Policies and Practices to Advance Global Health Technologies

A Report of the CSIS Global Health Policy Center

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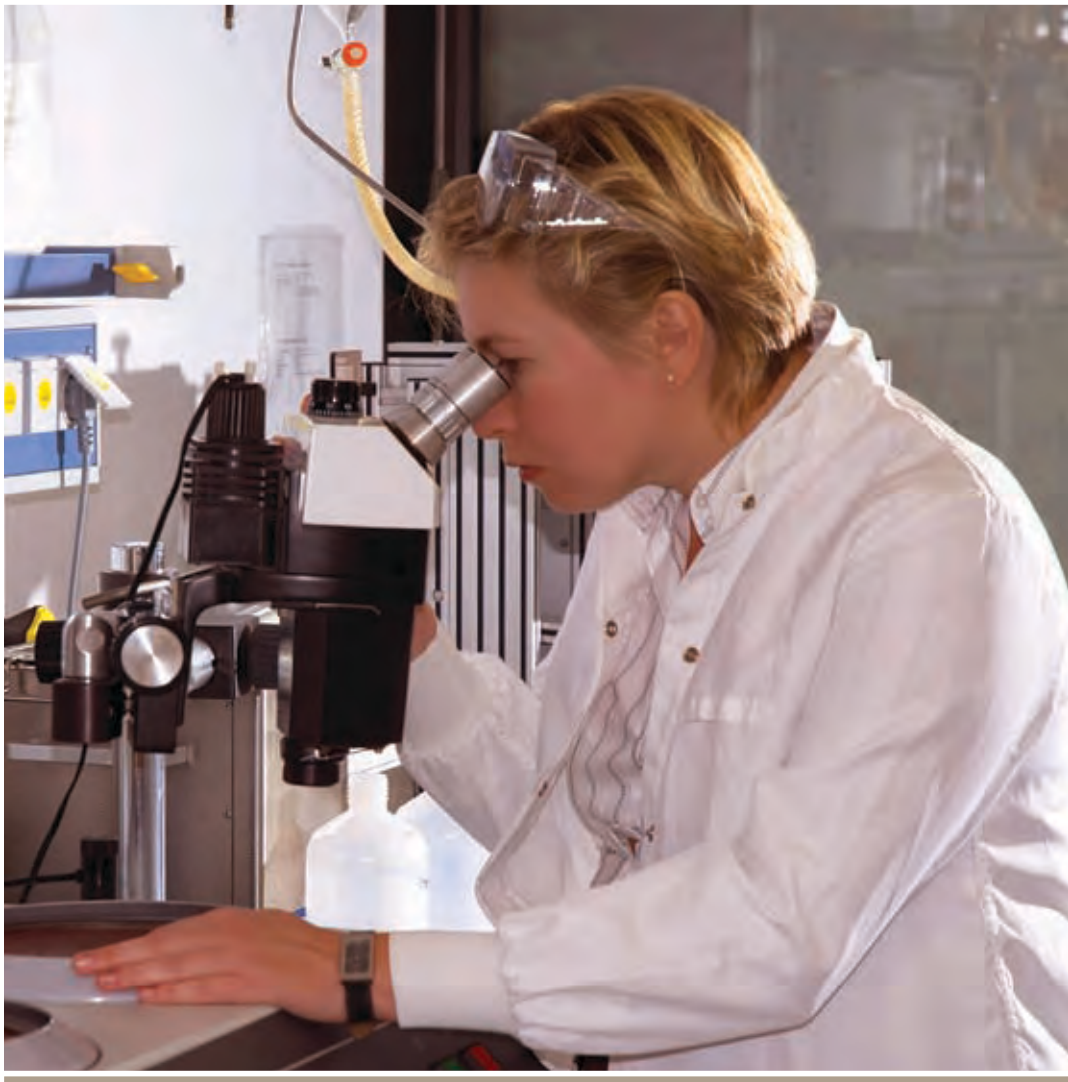

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POLICIES AND PRACTICES TO ADVANCE GLOBAL HEALTH TECHNOLOGIES

Christopher J. Elias[1]

Executive Summary

Innovation in global health technologies has been a hallmark of the past century. Often advanced through U.S. leadership, these new technologies have contributed to enormous progress in the battle against some of the world's greatest public health challenges. Significant barriers remain, however, and the world lacks many important tools to address existing and emerging health threats. Continued support for the development and delivery of global health technologies is critical to ensuring better health for all.

The value chain for developing global health technologies is complex. Significant political, financial, and intellectual support is needed to advance new products through five stages: (1) discovery and research; (2) development of discoveries into usable products; (3) regulatory processes to ensure product safety and licensure; (4) introduction of new technologies into health systems; and (5) scale-up and effective use of products by populations. Achieving the desired public health impact requires successful and timely progression through this value chain, which depends not only on financial commitment and political leadership from key stakeholders but also on meaningful engagement with affected communities.

New global health technologies do not progress on scientific merit alone. Ensuring that life-saving technologies get to those who need them most requires political leadership, innovative and sustained financing, and strong partnerships. Creative solutions are needed as the United States considers its role in prompting global health technologies amid an insecure economic climate. Congress and the new administration are urged to give special attention to:

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[1] Christopher J. Elias, MD, MPH, is president and chief executive officer of PATH, an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. Dr. Elias is deeply grateful to Rachel Wilson and Kaitlin Christenson for their significant contributions in producing this paper. The paper also benefited from the expertise of Eileen Quinn and from editing by John Ballenot and Ingela Ziemek.

- Maintaining secure, robust, and long-term financing for global health research and development
- Supporting and monitoring innovative mechanisms to encourage private sector investment in the development of global health technologies
- Enhancing regulatory pathways and capacities for reviewing and approving new technologies
- Preparing health systems for new products

Each of these policy priorities is critical to ensuring that new technologies are developed in a timely manner and delivered successfully to those most in need.

Investing in Global Health Technologies

Advances in science and technology have been effectively applied to solve some of the world's biggest health problems. For example, past investments in U.S. research have helped dramatically curtail polio and measles around the world and eradicate smallpox. Technology-driven progress against these diseases has saved countless lives and billions of dollars. In the United States alone, polio vaccination over the past 50 years has resulted in a net savings of $180 billion—money that would have been otherwise spent on treating individuals who succumbed to the disease.[2] Other examples of effective health innovations include artemisinin-based combination therapy to treat malaria, highly active antiretroviral therapy to treat HIV infection, and contraceptives not only to prevent unintended pregnancies but also to protect the health of women and promote the well-being of young mothers. Without these innovations—and the systems that support their delivery and use—the current status of global health would be vastly worse.

Despite these scientific advances, the package of tools for global health is still quite limited, and we lack effective technologies for tackling many problems. For instance, we lack a vaccine to prevent HIV, a simple and effective regimen to treat tuberculosis (TB), and proper tools to diagnose many infectious diseases. Though the absence of these technologies affects the industrialized world, the consequences in developing countries are especially dire.

In many poor settings, health care providers must rely on antiquated treatments of limited effectiveness because they have no other options. Even relatively simple tools to ensure clean water are not easily accessed in the developing world, contributing to diarrheal disease, the second most common cause of childhood deaths globally. Historical disparities in the application of technological innovation have exacerbated the inequities between rich and poor countries. It is both possible and necessary for emerging technologies to help bridge this equity gap and not contribute to widening it further.

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[2] K.M. Thompson and R.J.D. Tebbens, "Retrospective Cost-Effectiveness Analyses for Polio Vaccination in the United States," *Risk Analysis* 26, no. 6 (2006): 1423–40.

Evolving health threats—such as increasingly drug-resistant HIV, malaria, and TB and the emergence of new infectious diseases such as SARS and avian influenza—make it impossible to rely solely on existing tools. The emergence of new public health threats is almost certain; consider that just 30 years ago, the world was unaware of HIV, a virus that now infects more than 33 million people globally, with an estimated 2.7 million new infections each year.[3]

For all of these reasons, investment in the development and delivery of global health technologies must be sustained—even increased—to ensure additional improvements in health status. New technologies to prevent, diagnose, and treat disease are critically needed to enable innovation to keep pace with—and ultimately get ahead of—existing and emerging global health needs.

Harnessing Innovation to Improve Health for All

Technological advances do not progress based on scientific merit alone. Realizing the potential of science to benefit everyone, regardless of where they live, requires significant political, financial, and intellectual support. This support forms the basis for the interface between government stakeholders and product developers, an interface that is complex and vital to achieving results. Managing and improving upon that relationship are central to future success. Ensuring that innovations are appropriately channeled to key populations in a timely manner requires significant public investment, political support, and an enabling policy environment to support the full "value chain" of global health technology development (see figure 1). The U.S. Food and Drug Administration (FDA) estimates that it takes on average between eight and nine years to study and test a new drug before its approval for use by the public.[4] The development of new vaccines is often more complex and takes even longer. Complicated decisionmaking processes and weaknesses in health system infrastructure can result in further delays in the adoption and use of new technologies in the developing world.

The typical value chain for the development of health products includes five steps: (1) discovery and research; (2) development of discoveries into usable products; (3) regulatory processes to ensure product safety and licensure; (4) introduction of new technologies into health systems; and (5) scale-up and effective use of products by populations. Achieving public health impact requires successful and timely progression through this value chain.

Interwoven into each of these five steps are factors that can either hinder or facilitate the development of new technologies. Financial commitment and political leadership, for example,

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[3] Joint UN Programme on HIV/AIDS (UNAIDS), 2008 Report on the Global AIDS Epidemic (Geneva: UNAIDS, 2008), http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp.

[4] U.S. Food and Drug Administration (FDA), "The Beginnings: Laboratory and Animal Studies," in *From Test Tube to Patient: Protecting America's Health through Human Drugs*, special report from *FDA Consumer Magazine* (January 2006), http://www.fda.gov/fdac/special/testtubetopatient/studies.html.

Figure 1. Value Chain for Health Product Development

Source: Christopher J. Elias.

are vital in catalyzing progress throughout value chain of product development. Such leadership is critical to marshaling the significant resources required to generate innovative scientific research, develop and license effective products, and deliver them in appropriate ways. Leaders in industrialized nations can influence research and funding agendas, and leaders from developing countries can effectively engage civil society and promote an enabling environment for clinical testing and deployment of new innovations.

Another important factor is the engagement of affected communities. Innovation and development must reflect the needs and demands of the communities that are most affected by global health problems. Strong collaborations between partners in developed and developing nations (including product developers, donors, research institutions, governments, and other key stakeholders) are critical at all steps, including product selection, clinical trial design and implementation, manufacturing, ethical and regulatory review, and product introduction. Civil society must be engaged at every step of the value chain so that communities are informed and prepared once products are ready for use. Given the importance that public perception plays in the eventual adoption and use of new products, community-level stakeholders must be involved even at the early stages of technology development. The involvement of social scientists has strengthened clinical trial design and implementation. The interface between new technologies and human behavior must be understood during the design and development of new technologies to facilitate their eventual uptake and use.

HIV and AIDS

The problem: More than 33 million people worldwide are currently infected with HIV. Two million of those infected died from AIDS-related causes in 2007, and 6,800 new HIV infections occur each day.

Existing interventions: There is currently no cure for AIDS. Antiretrovirals (ARVs) can be extremely effective in treating HIV infection and mitigating progression to AIDS, but many in need are unable to access these lifesaving treatments, and ARV treatment regimens can have severe side effects. Currently, a number of interventions exist to help prevent infection, including male and female condoms, ARVs for prevention of mother-to-child transmission, and male circumcision. Although good diagnostic technologies exist, better tests that are noninvasive, inexpensive, and simple but reliable are needed. Affordable diagnostic tools to monitor ARV treatment are also a priority.

Interventions under development: The science behind innovation for new HIV/AIDS technologies has proven complex, though a number of different products are under development. ARV medicines are being reformulated and tested as prevention interventions in the form of vaginal gels (microbicides) and oral pills (for pre-exposure prophylaxis). Promising data emerging from a recent microbicide trial provide the first "proof of concept" that a microbicide could prevent HIV infection. A preventive HIV vaccine remains elusive despite significant research efforts.

Research

Research and development begin with understanding the underlying disease process and identifying potential targets—or vulnerabilities—within a disease-inducing pathogen. Scientists may spend years, even decades, working to understand the mechanisms of the disease in an effort to develop pharmaceutically active compounds. Hundreds or even thousands of molecules are screened, and a promising compound may fail for many reasons. The discovery of new research leads is an iterative process of inquiry and testing whose success depends upon a strong scientific community with adequate resources to develop and evaluate multiple hypotheses.

Product Development

Once a lead has been identified, a specific product must be formulated and subsequently tested in a variety of preclinical models, including living animals, to show whether it has toxic side effects and to understand its safety at varying doses. Many products are not deemed successful or safe enough to continue beyond this preclinical step. For products deemed safe, the information gathered in preclinical testing is used to inform future clinical trials.

Clinical development of a product typically involves three phases. During phase 1 clinical trials, a product is tested in very small groups of healthy individuals (20 to 80) to evaluate its safety. Phase 2 trials include a slightly larger group of people (typically 100 to 300) and are designed to expand the safety profile and demonstrate preliminary evidence of a product's effectiveness against the target disease. Phase 3 trials, conducted in even larger groups of participants (often up to 3,000 or more), confirm a product's efficacy against a comparable product or intervention (or, in some

Diarrheal Disease

The problem: Diarrheal disease, the second leading cause of death in children under the age of five, kills approximately 1.6 million children each year.

Existing interventions: Although effective interventions against diarrheal disease already exist, they are not implemented to their full potential. These include oral rehydration therapy, zinc treatment, and rotavirus vaccines. Many cases of diarrhea could also be prevented through other simple interventions, including breastfeeding and improved hygiene and nutrition. Diarrheal disease is often treated with antibiotics, which contributes to emerging drug resistance.

Interventions under development: The highest priority for combating diarrheal disease today is effective and widespread implementation of existing tools, including rotavirus vaccine, oral rehydration therapy, and zinc treatment, as well as the scale-up of basic prevention practices, such as improved water, sanitation and hygiene, and exclusive breastfeeding. Research and development efforts are also underway to develop more affordable drugs for use in the developing world, as well as vaccines against shigella, cholera, and other pathogens that cause diarrheal disease.

cases, a placebo) and can last several years. If phase 3 trials are successful, product manufacturers will submit the product for regulatory review and licensure. Sometimes, a phase 4 clinical trial occurs after licensure of a product to continue monitoring safety and side effects as it goes into widespread use in the general population.

Clinical trials—particularly later phase trials—are massive undertakings, and significant coordination is required to implement them satisfactorily. For instance, phase 3 clinical trials of the most advanced malaria vaccine candidate (GlaxoSmithKline Biologicals's RTS,S vaccine), set to launch in 2009, will enroll 16,000 infants and toddlers at 11 different trial sites in seven countries in Africa—perhaps the largest ever clinical trial of a malaria vaccine. This effort will require substantial organization and collaboration among partners and research sites.

Role of Product-Development Partnerships

The public sector often lacks key product-development capacities that exist within the private sector: the ability to manage the product-development process optimally, to manufacture products once they are developed, to navigate the regulatory landscape, and to develop strategies to introduce products to market. Similarly, the private sector in developed countries often does not have the expertise required to develop and introduce products for poor countries: a keen understanding of the intricacies of developing-country health systems and markets, specific knowledge about neglected diseases and their public health impact, and strong relationships with researchers and clinical testing sites in developing countries.

Product-development partnerships (PDPs)—structured collaborations between commercial and public-sector partners—play an important role in the research and development of lifesaving products to address neglected diseases. PDPs combine private-sector industry expertise in ushering new products through rigorous clinical trials and regulatory processes with public-sector

Pneumonia

The problem: Pneumonia—or acute lower respiratory illness—affects all age groups but is of primary concern among children. Between 2 and 3 million infants and children die each year from pneumonia, making it the leading cause of death for children under the age of five worldwide.

Existing interventions: Pneumonia can be prevented through the delivery of lifesaving vaccines during infancy: the *Haemophilus influenzae* type b vaccine and pneumococcal conjugate vaccine, which target two of the most common causes of pneumonia. Adequate nutrition, exclusive breastfeeding, and zinc intake can also help reduce the incidence of pneumonia. For children who are diagnosed with pneumonia, antibiotics can be an effective source of treatment. Antibiotics are often inappropriately prescribed, however, and their misuse has resulted in emerging antibiotic resistance.

Interventions under development: Despite high rates of illness and death due to pneumonia, development of new technologies to combat this disease is drastically underfunded. Efforts are underway, nonetheless, to develop new low-cost vaccines and second-line drugs for treatment.

experience in addressing the health issues of those most in need of innovative tools. For instance, the Meningitis Vaccine Project (MVP) is a partnership between PATH and the World Health Organization (WHO) aimed at eliminating meningitis in sub-Saharan Africa. MVP partners with a commercial vaccine producer to develop, test, license, and introduce meningococcal vaccines. Private-sector partners bring technical expertise in developing vaccines, and PATH and WHO bring vast experience working to improve health around the world. Throughout the development process, MVP works closely with African stakeholders to understand their priorities.

PDPs are designed to serve the needs of places where markets have failed (for example, where private-sector pharmaceutical developers have provided little investment because they believe that the costs and risks outweigh the expected financial returns). PDPs operate in a number of different ways to lower costs and share risks so that the commercial sector will have the incentive to apply its innovation capacity to solving problems it would otherwise not address. Although some PDPs conduct their own in-house research and manufacturing, others leave these functions to their industry partners and serve a more brokering role. By harnessing the expertise of the commercial sector, PDPs save time and money in accelerating the product-development process.

Regulatory Processes

Regulatory processes ensure that new products are safe and effective before they are distributed widely to populations. Products must be reviewed and licensed by the national regulatory authority of each country in which they will be marketed and distributed. Regulatory processes within developing countries can range from complex to nonexistent, making licensure particularly challenging for many product-development partners. Although some regulatory authorities in developing countries have the capacity to conduct these stringent regulatory reviews, most do not. WHO is making important contributions in addressing this challenge through its prequalification process but will need increased support to address the growing

volume of products requiring such review. The lack of sufficient capacity for stringent regulatory review could result in substandard products, increased cost of products, or substantial delays in product licensure and access.

To ensure that products for use in the developing world meet the same stringent guidelines as those used in industrialized nations, regulatory authorities such as the FDA and the European Union's European Medicines Agency (EMEA) are also involved in the review of these products. WHO has strategic advisory committees that provide periodic review of new drugs and vaccines and issue recommendations about their use—an important step in the regulation and decisionmaking process. In fact, many national regulatory agencies in developing countries will not conduct regulatory review of a product before WHO grants this recommendation.

The role of bodies like the FDA and EMEA becomes more complex when products are intended exclusively for use by populations in developing nations (e.g., a malaria vaccine). Given that the risk profile of a disease may differ substantially in the country of manufacture from that in the destination country, decisions on the best risk-benefit ratio can be complex and challenging.

To address this issue, the EMEA developed guidelines for products that fall within this category, and the FDA is not far behind. The EMEA's Article 58 established a mechanism through which the EMEA may issue a scientific opinion on products intended exclusively for use outside of Europe.[5] In 2008, the FDA issued new guidance on the review of vaccines that indicates that the FDA can license vaccines that protect against diseases or conditions that are not endemic in the United States.[6] These are significant accomplishments, but the complexities in their implementation are still being resolved. In addition, expanded efforts by U.S. and European regulatory bodies are needed to help strengthen the capacity of regulatory bodies in developing countries so that, in the future, these bodies may play a stronger, more coordinated role in the regulation of interventions designed for use within their countries.

Product Introduction

Product introduction is a complex and multifaceted process, and planning for introduction must begin far in advance of product availability to ensure successful and timely introduction. Many elements can affect the decision to introduce a new global health technology: product cost, programmatic costs to support product use, documentation of national disease burden, and health system capacity are just a few. Information about each of these must be readily available to enable policymakers to make informed, data-driven, and timely decisions. Experience shows that many diverse activities must be undertaken to ensure that health systems are prepared to absorb new health technologies:

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[5] Available online at http://www.who.int/immunization_standards/vaccine_regulation/article_58_guidelines_0505.pdf.

[6] Available online at http://www.fda.gov/cber/gdlns/gidvacc.pdf.

- Developers must take steps to prepare a product for market entry, including defining the market for the product, determining the most effective distribution channels, and developing strategies to market the product to diverse audiences.
- Product developers must work with developing-country governments and global stakeholders to ensure that supply, procurement, and financing mechanisms are in place.
- Health systems and service providers must be oriented to the new product and prepared for its introduction. To the extent possible, integration within existing delivery systems should be prioritized (e.g., a malaria vaccine should ideally be delivered through the existing Expanded Programs on Immunization currently supported by ministries of health).

Because health-system capacity varies widely, it is critical that introduction strategies be specific to the region and country where products will be introduced. In addition, during this stage, product developers and developing countries must work together to prepare for product scale-up.

When products are not introduced in a timely way, vulnerable populations can suffer mightily. Though unfortunate, lengthy lag times between product availability and product introduction are all too common. For example, Haemophilus influenza type b (Hib) is an important cause of pneumonia and meningitis in children worldwide, causing up to 3 million cases of severe disease each year. Despite the availability of a safe and effective Hib vaccine—which has been licensed since 1991 and used routinely in the developed world—most infants in the developing world still do not have access to this lifesaving intervention. This is in spite of the fact that the vaccine has proved effective in developing countries that have introduced it: when Kenya, for instance, introduced the Hib vaccine to its Expanded Program on Immunization in 2001, the incidence of Hib in children under the age of five fell by 88 percent.[7] Results from Kenya and other countries show that widespread use of the Hib vaccine in developing countries could have a major impact on the health of children.

Scaled-Up, Effective Use

So that technologies get to all those who need them, developing-country health systems must be prepared to articulate demand, provide widespread access to the technology, implement tracking systems to understand the impact of the technology on preventing or mitigating disease, and document their experiences during product introduction. Scale-up requires significant focus, energy, and resources, and it is critical to develop a strategic scale-up plan so that the strain of scaling up one intervention does not overburden the entire health system.

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[7] K.D. Cowgill, M. Ndiritu, J. Nyiro, et al., "Effectiveness of Haemophilus Influenzae Type b Conjugate Vaccine Introduction into Routine Childhood Immunization," *JAMA* 296 (2006): 671–78.

Neglected Tropical Diseases

The problem: The term *neglected tropical diseases* (NTDs) refers to 13 parasitic and bacterial infections that primarily affect individuals in developing countries. Examples include dengue, Chagas disease, schistosomiasis, and leishmaniasis. NTDs cause more than half a million deaths each year, with significantly more individuals falling ill but eventually recovering, and are among the most important health issues facing developing nations.

Existing interventions: Drugs exist both to prevent and to treat many of these diseases, but they are often outdated and less effective in part because of the development of resistance. Research is needed to develop a wider range of safer and more effective drugs. The lack of appropriate diagnostic tools also hinders treatment efforts.

Interventions under development: Efforts are underway to revive research and development of new drugs for both prevention and treatment. Several vaccines for NTDs are under development as well.

New technologies can take years to be accepted fully by communities, and "overnight success" is an unlikely phenomenon. Because generation of demand takes time, long-term planning for scale-up is important. A critical component of scale-up is engaging champions at the country and local levels and working with communities to plan effective rollout strategies.

Because slow uptake of new products by developing countries has been a major disincentive for manufacturers in the past, delivery systems must be prepared before new technologies are introduced. One of the strongest incentives for industry to invest in the development of new global health technologies—either on their own or through PDPs—is the successful and wide-scale use of existing innovations, ensuring that the procurement, delivery, and logistics needed for new technologies are in place.

The U.S. Role in Advancing Global Health Technologies

Ensuring that lifesaving technologies get to those who need them most requires not only scientific innovation but also political leadership, innovative and sustained financing, and strong partnerships. As the United States considers its role in advancing global health technologies during this time of financial insecurity, creative solutions will be needed to determine not only what levels of support are needed but also how support should be used most efficiently. The following policy recommendations provide a framework for rising to this challenge.

Tuberculosis

The problem: Tuberculosis (TB) kills more than 1 million people each year, and up to 2 billion people worldwide are estimated to be carriers (though not all will become ill). TB is the leading infectious cause of death among individuals with HIV/AIDS. Drug resistance—including multidrug resistant (MDR) and extensively drug resistant (XDR) TB—continues to grow, in part due to inconsistent adherence to treatment regimens that are lengthy and difficult to manage.

Existing interventions: The Bacille Calmette-Guérin (BCG) vaccine provides protection against severe TB in children but offers no protection for adults. The current treatment for TB is burdensome and difficult to adhere to, consisting of four different drugs that must be taken daily for six to nine months. Diagnostic tools for TB are equally antiquated and do not fit the needs of health care settings in the developing world.

Interventions under development: Efforts are underway to develop a more effective vaccine against TB that will work to prevent all forms of the disease (including MDR and XDR TB). Multiple drug candidates, designed to be safer and have shorter regimens, are in clinical trials.

Ensuring Sufficient Investment for Research and Development

A recent report by the George Institute shows that the United States is by far the largest funder of global health research and development, accounting for 70 percent of total investments.[8] Although such investments are significant, actual funding amounts have not kept pace with need. In this time of economic uncertainty, the U.S. investment in global health could be seen as an easy target for savings. However, with the United States contributing such a large share of the funding, any reduction in U.S. investment could have dire consequences for both current and future advances. The long-term nature of research and development for new global health technologies can create challenges for policymakers seeking to report back to their constituents with results—particularly as so many of their constituents struggle in the current economic climate. For policymakers who support global health, the immediacy of delivering on promises can make focusing solely on nearer-term solutions highly appealing—for example, by devoting more funding for the delivery of existing HIV/AIDS drugs rather than for the research and development of new HIV/AIDS preventive tools. Though investments in providing access to existing technologies should never be sacrificed, history has proved that it is also critical to maintain a strong pipeline of candidates for new products to meet the global health needs of tomorrow.

The benefits to U.S. stakeholders of investing in development of global health technology are many. Even in times of financial hardship, the American people have indicated that global health

[8] M. Moran, J. Guzman, A. Ropars, et al., *Neglected Disease Research and Development: How Much Are We Really Spending?* (Sydney: The George Institute for International Health, 2009), http://www.thegeorgeinstitute.org/shadomx/apps/fms/fmsdownload.cfm?file_uuid=409D1EFD-BF15-8C94-E71C-288DE35DD0B2&siteName=iih.

Malaria

The problem: Almost 1 million people die each year from malaria, with most of these deaths occurring among infants and young children. Hundreds of millions more fall ill from malaria infection every year, taking a significant toll on the workforce and economies of developing nations.

Existing interventions: Tools used to prevent and treat malaria include artemisinin-based combination drug therapy, insecticide-treated bednets, intermittent preventive therapy for women during pregnancy, and indoor residual spraying. All of these interventions require health-protecting behaviors to be effective, and resistance to malarial drugs has become a problem in some populations.

Interventions under development: Although no vaccine for malaria currently exists, efforts to develop one have progressed significantly in recent years. The most advanced vaccine candidate, GlaxoSmithKline's RTS,S vaccine, is ready to enter large-scale phase 3 clinical testing and, if successful, could be available for use as early as 2014. Although first-generation malaria vaccines are not likely to be 100 percent efficacious and will need to be used in combination with other prevention efforts, they will be an important new prevention tool.

remains a high priority. In fact, a recent Research!America poll shows that nearly 60 percent of Americans believe the new Congress should prioritize global health.[9] In addition, many of the investments in global health research and development benefit U.S. academic institutions and private partners, a fact reflected in the $10 billion investment made in the National Institutes of Health in the recently passed economic stimulus bill. Finally, many of the benefits of global health research and development have implications for health in the United States. Examples include a vaccine to prevent HIV, which is present in more than 1 million Americans; better drugs to reduce the risk of TB drug resistance, which has already caused fear among U.S. citizens as well as significant expense to protect them from it; and new medicines to prevent and treat malaria among U.S. troops in malaria-endemic countries.

The need for robust, long-term financing for global health research and development is not just a matter of the amount; it is also about the efficient use of those dollars. While each U.S. agency currently supporting this work has unique expertise that is critical and must not be sacrificed, cross-agency strategies and plans are greatly needed to ensure that the dollars are complementary and not duplicative. Although no cookie-cutter approach to inter- or intra-agency coordination would be appropriate, mapping and understanding the various strategies implemented by each agency will go a long way toward reducing any duplication and filling potential gaps that could lead to bottlenecks in progress.

[9] National Global Health Survey conducted by the Charlton Research Company for Research!America, November 5–11, 2008, http://www.researchamerica.org/uploads/2008NationalGlobalHealth.pdf.

Exploring Incentives for R&D on New Technologies

One of the major challenges in stimulating research and development for global health technologies is the risk that private industry will not invest if it believes that the primary beneficiaries—people in developing countries—may be unable to afford the new products. As a result, the development and supply of such products often fall short of the need, and developing countries are frequently forced to use or repurpose drugs, vaccines, and other interventions that were originally designed for use in the developed world. The recent economic downturn will make it even more challenging to leverage private dollars for investment in global health technologies in the near term.

Incentive mechanisms can help drive innovations to meet developing world needs in the absence of a sufficiently compelling market. Different mechanisms will be needed to offer incentives for products at different stages, depending on their complexity and level of advancement. Therefore, a variety of such mechanisms must be piloted and carefully monitored for potential success in overcoming market challenges.

Incentives to drive the development of new global health technologies can be classified as either "push" or "pull" mechanisms. Push mechanisms are designed to alleviate some of the costs of research and development and can be especially helpful in stimulating the early stages of research, where both scientific and commercial risks are high because of the uncertainties inherent in this step. Tax credits and funds directed toward small-businesses for innovation research are two examples of push mechanisms that can make private investments in global health technologies more appealing.

Pull mechanisms are designed to reward research outputs by creating market-like incentives for the generation of particular outcomes. For example, priority review vouchers (PRVs) can be granted to any company that gains FDA approval for a new drug or biological product that addresses a neglected tropical disease. The company that holds this PRV is then entitled to receive an expedited FDA review of a future product (which can be transferred—or sold for profit—to another company). This expedited review means that a future product would be ready for licensure several months earlier, which could translate into tens of millions of dollars in additional revenue for the product.

Another example of a pull mechanism is the advanced market commitment (AMC), an innovative funding mechanism that provides incentives for private industry to develop vaccines for diseases that primarily affect the developing world. With an AMC, donors commit funding to guarantee the price of a vaccine once it has been developed, thereby creating a predictable market for the vaccine. Developers then make binding commitments to provide vaccines at fixed, lower prices. This benefits long-term planning, as developing countries are then better able to develop sustainable financing plans.

Consideration of U.S. support for a future vaccine AMC was recently urged in language included in the *United States Global Leadership Against HIV/AIDS, Tuberculosis and Malaria*

Reauthorization Act of 2008 (the act reauthorizing the U.S. President's Emergency Plan for AIDS Relief, or PEPFAR), sponsored by Tom Lantos and Henry J. Hyde.[10] The United States did not join Italy, the United Kingdom, Canada, Russia, Norway, and the Bill and Melinda Gates Foundation in supporting the first AMC pilot for a vaccine to prevent pneumococcal disease, which is expected to be officially launched before the summer of 2009. U.S. support for the next vaccine AMC, however, should be important to an administration that values partnership and innovation for new solutions to longstanding challenges in reaching greater health equity. The date or product that will be the focus of the next AMC has not yet been determined, but an expert committee is expected to make a recommendation later this year and is likely to select a vaccine in the early stages of development.

Strengthening Regulatory Systems Worldwide

Licensing and other regulatory systems must be modified to streamline the approval process for health technologies that may be developed in the United States for a non-U.S. population. As noted previously, the FDA has recently shifted its policies to address this issue for new vaccines, but additional clarifications and policies are needed to address the remaining challenges related to approval not only of vaccines but also of drugs, diagnostics, microbicides, and devices intended for a non-U.S. population.

Strengthening the capacity of national regulatory agencies in the developing countries where clinical trials are taking place could also eliminate some of the delay that currently exists as a result of slow and uncoordinated regulatory processes. The FDA (in partnerships with the EMEA and WHO) is uniquely positioned to provide guidance and support to developing countries and their regulatory bodies that can help them improve their capacity to manage regulatory and ethical review. WHO has led efforts to strengthen the capacity of national regulatory agencies and has made some significant progress to date in improving their capacity to conduct regulatory review and quality control. Stronger U.S. engagement and partnership with WHO should be prioritized to help streamline and accelerate more robust and coordinated regulatory processes.

Ensuring That Health Systems Can Deliver Products

Health technologies are worth little if they do not get to their intended target populations. Well-functioning and well-staffed health systems are necessary for delivering not only existing interventions but also products currently in development. These systems require sufficient investment and strategies to increase human resources, improve procurement and logistics, enhance management information systems, and provide adequate quality assurance and other key functions related to product storage and delivery.

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[10] Available online at http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname =110_cong_bills&docid=f:h5501enr.txt.pdf.

New technology can also be targeted to improve a health system's ability to deliver health services effectively. For instance, innovations in vaccine delivery tools—such as vaccine vial monitors that change colors when a vaccine is no longer usable and prefilled single-use injection devices that can be used by low-skilled health workers in remote areas—have saved millions of dollars and millions of lives by making vaccine delivery simpler and safer. The United States has been the leader in developing such devices and should continue to pursue similar innovations so that future products reach their intended recipients safely and effectively.

Developing Advocates for Research, Development, and Delivery

Political champions who understand the importance of global health technologies and are willing to publicly advocate on their behalf are vital to helping the United States maintain its leadership in the development of new technologies. Such champions are hard to find. Even policymakers who consider global health a high priority sometimes have little knowledge of the current status and needs of global health research and development. Therefore, a robust and continued effort by government, nongovernmental organizations, academics, advocates, and others—those who have a solid understanding of the research and development process and how it has benefited people around the world—is needed to educate and support U.S. policymakers willing to take a leadership role on this issue.

These champions are critical for instilling long-term vision and maintaining optimism for the development of future health technologies. Time and patience coupled with innovation and confidence will be needed, but the final outcomes will be well worth the wait.

Policy Recommendations

The United States has a clear and important role in ensuring that the discovery, development, and delivery of new global health technologies continue to be a high priority on the world stage. To ensure that the United States remains a leader in global health research and that development continues to support the necessary pipeline of health products needed for the developing world, we urge Congress and the administration to focus on the following key policy areas:

- *Long-term financing for global health research and development:* Continued and enhanced financial support for global health research and development at the U.S. National Institutes of Health, the Centers for Disease Control and Prevention, the U.S. Agency for International Development, the U.S. Department of Defense, and the FDA must be ensured. To facilitate coordination and collaboration and eliminate duplicative research, government agencies should be encouraged to report their research and development strategies.
- *Mechanisms to encourage private-sector investment in the development of global health technologies:* The United States must support mechanisms that will attract private-sector involvement in the development of new tools. These mechanisms include innovative financing (especially priority review vouchers and advance market commitments) and public-private partnerships, including product-development partnerships.

- *Regulatory pathways and capacities:* Congress and the administration must pursue full implementation of policies to enhance the FDA's regulatory process for reviewing and approving technologies for non-U.S. populations; support and collaborate with WHO to strengthen the national regulatory capacity of developing countries; and support WHO in streamlining and accelerating prequalification processes.
- *Health systems for new products:* The United States must give priority to ensuring that health systems in developing countries—including surveillance, logistics, and procurement systems—are strengthened to guarantee timely access to new products by those most in need.

Conclusion

Historically, technology has played a critical role in combating the world's most severe diseases, and the United States has played a leading role in developing many of the world's global health innovations. From the eradication of smallpox to the development of antiretroviral drugs for HIV/AIDS, significant improvements in health status around the world have resulted from scientific innovation and discovery. Despite improved health statistics in developed nations over the past century, however, rates of death and illness in many developing countries have stagnated or even worsened over the past few decades. These trends highlight the need for greater investment in the development of innovative technologies for infectious diseases that primarily affect developing nations. Long-term vision and political leadership, innovative mechanisms for supporting the development of new technologies, effective health systems to deploy new products, and stronger U.S. leadership in improving regulatory processes will each be critical to ensuring that those who are most in need have timely and equitable access to technologies developed for their benefit.