



**5**  
\$3 billion  
per disease

# Chapter at a glance

- Our aim is to set a market size large enough to attract serious commercial investment from several pharmaceutical companies that see technological opportunities, while ensuring that the cost of the vaccines purchased is less than the social value and better value for money than alternative uses for the funds.
- A market of \$3.1 billion is comparable to the value of lifetime sales of an average pharmaceutical product. Given that expected sales for existing products were sufficient to attract commercial investment from pharmaceutical firms, we recommend commitments worth about \$3 billion per disease for early stage products such as malaria.
- Our recommendation is not based on any estimated cost of vaccine R&D. It is based on the realized sales revenues of existing commercial products.
- As an example, taking account of (modest) expected revenues from other markets, a price of \$15 per malaria treatment, for 200 million treatments, would provide this revenue and would be exceptionally good value for money in terms of health cost-effectiveness.
- Larger commitments would likely further accelerate development of vaccines; even with higher costs, vaccines would still be a bargain in development spending.

## Determining the size of the market needed

### Goals

In setting the parameters of the advance market commitment, the sponsors should aim to:

- Set the guaranteed market revenue high enough to accelerate R&D in the selected vaccine.
- Set the size of the commitment below the social value of the vaccine, so that the sponsors do not commit themselves to paying more for the vaccine than it is worth to society. Specifically, the commitment should be low enough that spending on the vaccine is cost-effective compared with alternative development interventions.

It turns out that there is a large window between these lower and upper bounds for setting a commitment. In other words, a wide range of guaranteed prices and maximum quantities would give firms a good return on investment in R&D and still represent an excellent bargain for sponsors seeking to maximize the effectiveness of their spending.

We do not believe that the optimal market commitment is the minimum level needed to lead to a vaccine eventually being developed, even if we thought there were some way to estimate this. If a larger market commitment is likely to lead to a vaccine being developed more quickly, with greater certainty or with more competition, accelerating the development of a vaccine by paying more for it would likely be a very good investment. The optimal market size, therefore, is likely to be somewhat above the minimum R&D cost needed to develop the vaccine.

### What market size is needed to accelerate vaccine development?

The larger the expected value of the potential market, the more firms will enter the field, the more research leads each firm will pursue and the faster a product is likely to be developed. In light of the enormous health burden imposed by diseases such as malaria, it is important to provide sufficient incentives for multiple researchers to enter the field and to induce major pharmaceutical firms to pursue many avenues of research simultaneously so that vaccines can be developed quickly.

In other words, the more sponsors are willing to commit to pay, the greater will be the likely number of firms, the larger

those firms' investments and the faster the development of a vaccine. Even though we cannot reliably predict how much faster a vaccine would be developed as a result of increased investments, both evidence and theory tell us that total commercial investments would be expected to rise with the increase in expected market size.<sup>1</sup>

We decided to calibrate the appropriate value for each advance market commitment by looking at the net present value of sales revenues of existing commercial products, the expected sales of which clearly motivated biotech and pharmaceutical companies to invest in the past.

The most recent comprehensive data on sales revenues for pharmaceutical products look at 118 new medicines introduced in the United States between 1990 and 1994.<sup>2</sup> Our analysis uses this sales revenue data and finds that the average net present value of lifetime sales revenue for products in that sample is \$3.1 billion (in 2004 dollars).<sup>3</sup>

Vaccine suppliers would earn some revenues from sources other than sales under the purchase commitment. For a malaria vaccine effective against the form of malaria endemic to Africa there would be sales to travelers and the military, and to the private sector in poor countries. We estimate that the net present value of purchases in these markets would be about \$850 million, so an advance market commitment would need to create a market of approximately \$2.3 billion in expected revenue to create total expected revenues of \$3.1 billion.<sup>4</sup>

Note that this is not an estimate of the cost of R&D for a new vaccine. It is simply an approximate measure of the realized sales revenues of the average of a sample of products whose expected sales were sufficient to spur R&D investments from pharmaceutical companies in the past.

We therefore conclude that an advance market commitment offering total market revenues of about \$3.1 billion (as a net present value) could be expected to stimulate pharmaceutical companies to invest in R&D on a commercial basis.

### What price would guarantee a return of \$3 billion?

For a malaria vaccine, under fairly pessimistic assumptions on uptake rates, this might correspond to a commitment to pay \$15 (in today's prices) for each of the first 200 million people immunized under the program.

Other combinations of price and quantity are possible. A lower price, with a correspondingly higher maximum quantity to which the guarantee applies, would create a smaller degree of front-loading of the return. This might be preferable to the extent that the first product to market is likely to be imperfect, and it is important to create incentives for improved products.

Some firms that we spoke to suggested a flexible pricing mechanism (such as cost plus some mark-up) instead of trying to set a price in advance. The rationale for this is that it is difficult to predict which technologies will succeed and thus to anticipate the cost of production. Firms could be sheltered from some of this risk through cost-plus pricing, albeit with a corresponding increase in the risk to sponsors. But this approach would reduce incentives to develop products that could be produced cheaply or to develop inexpensive manufacturing processes—and it might add uncertainty to the commitment. Moreover, if a product were too expensive, it would not be a cost-effective use of a sponsor's funds to purchase it. For simplicity, the term sheets include a simple cost-plus formula, subject to a cap.

### What price is worth paying for vaccines?

Developing countries—and donors on their behalf—currently pay less than \$0.50 a dose for most vaccines. This has the advantage of reducing the cost to highly stretched health budgets. But as set out in chapter 1, it means that the introduction of new vaccines to poor countries is significantly delayed and that there is insufficient incentive to develop new vaccines for diseases in developing countries.

Some of the most significant benefits of an advance market commitment would come from enhancing the size and predictability of the market, by committing to pay a price for new medicines that meets the cost of innovation. In fact, a guaranteed price considerably higher than pennies-per-dose would still be highly cost-effective relative to other health, and other development, policies.

We used malaria as an example to illustrate the orders of magnitude involved. Consider a commitment to purchase a malaria vaccine at a price of \$15 (in today's prices) per person immunized for the first 200 million people immunized. This commitment, together with estimated revenues from other markets, provides an expected return to developers of approximately \$3.1 billion, comparable to average revenue for commercial products as discussed

above. In return for this revenue, the developers guarantee to sell subsequent treatments at \$1 each.

The cost-effectiveness of such a commitment would depend on a number of assumptions. These assumptions were employed for the example developed by the Working Group, and should be refined with additional analyses and consultations. To get an idea of the magnitudes, assume that:

- The contract covers all countries with a GNP of less than \$1,000 a year with sufficient disease prevalence to make vaccination worthwhile (in terms of being cost effective at less than \$100 per DALY saved; see box 3.1).
- Countries adopt the vaccine over seven years and eventually attain a steady-state immunization level five percentage points above that of the basic childhood immunization program.
- The vaccine requires three doses but could be delivered with the childhood immunization package at an incremental delivery cost of \$0.75.
- The vaccine is 60% effective, protects against infection for five years and does not lead to a rebound effect by weakening limited natural immunity.

Given these assumptions and data on population, fertility and disease prevalence, the cost—including incremental delivery costs—per DALY saved would be about \$15 (discounted in 2004 dollars), making vaccine purchases under the program one of the world's most cost-effective health interventions.<sup>5</sup>

The value-for-money from such a program is robust to changes in assumptions about efficacy, uptake rates or the price offered. Furthermore, this is a highly conservative estimate of the program's cost-effectiveness. The calculation does not include epidemiological benefits—vaccinating a significant fraction of the population may slow the spread of a disease, and thus benefits may spill over to the unvaccinated. It does not include savings to developing-country health systems from lower rates of illness and morbidity. It does not include health benefits to people in middle- and high-income countries or benefits to adults in low-income countries who purchase a vaccine privately. It assumes that the vaccine would be given randomly throughout a country and thus does not include the efficiency benefits of targeting vaccine delivery within countries to areas that have the most severe disease problems. Finally, it does not include any benefits of increasing vaccination rates for other diseases that might arise

if parents know they can vaccinate their children against malaria by bringing them to a clinic.

These estimates demonstrate that, once a vaccine is developed, purchasing it at a price well above current prices paid for vaccines in developing countries would still be one of the most cost-effective health interventions, more cost-effective than a wide range of other development expenditures.

### Is the commitment the right size?

If an increase in the size of the commitment would accelerate development of a vaccine, is it worth making a commitment to a higher price or paying for a larger number of doses? For example, paying \$17 per person for the first 200 million people immunized rather than \$15 per person would increase the overall market size to \$3.6 billion, comparable with the revenues for the average drug in the 70th to 80th percentile, at a cost of \$16 per DALY saved. Or paying \$25 per person immunized for the first 250 million people immunized would increase the overall market size to \$5.7 billion, comparable with the average drug in the 80th to 90th percentile of drug revenues, at a cost of about \$23 per DALY saved. Either of these commitment sizes would create attractive markets for developers and still be cost-effective from a public health perspective.

These calculations demonstrate that once a vaccine is developed, purchasing a vaccine at the pre-specified price would be very cost-effective. A more complex issue is the value of a commitment in accelerating the development and distribution of a vaccine, which requires assumptions about what would happen in the absence of a commitment. We estimate that if a vaccine purchase commitment advanced vaccine development by 10 years and accelerated access in poor countries by 10 years, it would cost only about \$23 per additional DALY saved. Even in the extreme case in which a price commitment accelerated vaccine development by only one year and adoption in poor countries by only two years, the program would cost about \$80–90 per additional DALY saved—still less than the \$100 per DALY cost-effectiveness threshold for the poorest countries.

Hence under a large range of assumptions and contract structures, a vaccine commitment could be priced at a level likely sufficient to stimulate substantial private R&D, yet still be cost-effective from a public health and donor perspective.

A commitment of \$15–25 for each of the first 200–250 million people immunized would be a bargain in terms of public health cost-effectiveness. Within this range larger commitments would be expected to lead to more firms to enter the search for a vaccine and shorten the expected time to development and distribution.

### Cost-effectiveness of an advance market commitment for HIV and tuberculosis vaccines

A spreadsheet model (available for download from the Center for Global Development website at [www.cgdev.org/vaccine](http://www.cgdev.org/vaccine)) allows users to analyze a large number of different scenarios and estimate the costs and benefits of commitments for malaria, tuberculosis and HIV vaccines under a variety of assumptions, such as about delivery costs, uptake, disease burden and eligibility.<sup>6</sup> Appendix E gives a short overview of the spreadsheet.

We present here estimates produced by this spreadsheet model under a set of conservative benchmark assumptions. Although we have used the example of malaria throughout this report, the spreadsheet estimates similar degrees of cost-effectiveness for commitments to purchase vaccines for tuberculosis or HIV (table 5.1). Note that additional analytic work would be required to refine the estimates.

Malaria has a particularly low cost per DALY because the burden of disease is highly geographically concentrated in Africa and hence it would be possible to economize on delivery costs by targeting the vaccine. However, given that the burden of disease from tuberculosis and HIV is estimated to exceed that of malaria,

**Table 5.1**  
Cost-effectiveness of an advance market commitment of \$3.1 billion

Disease	Estimated cost per DALY would be less than . . .
Malaria	\$15
HIV	\$17
Tuberculosis	\$30

Source: Spreadsheet model available at [www.cgdev.org/vaccine](http://www.cgdev.org/vaccine).

the cost per DALY alone should not be the sole determinant of policy priorities.

The International AIDS Vaccine Initiative and the Malaria Vaccine Initiative are both conducting more detailed investigations of the appropriate parameters for an advance market commitment for a vaccine for each of those diseases, with the aim of making recommendations for how the commitment should be tailored to the circumstances of those diseases.