



Summary

A legacy
of our
generation

This generation has a unique opportunity to leave a legacy of which we can be proud. Current and near-future scientific knowledge can be used to conquer diseases that kill millions of people each year and disable millions more. In the development of vaccines, in particular, scientific breakthroughs have the potential to transform the health of the developing world much as they have been instrumental in almost eliminating the burden of life-threatening infectious disease among children in affluent nations. The most significant challenges are ahead: we have not yet developed effective vaccines against diseases of the poor, such as malaria, HIV and tuberculosis.

Governments and private foundations have made enormous strides in recent years toward establishing arrangements that will facilitate investment in R&D needed to develop new vaccines for these diseases. Now the resources and talent of the private sector are needed to translate those investments, and the scientific breakthroughs they are producing, into new vaccines, which once developed would be manufactured in adequate quantity. Unfortunately, the absence of an adequate market for those vaccines makes it impossible for the private sector to make investments in these diseases on a commercially viable basis.

We could make it worthwhile for the pharmaceutical industry to invest much more in R&D on vaccines for diseases occurring mainly in developing countries—and in the mass production of those vaccines when they have been developed. This can be done simply and cheaply by ensuring that there is a market for the vaccines if and when they become available.

Why vaccines: The unrealized potential of immunization

Immunization has had a profound impact on global health, in rich countries as well as poor. Immunization is cheap, reliable and effective, and is reaching the majority of children in low-income countries. But we have not capitalized on the full potential that immunization offers. Many more lives in the developing world could be saved and improved with increased access to existing and new vaccines.

First, we need to improve the availability of existing vaccines. That 3 million people die every year of diseases that can be prevented with existing vaccines is evidence of a profound failure in the current system. This failure can be remedied with more predictable financial resources, stronger political commitment to

public health, greater investment in both immunization-specific and broader elements of health systems and better management at all levels, global to local.

Second, we need to accelerate the development of new vaccines targeted to and appropriate for the epidemiological conditions and health systems of developing countries. Part of the solution lies in establishing secure financing for the medium term so that countries are willing to introduce vaccines that cost more than the “pennies per dose” that ministries of health (and donors) have come to expect. Another part of the solution is to ensure sufficient funding and the right incentives for innovation to develop new health technologies, both in the short and long term. Given the range of what is needed—investment in basic science, conduct of clinical trials, development of new manufacturing capabilities for cutting-edge products and scaling up of manufacturing over the long term—these incentives should be designed to attract investment by private firms of many types: biotechnology firms, multinational pharmaceutical companies and emerging suppliers, including in developing countries such as India.

Intensive and growing efforts are being directed along many but not all of the necessary fronts:

- The Global Alliance on Vaccines and Immunization’s (GAVI) recent investments in vaccines and strengthening health care systems, along with the long-standing efforts of national governments and international donors.
- The International Finance Facility for Immunization initiative (IFFIm) and other efforts seeking to establish an adequate and predictable funding base.
- GAVI’s Accelerated Development and Introduction Plans (ADIPs) to generate information for good decisionmaking about introducing new products.
- Increased funding for research on neglected diseases, for example through product development public-private partnerships as well as traditional publicly funded research.

These efforts are beginning to show results with improvements in immunization coverage and introduction of newer vaccines, as well as the accumulation of scientific knowledge and the development of promising new vaccine candidates. But one dimension of the problem has gone largely unaddressed by policymakers: the lack of market-based incentives for pharmaceutical companies to complement these existing efforts with the R&D necessary to move promising vaccine candidates from the lab through to scaled-up manufacturing.

New medicines are a shared endeavor

Developing a new vaccine or drug is expensive because of formidable scientific challenges and stringent regulatory requirements.¹ Candidate medicines must be tested, first in small and then in large trials. Regulatory approval must be obtained. Investment is needed in manufacturing and distribution capacity, meeting a high standard for safety and quality. Estimates of the total cost of developing a new medicine vary from hundreds of millions of dollars to well over \$1 billion.

For most medicines available today, this investment has been financed by a mixture of public funding by government, philanthropic and charitable giving and private investment. Firms make those investments in R&D with the expectation of being able to sell the finished product for a profit and so recover their investment.

For health conditions that affect affluent countries, basic scientific development is the result of a mixture of publicly funded research in tandem with a more limited amount of commercial investment in basic science. The later stages of product development, including clinical trials, approval and manufacturing—stages that make up more than two-thirds of the total costs of developing new medicines—are funded primarily by commercial pharmaceutical companies. While nearly all medicines depend to some extent on publicly funded science, the private sector is the single largest funder of medical R&D, and typically takes on the challenge of converting scientific advances into usable products. Those costs are then passed on to the consumers and governments, directly or through insurance.

It is difficult to overstate the importance of commercial investment in medicine. Market incentives are particularly effective in ensuring that R&D is targeted at strategies that will bring the best possible products to market as quickly as possible.

A piece of the puzzle is missing

Commercial biotech and pharmaceutical companies have to target their R&D on products that will produce a commercial return; this usually means medicines for the high-value markets of high-income countries. As things stand today, the markets for vaccines and drugs for diseases occurring mainly in developing countries are not valuable enough to offer sufficient returns to provide commercial justification for the necessary expensive research and product development.

So for health conditions that primarily affect poor countries, there is little or no commercial investment to complement publicly

financed R&D. An estimated 10% of the world's R&D investment is in solutions for diseases that affect 90% of the world's people.² Even where public investment results in promising scientific leads, limited resources mean that many of those leads languish in the laboratory, with insufficient resources and few champions to bring more than a few of them through to the next, more expensive stages of product development and clinical trials.

Commercial investment would accelerate new medicines

The prospects for R&D for products that would prevent or treat diseases concentrated in developing countries has been significantly improved in recent years by the establishment of partnerships³ that, largely through funding from philanthropic foundations such as the Rockefeller Foundation and the Bill & Melinda Gates Foundation, have greatly increased the resources available to accelerate the development of medicines for developing countries.

While these efforts have vastly enhanced the prospects for finding vaccines for these diseases, resources are still too small to fund the development of more than a small number of candidate medicines. Moreover, incentives for the full engagement of the private sector, which will be essential for efficient scale-up and manufacture, are not in place. The result is slow progress through clinical trials and the commercial development of new vaccines, and potentially a premature narrowing of the field of candidates. Were it available, commercial funding would increase the number of products under development and accelerate clinical trials, and so raise the chances of success for second-generation products and a greater diversity of new vaccines. This is particularly important in the case of malaria and AIDS, where the first-to-market vaccine may be only partially efficacious, and there will be a strong need to push the science further.

We can create incentives for commercial investment

Incentives for commercial investment in R&D and manufacturing can be created through an advance market commitment, in which donors make a legally binding pledge to pay for a new vaccine, if and when one is developed (box 1).⁴ Such a commitment would create a larger and more certain market. It would imitate the market conditions that stimulate research for diseases common in developed countries. It would create incentives for more firms to

identify and pursue promising avenues of research and to compete to bring them to market as quickly as possible. It would attract firms to develop new products for these diseases.

Such a commitment would enable donors to increase the incentives for commercial investment without reducing the resources available for immediate investment in R&D through public-private partnerships and other existing arrangements.

Create a market not a prize

The Center for Global Development Advance Market Commitment Working Group has designed an advance market

commitment that would be practical and effective. It would create a market, not a prize, and so avoid some of the pitfalls of a “winner-take-all” mechanism.

The main elements of our findings are that:

- A legally binding commitment can be made within the conventional framework of existing contract law (we include draft contract term sheets to illustrate the arrangement).
- Government donors can make this commitment within existing budget processes; it would have no impact on public spending unless and until a vaccine is developed.
- Government and philanthropic investments in research and the creation of an advance market commitment are mutually reinforcing, collectively accelerating progress.
- A market of approximately \$3 billion for each priority disease for which substantial R&D is needed would create revenues comparable in value with revenues that firms obtain for pharmaceutical products in affluent countries.
- For diseases that impose the largest health burden on developing countries, the cost of vaccines under such a commitment would be outstanding value for money for donors, more cost-effective than almost any existing development assistance. Purchases under an advance market commitment for a malaria vaccine are roughly estimated to cost less than \$15 life-year saved.
- Consistent with current thinking in development assistance and aid effectiveness, payments are linked to results. If a commitment is put in place and no vaccine is developed, there will be no financial cost. If such a commitment succeeds, millions of lives will be saved at very low cost.
- This would create a set of incentives comparable to those that exist for diseases of high-income countries. Firms would be likely to respond to a commitment by increasing investment in R&D and scaling up production capacity, thereby accelerating the development of new vaccines, increasing competition and fostering long-term affordability.

Box 1

The main features of the proposed commitment

- An agreed technical specification—in terms of outputs—required of a new vaccine.
 - A price guarantee, consisting of small payments from eligible countries and a co-payment by sponsors, would apply to a maximum number of treatments. (For example, the price might be guaranteed at \$15 per treatment, with the eligible low-income country paying \$1 and sponsors topping up the payment with an additional \$14 for the first 200 million treatments.)
 - An overall market size of about \$3 billion—enough to make it worthwhile for firms to accelerate investment in research and development for new vaccines, but well below the social value of the vaccine.
 - An independent adjudication committee to oversee the arrangements and commitments enforceable under the law.
 - In return for taking up the guaranteed price on the first treatments sold, the producer would be obliged to commit to produce and sell further treatments in eligible countries at a fixed, low sustainable 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 available alternatives.
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Benefits to developing countries, donors and industry

Carefully designed advance market commitments can offer substantial benefits to donors, industry and—most importantly—developing countries. For donors, this is a low-risk, transparent,

cost-effective investment that guarantees widespread access to vaccines if and when they are developed. In this results-oriented approach, there is a financial cost to sponsors only if a vaccine is developed. In addition, the structure of these commitments guarantees that this would be a financially sustainable donor investment. For industry, an advance market commitment creates a risk-reward structure with which firms are already familiar: they will be rewarded if they bring to market a product for which there is real demand. Unlike many alternative proposals, access issues are addressed without weakening incentives or dismantling the system of intellectual property rights. Most important, for developing countries an advance market commitment is likely to significantly accelerate the development and distribution of essential vaccines, of great value to 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.

Next steps

We recommend that donors, industry and the public health community work together to develop an advance market commitment for critical diseases occurring mainly in developing countries, including (but not necessarily limited to) HIV, tuberculosis and malaria. In doing this, we recommend further and more targeted analytic work by governments, industry and public health experts on several key topics.

Priorities for further work include:

- Strengthening financing for the purchase of existing vaccines, and strengthening health systems in developing countries to increase vaccine coverage.
- Developing long-term advance market commitments with producers of vaccines that will be available in the near future, using the commitment to negotiate on price, timing

of supply and characteristics of the vaccines and their presentation.

For vaccines that are at an early stage:

- Considering the specific issues with respect to individual diseases (such as the likely demand from high-income and middle-income markets).
- Validating our estimates of the market size needed to induce private sector investment in R&D, using alternative datasets for market revenues.
- Working closely with industry and the public health community to develop the contractual framework, including addressing the various design choices highlighted here.
- Developing technical specifications for each product, in collaboration with developing country health specialists and the scientific community.
- Considering what adaptations, if any, should be made to mechanisms for funding R&D in the context of an advance market commitment.
- Considering how this approach might be extended to other diseases that affect the developing world, such as schistosomiasis or leishmaniasis, and for drugs and medical diagnostics.

This report lays out the rationale for this approach. More important, it sets out a blueprint for implementation.

We have been heartened and impressed by the speed of policymakers in responding to the Consultation Draft of our report. Policy processes are now in place to establish a commitment for such diseases as malaria and HIV. We fully acknowledge that there is more work to be done, and that the Working Group's ideas will likely require modification as they are put into practice. We hope that this report will encourage the continuing discussion between donors, industry and the public health community in agreeing on the details of advance market commitments.