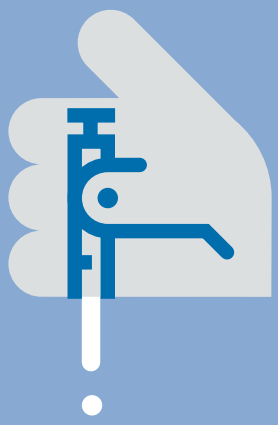

2 Promoting private investment in vaccine development

Chapter at a glance

- The development of a new medicine depends on the work of scientists based in academic, government and private research institutions, focusing on challenges that range from understanding a particular type of immune response to determining what type of packaging will maintain the viability of heat-sensitive products.
- Commercial investment is complemented in essential ways by public and philanthropic funding, which is especially important for the basic science and early-stage research on which pharmaceutical development depends. But the most expensive, later stages of vaccine development—such as clinical testing, regulatory approval, production and distribution—are mainly the result of private sector investment.
- For drugs and vaccines that are produced for populations in affluent countries, the single largest source of funding for R&D is commercial investment.[1]
- R&D on products that address health problems in developing countries receives neither the level nor the type of funding that health problems in developed countries receive. Of more than $100 billion spent on health R&D across the world, only about $6 billion is spent each year on diseases of developing countries, almost all of which is from public and philanthropic sources. There is little commercial investment because the market is not large enough to provide financial returns to cover the costs.
- A number of different approaches can be used to make investments in neglected diseases more attractive—and some have already been tried in a limited context and have demonstrated a positive effect.
- An advance market commitment would have important benefits:
  - First, it would mobilize additional resources, particularly for the clinical testing phases of development.
  - Second, strong market incentives would mobilize the ingenuity, energy, intellectual assets and managerial capacity of the pharmaceutical sector—from biotechs to multinational firms.
  - Third, it would allow public sector and philanthropic funders to stand at arm's length from complex scientific choices and tradeoffs, allowing firms to make their own judgments about the scientific feasibility and risks of alternative strategies.
  - Fourth, it would pay only for results, providing sponsors with the assurance that large-scale funding would be provided if and only if an effective and safe product that is appropriate for the developing world is manufactured in large enough quantity to meet demand.
  - Finally, such an arrangement would speed up access to vaccines when they are developed, and would ensure long-term sustainable and affordable supply.

Drug development depends on both public and private investment

Bringing new drugs and vaccines to market is costly. For one drug to be approved by the Food and Drug Administration (FDA), a firm typically screens 5,000–10,000 compounds. Of these, an average of 250 compounds survive preclinical testing, only 5 are approved for clinical testing, and only 1 succeeds in obtaining FDA approval.[2]

Most of the R&D costs are concentrated in the clinical testing phases, and during the start-up of the manufacturing process. About 70% of R&D costs for a typical new medicine are incurred after clinical testing begins.[3] Clinical trials for vaccines tend to be larger, and thus more expensive, than those for drugs, so the proportion of costs for clinical testing is likely to be even higher.

For R&D on health conditions that affect affluent countries, a large share of the basic scientific research is funded by the public sector, while the greater part of clinical testing and drug development is financed by private sector investments. Of the total investments in health R&D across the world (about $106 billion in 2001), governments provided about 44% of the total, the pharmaceutical industry about 48% and private, nonprofit and university funds provided the remaining 8%.[4, 5]

Public and philanthropic programs in industrialized countries are focused mainly on basic research

About half of total global government funding for health research is financed by the U.S. government. U.S. funding is channeled mainly through the National Institutes of Health (NIH), part of the U.S. Department of Health and Human Services. NIH invests more than $28 billion a year, with about 80% awarded to more than 200,000 researchers in universities, medical schools and other research institutions in the United States and around the world. About 10% of the NIH budget supports projects conducted by nearly 6,000 scientists in its own laboratories.

A study of 21 drugs introduced between 1965 and 1992 and considered to have the highest therapeutic value found that public funding was instrumental in the development of 15 of them.[6] NIH notes that the work that it funds is basic research, requiring extensive further development, and that development and production of an FDA-approved therapeutic drug occurs, on average, 8–12 years after the basic research has been completed.[7]

The private nonprofit sector, including foundations, charities and universities, provided approximately $8 billion in 2002, about 8% of total global health R&D.

Public investments are complemented by commercial private investments, when the promise of a market exists. Global investment in health R&D by the for-profit sector was estimated at more than $50 billion in 2002, of which the U.S. pharmaceutical industry comprised about half. The trade association, PhRMA, estimates that the U.S. industry spent $34.4 billion on R&D in 2003.[8] However, definitions of R&D vary so this figure should simply be regarded as confirming the orders of magnitude, but not necessarily comparable to the overall figures.

Private investment in health R&D is spent primarily on developing products and turning promising candidates into drugs. A study by the National Science Foundation found that 18% of the U.S. pharmaceutical industry's spending on R&D is devoted to basic research; the other 82% toward applied research and product development.[9] Other observers estimate that about 10% of industry investment is in basic research.[10] The trade association puts the figure higher, which may again reflect differences in definition.

It is difficult to overstate the importance of private sector investment in medicines. As well as providing the majority of the investment, the incentives are particularly effective at ensuring that research is targeted at the strategies that will bring the best possible products to market as quickly as possible. Decisions about where to allocate resources are made by those with the most at stake and the most direct knowledge of the prospects of scientific success, and investment decisions are based on a hard-headed analysis without political or bureaucratic influence.

R&D funding for products for the developing world

This picture of complementary private and public investment is quite different for R&D on products for primary use in the developing world. Overall, only a tiny proportion of total R&D addresses poor country health problems—about $6 billion of a total of more than $100 billion annually; of that, less than $1 billion is devoted to vaccine research. The funding mechanisms also are markedly different: under current arrangements, progress toward drugs and vaccines for these diseases depends on public and philanthropic funding, largely through grants—with about $1 billion from philanthropic sources and $5 billion from the

public sector. Very little is invested by commercial firms themselves in products specific to health problems of developing countries—which is unsurprising given the small potential returns and the high risks associated with developing country markets.

The total resources committed to developing vaccines against the three biggest global infectious diseases (HIV/AIDS, tuberculosis and malaria) is less than $1 billion a year, compared with about $100 billion spent on diseases of rich countries. This disparity is reflected in the number and type of drugs that make it to market: among 1,223 new chemical entities brought to market from 1975 to 1997, only 13 (1%) were specifically for tropical diseases; of these, only 4 were the direct results of research and development activities of the pharmaceutical industry targeted at new human products.[11]

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.[12]

Despite the lack of commercial incentives, some pharmaceutical companies are investing in the development of vaccines to prevent rotavirus, malaria, HIV and the forms of pneumococcus prevalent in many poor countries. But these efforts, while very welcome, are modest relative to the size of problem and the amount of investment needed. To accelerate progress toward these vaccines, it is necessary to move beyond investments motivated primarily by corporate social responsibility, toward a model in which these investments can become part of the mainstream commercial business, driven by the same incentives and commercial imperatives as products for affluent markets.

Product development partnerships

A large share of R&D philanthropic spending since the mid-1990s has been channeled through about 20 product development public-private partnerships (PDPPPs), which were established to provide direct support for basic research and clinical trials in particular disease areas. Both the Rockefeller Foundation and the Bill & Melinda Gates Foundation have been instrumental in the development of the PDPPP concept and its implementation. While ad hoc collaboration between pharmaceutical companies and public sector bodies had previously existed around individual candidate projects, there were no systematic attempts to promote the parallel development of a portfolio of candidate products—as the PDPPPs now attempt to do. Some PDPPPs are relatively new, with small portfolios; the older ones, with seven or more years' experience, manage sizeable portfolios, in some cases more than 25 products (box 2.1).

For vaccines, the main PDPPPs include the Malaria Vaccine Initiative (MVI), the International AIDS Vaccine Initiative (IAVI) and the Aeras Global TB Fund (Aeras). The majority of the funding for PDPPPs comes from philanthropic foundations—again, the Bill & Melinda Gates Foundation is the biggest contributor.

MVI, founded in 1999, has spent more than $43 million on malaria vaccine R&D and now supports 20 vaccine candidates in various stages of preclinical or clinical development. This is about 15% of total noncommercial malaria vaccine R&D expenditures from 1999 to 2003. NIH (specifically, the National Institute of Allergy and Infectious Diseases, or NIAID) accounts

Box 2.1
Examples of product development public-private partnerships

HIV/AIDS
- International AIDS Vaccine Initiative (IAVI)
- South African AIDS Vaccine Initiative (SAAVI)
- Global Microbicide Project (GMP)
- International Partnership for Microbicides (IPM)
- Microbicide Development Project (MDP)

Malaria
- Medicines for Malaria Venture (MMV)
- Malaria Vaccine Initiative (MVI)
- European Malaria Vaccine Initiative (EMVI)

Tuberculosis
- Global Alliance for Tuberculosis Drug Development
- Aeras Global TB Vaccine Foundation
- Foundation for Innovative New Diagnostics

Other
- Drugs for Neglected Diseases Initiative (DNDi)
- Institute for OneWorld Health (IOWH)
- Pediatric Dengue Vaccine Initiative (PDVI)
- Human Hookworm Vaccine Initiative (HHVI)

for more than 50% of total funding; other funders include the European Community, the World Health Organization's (WHO) Special Programme for Research and Training in Tropical Diseases (TDR), the U.S. Agency for International Development (USAID) and the U.S. Department of Defense.[13] MVI works through targeted partnerships with scientists, vaccinologists and development projects, and seeks to link government, industry and academic partners with field trial sites in malaria-endemic countries as early as feasible in the development process. Increasingly, MVI is recognizing the importance of working during the R&D phase to support the development of financing and introduction strategies.

A slightly different model has been used by IAVI, which was founded in 1996. IAVI is focused mainly on providing financial and technical support for product development—according to IAVI's strategic plan, it will use 75% of its budget ($340 million donated to date) to support promising vaccine candidates. IAVI currently has 20 preclinical vaccines, 5 Phase I vaccines and 1 Phase II vaccine in its portfolio.[14]

The Aeras Global TB Foundation received a grant of $82.9 million from the Bill & Melinda Gates Foundation in February 2004 to support research of promising tuberculosis vaccines in three main areas: clinical trials of two promising vaccine candidates, improving the effectiveness of animal models to indicate efficacy in humans and basic research on early-stage "next generation" candidates.[15]

These and other PDPPPs are not resourced to take a portfolio of vaccine candidates through late stage clinical trials and commercial development. Even to meet their existing mandate—that is, not including commercial product development—they are estimated to need an additional $1–2 billion over the coming two to three years.[16]

The roles of public and private investment: the malaria example

Despite the best efforts by PDPPPs, the small volume of resources for R&D and the absence of dynamic commercial investment have serious negative consequences for progress toward good—and then better—products for the world's most serious health conditions.

Consider R&D for a malaria vaccine. Total global funding of R&D for a malaria vaccine in recent years has been about $65 million annually; in addition to this, MVI recently received a $100 million grant from the Bill & Melinda Gates Foundation. This funding has enabled several candidate vaccines to move from the lab to clinical trials. So far, the scientific results are promising.

This level of funding—remarkably generous in comparison with what was previously available—represents only a fraction of the likely costs of getting a product to market. The lowest estimates of the costs of pharmaceutical development predict a total of at least $300 million per new medicine; the most widely used estimate is $802 million (in 2000 dollars).[17] Even at the lower estimates, pursuing a single candidate vaccine through the remaining phases of clinical trials, regulatory approval and production would exceed the total public and philanthropic funds presently available for the development of a malaria vaccine.

Using any plausible scenario for public and philanthropic financing alone, the available funds might allow at most one candidate to be pursued through large trials to licensure. If MVI has to bet all its available funding on a single candidate, this would eliminate its ability to fund other prospects. So there would be no fallback if the lead candidate does not succeed—or has unforeseen adverse effects. There would be no competitive pressure to improve the efficacy or reduce costs, and no prospect of second-generation products following behind.[18]

Even if funding were increased to allow a limited set of clinical trials, and if these trials demonstrate high levels of safety and efficacy, there are no guarantees that the product would be commercialized or produced in sufficient volume to support rapid uptake. The lead time for development of significant manufacturing capacity, which is beyond the scope of any public or philanthropic program, can be up to six years, and this investment is very costly and risky. "Right now, the markets don't justify the risk, from a pharmaceutical company's perspective," according to Melinda Moree, Director of Malaria Vaccine Initiative, PATH. "We have to find ways to make this work for both the private and public sector. If the market is not there, the products won't be there. Getting the incentives right could make the difference."

With the right market incentives, pharmaceutical companies have the experience, cost advantage and structure that would enable them to test and develop scientific leads and progress them as rapidly as possible through the development pipeline.

An effective vaccine against malaria would be of enormous social value. Malaria is one of the world's biggest killers of

children, and through the Expanded Programme on Immunization (EPI) we have a proven and effective mechanism to deliver vaccines to children. But as things stand, the likely revenues to industry from developing a vaccine remain small. Governments in Sub-Saharan Africa cannot afford large increases in health spending. While donors might be willing to pay for life-saving products, at least for a time, a rational firm would discount that market heavily because of the downward pressure that donors collectively place on pharmaceutical prices.

Possible incentives for commercial investment

To understand better the potential for altering the behavior of pharmaceutical firms through the use of targeted incentives, we looked at several examples of how policies have affected private sector R&D activities: the U.S. Orphan Drug Act, procurement of meningitis C vaccine in the United Kingdom, incentives generated by government procurement guidelines, the Bioshield legislation in the United States and increasing the financing for existing products, with enhanced forecasting of demand.

U.S. Orphan Drug Act

The U.S. Orphan Drug Act of 1983 uses market exclusivity and other mechanisms to enhance the market and thereby stimulate R&D on products for diseases that are rare in the United States (defined as those that afflict fewer than 200,000 Americans).[19]

The Orphan Drug Act provides the following incentives:

- Seven years' marketing exclusivity on FDA approval (the FDA cannot approve the "same" drug for the same orphan indication without the sponsor's consent for seven years). If a drug demonstrates clinical superiority, the new drug can then be authorized for the same orphan disease.
- Tax credit for related clinical research, up to 50% of clinical testing expenses.
- Grant support for investigation of rare disease treatment.

The act has increased R&D. According to the FDA, more than 200 drugs and biological products for rare diseases have been brought to market since 1983, up from fewer than 10 in the previous decade.[20] Of these, only 8 preventive vaccines have been designated. The main feature that makes the act attractive to pharmaceutical companies is believed to be the promise of a period of market exclusivity.[21]

Advance contracts for meningitis C vaccine in the United Kingdom

The establishment of a more certain and commercially attractive market in the United Kingdom stimulated the development of a meningitis C vaccine.

In 1994 officials in the U.K. Department of Health noticed an increase in the notifications and laboratory-confirmed cases of meningococcal disease. While some of the increase was the result of improvements in reporting, there had also been a disproportionate increase in group C cases, particularly for older teenagers. The department conducted talks with all major pharmaceutical manufacturers to understand the status of research on a vaccine for meningitis C. These talks revealed that a product was in the early stages of development.

In 1996 the United Kingdom announced that a tender would be issued for a meningitis conjugate vaccine, and a tender for 18 million doses of vaccine was duly issued in 1999. Three companies responded to the tender and negotiations were conducted with each company separately. Clinical trial support and help by way of expedited regulatory reviews shortened the time to market for the companies in the United Kingdom and through the mutual recognition process in other European countries. The guaranteed purchase was negotiated with each company participating in the tender; the first to market would receive the lion's share of the purchase.

The first vaccine was licensed in October 1999 by Wyeth Lederle, which received a contract for approximately 10 million doses. This was followed by contracts for Chiron (5 million doses) and Baxter (3 million doses) in March and July 2000. The price was about $21 a dose. In subsequent tenders, in which only the annual birth cohort was vaccinated (approximately 240,000 births at three doses per infant), prices fell substantially and fluctuated at around $12–18 a dose. The combination of accelerated approval and guaranteed purchase brought forward the development of a conjugate meningococcal vaccine.[22]

Incentives generated by government procurement guidelines

Vaccines for Children (VFC), a U.S. government program established in 1994, provides vaccines to needy children free of charge. The Advisory Committee on Immunization Practices (ACIP),

experts selected by the Department of Health and Human Services, makes recommendations on vaccines to be administered in the United States. In practice, the recommendations typically set policy for immunization requirements and determine which vaccines will be available under VFC. Hence, if a vaccine is recommended by ACIP, producers of that vaccine are assured a reasonably large market. Vaccine prices are typically negotiated after the ACIP recommendation, so once it has issued a recommendation, a vaccine producer is in a strong position to set the price close to the vaccine's social value. In this way the ACIP system shares some of the characteristics of an advance market commitment.

Similarly, the private response to the 1993 Medicare policy to cover influenza vaccinations without co-payments or deductibles, which substantially enlarged the expected market for flu vaccines, offers evidence that policies can induce R&D in the private sector.[23] The best flu vaccines in existence at the time the policy was put in place had an efficacy rate of 58%, and the 1993 flu policy helped stimulate the research responsible for the approval (in 2003) of the first new flu vaccines since 1978, as well as the first intranasal flu vaccine, FluMist, which has an 85% efficacy rate in healthy adults. The annual potential benefits from the 1993 flu policy (in particular, the combination of greater efficacy and wider use of the new vaccine) were estimated to range from $4.3–9.5 billion.[24]

Project Bioshield I and II

Project Bioshield legislation uses market enhancement mechanisms to stimulate development of bioterror countermeasures for 57 diagnostics, vaccines and therapeutic products prioritized by the Defense Science Board in the United States. Enacted in 2003, Bioshield provided for:

- Spending authority of nearly $6 billion for the procurement of qualifying countermeasures available in five years.[25]
- Greater authority of NIH and NIAID to award R&D grants and contracts and to hire technical experts.
- FDA emergency-use authorization—for example, to waive licensing requirements if a product is needed in an emergency where alternatives are not available.

A feature of the original design of Project Bioshield is that it established spending authority generally without committing to a particular price for the product. This reduces the certainty of returns to the producer: once a product has been developed, the U.S. government would still have an incentive to bargain for a low price. Moreover, the budgetary authority expires after five years, even though it is likely to take longer to develop new products. Accordingly, the reaction of industry has been mixed. In interviews with pharmaceutical and biotech companies the Working Group found support for the need for explicit market creation, but also a widespread feeling that the proposals in the legislation had not gone far enough to achieve this

Congress is now considering a further piece of legislation, Project Bioshield II, to create incentives to encourage research including in infectious diseases, which could include tax credits, intellectual property incentives, "wild card" patents (allowing companies to recover their R&D costs by extending the patent on a different product) and liability protection

Enhancing incentives by demonstrating demand

One way to increase firms' assessment of the likely returns on investment in future products is to buy larger quantities of products that are available today. The existence of GAVI and the Vaccine Fund, which have pledges in excess of $1.3 billion for the purchase and delivery of existing vaccines, may encourage some manufacturers to look again at developing-country markets. The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) has said, "This global initiative...has led to significant improvements in financing higher levels of immunization in developing countries, making the development of new vaccines for developing countries feasible."[26]

Options for financing R&D for neglected diseases of developing countries

The question of how to provide incentives for R&D on developing-country drugs and vaccines has intrigued economists, public-policy specialists, public health experts and others for a long time, and has taken on an increasing intensity in the debates about the best way to use donor resources in the fight against AIDS, tuberculosis and malaria.

Table 2.1 provides a thumbnail sketch of various approaches that have been suggested, along with their advantages and risks. Of the "pull" proposals, an advance market commitment has the advantage that it simultaneously meets the goals of creating effective incentives for commercial investment in R&D, ensuring

Table 2.1
Possible incentives for commercial investment

Approach	Description	Advantages	Risks and challenges
Advance market commitment	Sponsor promises to fully or partially fund purchases of vaccines meeting specified conditions.	• Creates link between product quality and the revenues that accrue to a developer. • Creates market for improved vaccines and progress. • Ensures access to new vaccines in both the short and long run. • Requires sponsors to pay only if a desired product is developed.	• Promises must be credible. • Must be designed to cover appropriate products. • Requires explicit financial commitment.
Patent buyouts	Sponsor offers to buy patent rights to a vaccine meeting specified conditions, then puts the patent in the public domain and encourages competition in manufacturing the vaccine.	• Allows competition among manufacturers. • May reduce prices and thus increase access.	• Promises must be credible. • Must be designed to cover appropriate products. • Manufacturer may have effective monopoly. • Uncertain link between payments and product quality. • Likely to be winner-takes-all.
Strengthened intellectual property right (IPR) protection	Public sector makes stronger commitment to enforce or extend IPRs (similar to Orphan Drug Act's guaranteed market exclusivity).	• Provides some additional incentive for industry.	• Difficult to implement. • Higher prices for longer will impede access. • May be politically unpopular. • Provides very little incentive for R&D on products specific to poor countries.
Sales tax credits	Government offers a tax credit on vaccine sales.	• Provides some additional incentive for industry to invest.	• Only of benefit to those with a tax liability (unless credits are transferable). • Must be credible; no recourse to legal challenge for changes in tax law. • Difficult to coordinate internationally.
Prizes	Offers cash or other reward to whoever achieves a certain, pre-specified goal.	• Provides immediate upfront payment—no need for long-term contract.	• Industry may not be enthusiastic about competing for prizes. • Does not address access. • Winner takes all. • Does not foster competition for subsequent improvements.

(continued on next page)

Table 2.1 (continued)
Possible incentives for commercial investment

Approach	Description	Advantages	Risks and challenges
Prizes based on incremental benefits[a]	Innovators are rewarded based on the incremental therapeutic benefits; plus compulsory licensing.	• Solves access problem. • Reduces wasteful duplication. • Applies to wide range of diseases.	• Difficulty of fairly determining social value after products have been developed. • May be insufficient to foster competition for subsequent innovation. • Uncertainty of value may deter investment.
Best entry tournaments	Offers cash or other reward to whoever progresses farthest toward a specific research goal by a given date.	• Provides assurance that reward will be paid.	• May have to pay without getting result. • Does not address access.
Patent extensions on existing pharmaceuticals ("wildcard patents")	Gives a manufacturer the right to extend the patent on any product in an industrial market, or allows a manufacturer to extend the customary time period that a patent is protected.	• Is attractive to larger pharmaceutical companies.	• Favors big companies and those with existing patents (unless patent extensions are transferable). • Places cost of developing new vaccines on users of drugs whose patent is extended. • Winner takes all—does not foster competition for subsequent improvements.
R&D treaty[b]	An international R&D treaty under which each signatory promises to devote a minimum fraction of its GDP to drug research through diverse mechanisms.	• Spreads R&D costs internationally. • Is consistent with different intellectual property regimes.	• Free-rider problem: individual countries may channel subsidies to within-country firms and universities rather than to fund R&D on usable products suitable for poor countries. • Does not directly address access.
Virtual pharma	A drug development strategy in which a small management team acquires and monitors most of its R&D services from outside vendors.	• Coordinates research. • Prevents unnecessary duplication. • Encourages information sharing.	• Lack of competition for innovation. • Funders may not be best-placed to choose which research strategies to pursue. • Absence of strong managerial incentives may lead to bureaucracy. • Does not take advantage of R&D cost advantage of pharmaceutical industry. • Uncertainty of future funding.

Table 2.1 (continued)
Possible incentives for commercial investment

Approach	Description	Advantages	Risks and challenges
Limiting patent protection in poor countries[c]	Allowing patent protection in rich markets coupled with unrestricted competition by generics manufacturers in poor countries.	• Ensures increased access with little loss to pharmaceutical industry. • Is cheap to implement.	• Is not intended to address problem of neglected diseases, but rather on medicines for which markets exist in high-income countries.
Fast-track regulatory approval	Rewarding pharmaceutical companies for developing vaccines for low-income countries by fast-tracking regulatory approval for them or for other, more profitable medicines.	• Benefits to pharmaceutical companies at little cost. • Complements other approaches.	• Reward insufficiently large and insufficiently certain. • If regulatory approval is being unnecessarily delayed, it should be accelerated anyway.

Note: This table draws on Glass, Batson and Levine (2001) and Kremer and Glennerster (2004), with additions.
a. Hollis (2005).
b. Hubbard and Love (2004).
c. Lanjouw (2003).

funding for rapid and affordable access to vaccines once they are developed and creating incentives for competition among suppliers and for further development of improved second-generation products. It is this approach that the Center for Global Development's Advance Market Commitment Working Group examined in detail.

The potential benefits of an advance market commitment

An advance market commitment, in which suppliers of vaccines that meet established technical specifications are guaranteed a price that provides the potential for a viable return on investment, closely mimics for the developing world the type of market incentives that exist in the developed world. In principle, such an arrangement could have important benefits:

- It would mobilize additional resources, particularly for the clinical testing phases of development. Despite generous funding by foundations, within current budget envelopes most of the product development public-private partnerships and other "push" programs that are engaged in drug and vaccine development for the developing world do not have sufficient resources to bring products through the full R&D process. As noted earlier in the case of malaria, without significant commercial investment it is not clear how multiple candidate vaccines will be moved through clinical testing and, potentially, into large-scale manufacture.
- It would engage the dynamism and energy of the commercial pharmaceutical sector—from biotechs to multinational firms. It would mean that decisions about which avenues to pursue, and which to abandon, would be put in the hands of those with the biggest stake and with the most knowledge about the prospects for success. It would harness the incentives and managerial capacity of the industry to develop new vaccines rapidly. It would thereby reproduce for developing-country diseases the market-based incentives that, together with public and philanthropic funding of R&D, have contributed to tremendous innovation in medicines for affluent countries, rewarding firms that move fastest toward the objective of developing and producing good products.

- It allows public sector and philanthropic funders to stand at arm's length from complex scientific choices and tradeoffs, avoiding the need for them to take a position on the feasible approaches and the likelihood of success. By clearly defining the objectives they wish to achieve with public funds, the sponsors can create conditions in which a variety of different approaches can be tried, not all of which may command a scientific consensus at the outset, promote competition and allow different firms to make their own judgments about the scientific feasibility and risks of alternative strategies.
- It would pay for results, providing sponsors with the assurance that large-scale funding would be provided if and only if an effective and safe product that is appropriate for the developing world is manufactured in large enough quantity to meet demand. This is consistent with innovations in development assistance, in which donors seek to pay for results rather than inputs.
- It would make the most of the untapped asset of information. By informing potential developers and suppliers about how much they would be willing to pay, and then locking it in, donors provide the type of signal that can, quite literally, be turned into capital.
- Properly designed, it would ensure access by helping to purchase vaccines in the short run and by ensuring a sustainable supply at an affordable price in the long run

There is widespread agreement that more must be done to accelerate progress toward new vaccines and other products for the developing world. Similarly, there is broad appreciation of the value of engaging the talent, resources and hard-nosed business sense of the private sector in developing and pursuing promising scientific pathways, and creating efficient manufacturing processes. From a conceptual perspective, providing an advance market commitment is appealing: it builds on the best aspects of markets, deploying public resources responsibly to stimulate private innovation.

But could it work? Would it work? What would be the potential costs and benefits? The findings of the Working Group on these questions are presented in the chapters that follow.