worldwide. Each year it causes more than 100 million cases of disease, 25 million clinic visits and between 350,000 and 590,000 deaths in children ages five or younger. Nearly every

child in the world is exposed to rotavirus before reaching age five, but, because of lack of access to health care, the children who die of rotavirus are in the very poorest countries.

At present, the only treatment for rotavirus involves preventing dehydration by providing fluids and salts until the disease runs its course; neither antibiotics nor other drugs can cure rotavirus.

A vaccine has recently been licensed in Mexico: a human-derived, monovalent, live, attenuated two-to-three-dose oral vaccine developed by Avant Immunotherapeutics and licensed to GSK Biologicals. This product has undergone Phase III trials in Latin America and is in Phase II trials in Bangladesh, Singapore and South Africa. A second vaccine is close to licensure: a bovine-human reassortant, pentavalent, live-attenuated three-dose oral vaccine developed by Merck is now in Phase III trials in Central and South America. In addition, Biovix has recently indicated that it will pursue licensing for a rotavirus vaccine that had previously been sold in the U.S. market but was withdrawn for fears of adverse effects.⁹

Box 3.2 What is a DALY?

A disability-adjusted life year, or DALY, is a unit used for measuring both the global burden of disease and the effectiveness of health intervention. DALYs were introduced as a unit of measurement in the World Development Report 1993: Investing in Health (World Bank 1993), and in 1996 a joint effort by WHO, the World Bank and the Harvard School of Public Health produced The Global Burden of Disease (Murray and Lopez 1996) in which the DALY methodology and findings were presented in more detail.

DALYs are intended to combine losses from premature death, defined as the differences between actual age at death and life expectancy at that age in a low-mortality population, and losses of healthy life resulting from disability. Because the benefits of all health interventions can be measured this way, DALYs allow comparisons between different interventions and overcome some of the problems associated with using analysis relevant only for specific conditions or that relies on placing a monetary value on saving lives.

Table 3.1
Some estimates of the cost per DALY of development interventions

Intervention	Cost per DALY (\$)ª
Malaria vaccine under advance market commitment of \$15 per treatment (conservative estimate)	15
Condom distribution	12–99
Integrated management of childhood illness	30–100
Tuberculosis prevention	169–288
Antiretroviral therapy for HIV	1,100–1,800 ^b
Family planning	20–30 ^c
Prenatal and delivery care	30–50
Water supply (village pump)	94
Malaria bednets	19–85
Malaria residual spraying	16–19

a. Data not adjusted for inflation. Some interventions may have changed in price substantially since these studies.

b. The cost of antiretroviral therapy has fallen since this study.

Source: Creese and others (2002); Murray and Lopez (1996); Cairncross and Valdmanis (2004); Hanson and others (2003).

Second-generation products—at the Lanzhou Institute in China, Bharat Biotech International in India, BioFarma in Indonesia and NIH—are in progress but several years behind.

The Rotavirus ADIP was established by GAVI to lay the foundation for rapid introduction and sustainable supply of first-generation rotavirus vaccines. One of the most important elements of this project is to secure the supply of affordable vaccines in predictable quantities.

Recent developments in a vaccine for pneumococcus

More children die each year from pneumonia than from any other disease—even more than malaria or AIDS—and nearly all these deaths occur in the world’s poorest countries.¹⁰ Unlike malaria and AIDS, vaccines are available to prevent these deaths. But without a coordinated effort and forward planning, it will probably take 20 years or more for these vaccines to reach even half the children in the world’s poorest countries—in part because of the high cost but also because of the lack of reliable and predictable demand.

A vaccine against the second-leading cause of bacterial pneumonia deaths—a bacterium called Hib (*Haemophilus influenzae* type B)—has been available since the late 1980s. It has been widely used in all wealthy countries, and as a result Hib disease has nearly disappeared altogether in those countries. But in 2002—15 years after the vaccine was first used in wealthy countries—fewer than 15% of the world’s poorest children were receiving the vaccine.

The leading cause of bacterial pneumonia deaths—a bacterium called *Streptococcus pneumoniae* (pneumococcus)—is now preventable by immunization with a vaccine very similar to the Hib vaccine. In 2000 the United States licensed a pneumococcal conjugate vaccine for prevention of severe pneumococcal infections in infants and young children. Like the Hib conjugate vaccines, this vaccine has proven to be safe and very effective in randomized clinical trials. In studies in Finland and the United States, the vaccine was shown to significantly reduce the incidence of severe pneumococcal infections, such as meningitis, pneumonia and septicemia, and to prevent ear infections. Since 2000 it has been routinely used in the United States and other wealthy countries but not in the developed world.

GAVI’s Pneumococcal ADIP aims to increase access to new life-saving pneumococcal vaccines and ultimately prevent

millions of deaths by getting vaccines where they are needed most, faster than ever. The ADIP has articulated a three-part mission: to establish, communicate and deliver the value of existing (and next-generation) pneumococcal vaccines. The ADIP is currently funding disease surveillance networks, clinical trials in target populations and cost-effectiveness studies. An important part of its mission will depend on delivering products to GAVI’s target countries at a price and volume that they can afford.

Goals of an advance market commitment for pneumococcus and rotavirus

Against this background, an advance market commitment will:

- Ensure that first-generation products are tested in the populations that need them most.
- Provide an incentive for suppliers to produce the vaccine in quantities that will meet the needs of the developing world over time.
- Influence decisions about the presentation and characteristics of the product so that it better meets the needs of the developing world.
- Influence the long-term pricing of the product.

There is a clear need for advance market commitments to secure the right profile, price and supply of these vaccines. Combined with more concerted demand-side interventions, this will be instrumental in shortening the gap of 10–15 years seen in the introduction of recent vaccines, such as hepatitis B and Hib vaccine. The ADIPs for pneumococcus and rotavirus are important steps in this direction and, while they do not yet have the mandate to negotiate such contracts, they consider long-term advance contracting as potentially critical to achieving their mission.

Proposed contract structure for a late-stage product

We considered an advance contract for late-stage products, which could be applied to vaccines for rotavirus and pneumococcus.

Unlike the early-stage contract, the late-stage contract in these cases will be with one or more specific suppliers. (The Framework Agreement stage included in the early stage contracts would be unnecessary.) The contract with the supplier will be very similar to the Guarantee Agreement of an early-stage product.

The main characteristics of the agreement will be as follows:

- The sponsor commits to pay a relatively high price for a course of immunization, up to a certain number (say, the first 100 million courses).
- In return for receiving the higher price at first, the supplier guarantees to provide vaccine indefinitely to qualifying countries, at a much lower price. The lower, long-run price would be set at a reasonable mark-up over the estimated production cost.
- If the supplier does not fulfill demand at this lower price, given adequate notice, the contract would provide for damages, or require that a restricted license be given to the sponsor or to the public domain (to supply only Vaccine Fund–eligible countries).
- The contract might commit the sponsor to guarantee some minimum order, but after the initial volume is reached, the vaccine may have to compete against other products, so there would still be an incentive for other firms to enter if they could produce superior products or manufacture more cheaply.
- The contract could be signed prior to regulatory approval, but it is conditional on regulatory approval and the expected performance of the vaccine.

There are a number of advantages to this approach for developing countries, for suppliers and for sponsors.

- The supplier obtains a more predictable revenue stream.
- The supplier has incentives to install capacity quickly, since the net present value of its revenue will be greater the faster the first 100 million people are immunized.
- There is no long-term commitment to buy the product if a superior product is developed later.
- Both suppliers and consumers are better off than they would be with a system of short-run contracts with a single supplier. Uncertainty will be reduced for both. If prices are chosen appropriately, overall revenue and profits will increase, making the supplier better off. But the number of immunizations will also increase significantly, lowering the average price per person immunized and improving cost-effectiveness.
- The contract ensures sustainability for countries and donors in the long run. Because countries know that they will have access to the vaccine at affordable prices over the long run, they can be more confident in adding it to their immunization

schedules without fear that they will not be able to afford the vaccine later and will have to reverse their strategy.

- The contract sets a good precedent for advance market commitments aimed at stimulating investment in early-stage products—and builds confidence in that commitment mechanism.

Risks and benefits of an advance market commitment

We have based our design of the advance market commitment on economic principles, practical realities and extensive consultation with donors, industry and the public health community. We set out here how the mechanism we have designed meets the principal objectives of the main stakeholders and the risks and challenges that the commitment must address.

Benefits for donors

- The commitment would likely accelerate the development of new vaccines, which are one of the most cost-effective ways to tackle poverty, improve the health of vulnerable populations and meet the Millennium Development Goals.
- There will be a cost to sponsors only if the program succeeds and a new vaccine is developed. If no vaccine is developed, there is no significant cost to the sponsors. If a vaccine is developed, it will save millions of lives at very low cost. The commitment is payment-for-results.¹¹
- If a vaccine is developed, it will be available rapidly to people who need it, in contrast to recent experience with new vaccines.
- Vaccine purchases under the commitment will be a highly cost-effective use of aid in comparison with other interventions.
- Existing and future donor support for R&D investment will be more productive as a result of complementary private investment.
- Donors will increase the productivity of their likely future expenditure by making it predictable.
- The commitment is sustainable; once the advance market at a guaranteed price has been exhausted, the suppliers will provide further vaccines at a guaranteed low price, unlike open-ended commitments to subsidize purchases indefinitely.

- Aid spending on R&D for, and delivery of, vaccines is low risk, with few opportunities for corruption and rent-seeking.

Points for donors to watch

- It is important not to be locked into a contract to spend \$3 billion on a vaccine that is not needed, for reasons unforeseen at the time the commitment is made. *The commitment to create a market, rather than a prize, protects donors by ensuring that their commitment is to underwrite the cost of vaccines for which there is actually demand.*
- The commitment should be structured in a way that does not require donors to move money from current priorities, including health R&D, so that it is available for uncertain future obligations to purchase a vaccine. *A commitment to purchase a vaccine if and when it is available does not score in public spending until the vaccine is supplied. In the meantime, existing expenditure priorities can continue to be funded (chapter 7 explains in more detail).*
- Donors should avoid unnecessarily driving up the price of vaccines. *The structure of the contract ensures that the higher prices paid for the initial doses leads more quickly to long-term sustainable prices, keeping long run costs down; by contrast, under current arrangements, increased funding of vaccine purchases is likely to push up prices. Furthermore, compared with a cost-plus arrangement, an advance market commitment creates stronger incentives to keep the costs of production as low as possible to recoup the highest profit.*
- Donors should not overpay for R&D costs of vaccine development. *We don't know for certain what it will cost to develop a new vaccine. Creating commercial incentives for competition in the most expensive phases of the process will allow firms to make judgments about the best use of available resources. A larger donor commitment will encourage more competition and faster development of a new vaccine—which would be money well spent.*

Benefits for industry

- The commitment would extend the overall size of the market in which firms operate, creating opportunities to expand the scope of their business and providing a new path for growth.

- The commitment significantly reduces the risk that, if a life-saving health product is invented, it will be subject to compulsory licensing, or that the firm will be forced to sell it at a loss, either because of pressure of public opinion or because of the purchasing power of public procurement.
- The advance market commitment creates a risk-reward structure that firms are already familiar with and that puts these decisions in the same framework as other investments: they will be rewarded if they bring a product to market that governments want to buy.
- Unlike many of the alternative proposals for increasing R&D in diseases concentrated in developing countries, the advance market commitment addresses the access issue without weakening incentives or dismantling the system of intellectual property rights.
- The opportunity for commercially driven investment in vaccines reduces the risk of growing activism and anger directed at pharmaceutical companies because of the perceived lack of investment in neglected diseases—and because of the need to charge prices that make essential medicines unaffordable to the very poor.
- The commitment does not reduce donor resources available for the purchase of existing vaccines and drugs or for the investment in health systems, which increase demand for existing products.

Points for industry to watch

- The donors must not be able to renege on their commitment when a vaccine is developed that meets the technical specification. *The advance market commitment would be legally binding and enforceable in the courts. The Independent Adjudication Committee, which decides if a vaccine qualifies for the co-payment guarantee, is an important safeguard for industry, and industry should pay close attention to its composition, funding and organizational arrangements.*
- The commitment must not allow copy products to take the guaranteed market. *The Independent Adjudication Committee is responsible for ensuring that second and subsequent products that meet the technical specification are superior, and not merely generic copies.*
- A substantial portion of demand risk remains with the firm. *The market guarantee removes the risk relating to the*

poverty of the final consumer and the incentives of the public purchaser to secure the best possible price once the R&D costs are sunk. The demand risks that (rightly) remain with firms relate to the quality of the product, the quality of competitors and the speed of making the product available. These are risks that firms are best placed to manage—and risks that firms are used to bearing in affluent markets. The two-stage pricing structure—with bigger returns early on—greatly reduces the risk to firms and encourages early innovation. As shown in chapter 4, even if uptake is somewhat slow, the risk to firms is still much lower than it would be with a constant price.

- The creation of a market for the final product may not be enough to create incentives for intermediate R&D. *A market of this size, combined with the response from the pharmaceutical industry, has been enough to spur the biotech sector and venture capitalist investment in R&D for pharmaceuticals for affluent markets.*

Benefits for developing countries

- An advance market commitment is likely significantly to accelerate the development of essential vaccines, the best hope for sustainably improving the health of people in poor countries.
- The commitment ensures that, if a new vaccine is developed, it will be rapidly available in developing countries at an affordable price, unlike previous vaccines, which have been available only after a long delay.
- There are many very poor people in countries that are not currently eligible for Vaccine Fund support, for whom it is a priority to increase affordable access to vaccines. For countries that are not eligible for vaccines purchased under the advance market commitment there would still be considerable benefits arising from the advance market commitment, because significantly more new vaccines would be likely to be produced.
- Experts and decisionmakers from developing countries could participate in the initial establishment of the technical specifications, ensuring that products developed are appropriate to in-country conditions.
- The commitment offers open competition for developing-country biotechs and larger firms to compete to provide new

vaccines, perhaps through joint ventures with multinational pharmaceutical companies.

- There are no adverse macroeconomic or exchange rate effects for developing countries as a result of increased development assistance provided in the form of co-payments for imported pharmaceuticals.

Points for developing countries to watch

- The contract must allow superior products to be bought if they are developed. *Because this is a market not a prize, developing countries can switch demand to superior products that qualify for the guarantee as soon as they are available.*
- Developing countries will have to make some payments for the vaccines. *The payments will be small, because donors bear most of the guaranteed price. The developing countries' contribution ensures that they are the ultimate customers for the vaccines and can decide their priorities. As is the case today, recipient countries can seek donor assistance for their contributions when the vaccines are available.*
- The long-term price must be affordable. *The commitment ensures that vaccines will be available to all eligible countries at affordable prices in the long term (and that the higher price will be subsidized by donors in the meantime). This ensures that vaccine programs are sustainable in the long run, and so enables governments to expand their vaccination programs with confidence.*

An advance market commitment is only a partial solution

Theory and evidence predict that an advance market commitment would substantially increase commercial investment in R&D on vaccines for developing countries and that it would accelerate the development and availability of new vaccines.

But much else can and should be done to accelerate R&D and improve access to vaccines. Steps that could make a substantial contribution include:

- Greater donor funding of the purchase of existing vaccines and drugs for diseases in developing countries, which will save many lives immediately and increase the perceived value of the market in the future.

- Increased upfront donor funding of R&D into health conditions concentrated in developing countries, including investment in R&D for new vaccines.
- Improved demand forecasting to enable producers to invest in manufacturing capacity of an appropriate size.

Advance market commitments are an additional tool, focused on an important deficiency in the current arrangements for the development of new vaccines: the lack of adequate incentives for commercial investment. We consider that commercial engagement in the development of new vaccines is critical for the rapid development and production of new vaccines. We believe that advance market commitments can and will make a substantial contribution to accelerating new vaccines and that they should be a high priority for donors and the industry. But in advocating their rapid introduction we are mindful of the need not to lose sight of the importance of other steps that would also improve the effectiveness of the market for vaccines.