

opportunity for commercial vaccine developers. In addition to the very profound fundamental scientific challenges, accelerating its development may require incremental investments to tailor a vaccine to the needs of developing countries once a successful approach is discovered as well as innovative ways to ensure affordable pricing.

INNOVATIVE MECHANISMS TO CHANGE THE ECONOMIC EQUATION

Decisions to invest in the development and commercialization of vaccines, while dependent on scientific progress, are based largely on an evaluation of the economic factors: the costs, risks, timing of investments, and expected return on future sales. To influence these economic factors, the public sector is exploring and implementing innovative ways to assess, share, and alter the risks and returns. There is no single solution. Not only do the risks vary by vaccine, but they are also perceived differently by public and private entities.

Both the public and private sectors seek to minimize risk. Given the choice, the public sector would avoid all risk, only committing to buy a product once it is developed, widely demanded, and available at a low price. In contrast, the private sector prefers to invest in a product only once solid market commitments were in place, that is, guarantees to purchase the product at an acceptable price. Creative public-private partnerships that share specific risks and costs and protect the interest of all partners are essential if low-income markets are to have rapid access to priority vaccines.

There are two generic approaches to accelerating the development and introduction of priority vaccines: push and pull mechanisms. Push mechanisms are those that reduce the risks and costs of investment, while pull mechanisms assure a future return in the event that a product is produced. There has been significant work over the last five years to develop and implement both kinds of mechanisms.

Perhaps most significant on the push side is the creation of new product development partnerships (PDPs). PDPs are typically not-for-profit entities mandated to accelerate the development and introduction of a product against a specific disease—such as the Malaria Vaccine Initiative (MVI). PDPs were created recognizing that the absence of a robust commercial market (defined as both need and the ability and willingness to pay for the appropriate product) and the consequent riskiness of commercial R&D investment required creative approaches.

PDPs are funded by donors to promote research and development, often through the creation of links between industrial and developing country academic programs, biotechnology companies, and pharmaceutical companies. PDPs have played a particularly important role in facilitating investment in product development such as large-scale clinical trials and process development for diseases of especial and unique importance to the poorest countries in the world (16).

Downstream PDPs, such as the GAVI-funded Accelerated Development Introduction Programs (ADIPs) for pneumococcal and rotavirus vaccines, focus more on supply and pricing issues that will affect introduction and uptake decisions. Both upstream and downstream PDPs have filled a critical gap—focusing attention and resources on the neglected development and introduction of priority products for low-income countries.

On the pull side, there have also been a number of partnerships and innovative financing mechanisms developed.

The GAVI Alliance is, itself, a public-private partnership that was designed to bring together the major partners in immunization; providing them a forum and a means to work together to achieve their common immunization goals. The GAVI Alliance comprises key immunization stakeholders, including developing country and donor governments, civil society, WHO, UNICEF, the World Bank, industry, the Gates Foundation, and others. Through GAVI, partners have channeled large increases in funding, raised through traditional donor contributions and through innovative financing mechanisms. Two interesting new financing mechanisms are the International IFFIm and the AMC. Both are intended to increase the impact of the pull side of the equation.

International Finance Facility for Immunization

IFFIm is a way to increase the predictability and quantity of development aid available today. It front-loads donor aid commitments through sales in the bond market, allowing for immediate investment into country immunization programs. Originally proposed by the U.K. Treasury, the International Finance Facility was envisioned as a tool to increase availability of development funding to achieve all the millennium development goals.

Immunization was selected to pilot the IFF because it offers a strong rationale for front-loaded funds where returns are large enough to offset the financial costs associated with a bond issuance. IFFIm funding is channeled through the GAVI Alliance to reduce the number of childhood vaccine-preventable deaths in the world's poorest countries and to scale up delivery systems. By assuring more predictable funding for underutilized vaccines like DTwP combinations, IFFIm funds help attract increased investment by existing and new suppliers to scale up production to serve the low-income country market. Because of economies of scale, rapidly ramped-up production capacity helps reduce costs more quickly than would otherwise occur. IFFIm funds are also provided to governments to strengthen immunization program delivery, thus reducing the risk of disease. The front-loaded IFFIm funds accelerate the scale-up of both vaccine production and delivery systems. GAVI estimates that the current pledges of \$3.9 billion of IFFIm funds will prevent 5 million child deaths between 2006 and 2015, and more than 5 million future adult deaths by protecting more than 500 million children in campaigns against measles, tetanus, and yellow fever (17).

How Does IFFIm Work?

Eight donors (the United Kingdom, France, Italy, Spain, Sweden, Norway, Brazil, and South Africa) have pledged payments totaling \$3.9 billion in current dollars over 20 years. The donor commitments are sovereign obligations and are used to guarantee "immunization bonds," which are sold in the capital markets. The money raised by these bond sales is then channeled through GAVI to support the agreed vaccines and immunization programs in low-income countries. Ultimately, IFFIm will repay its bondholders with the long-term funds committed by the donors. The World Bank is IFFIm's Treasury Manager providing services such as the development and implementation of financing strategies and funding operations, handling the donor grants and payments, and managing the liquidity of IFFIm funds as they become available.

IFFIm had its first bond issuance in November 2006. The \$1 billion bond offer was substantially oversubscribed, with