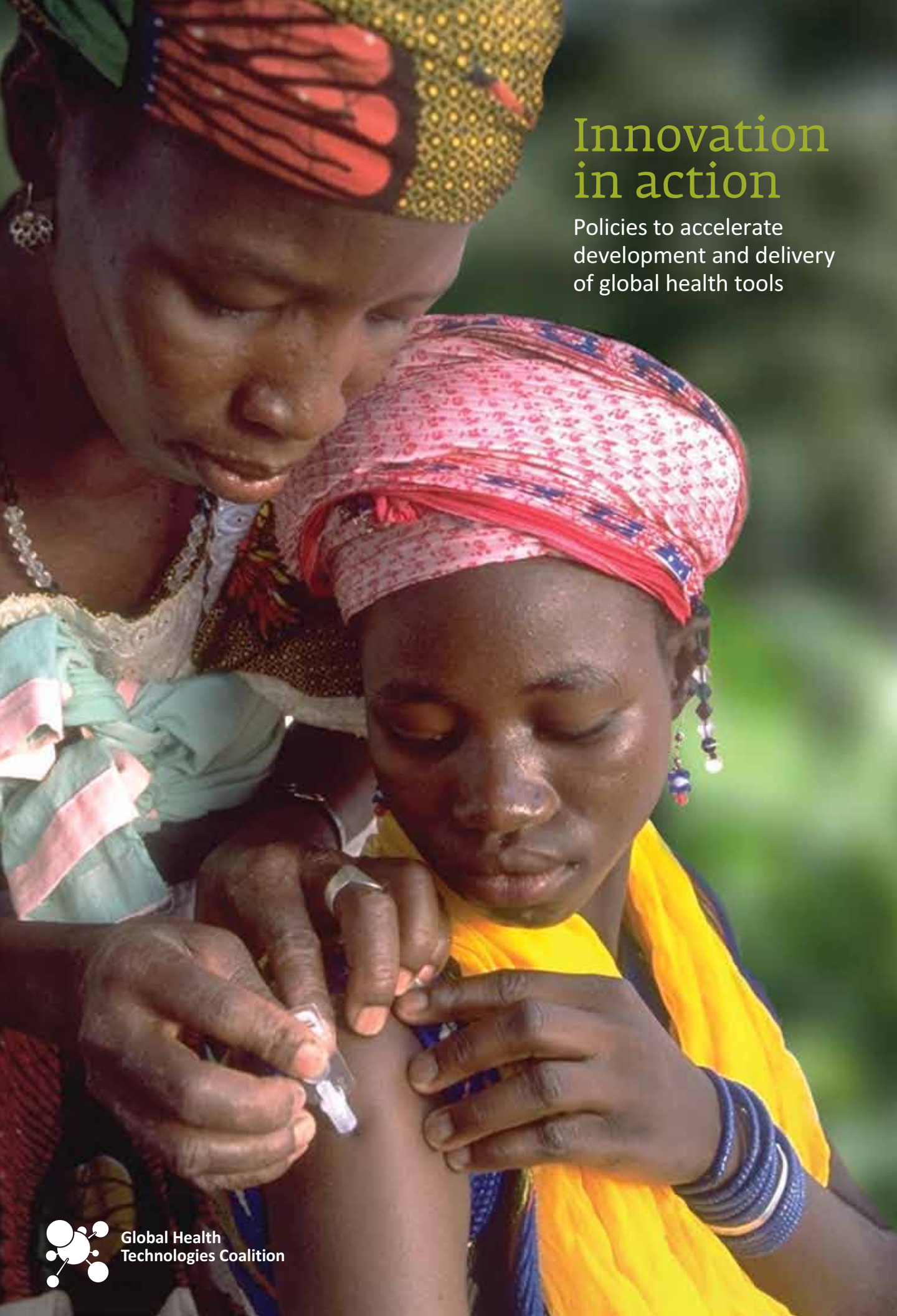

Innovation in action

Policies to accelerate development and delivery of global health tools

Global Health Technologies Coalition

CONTENTS

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The Global Health Technologies Coalition

The Global Health Technologies Coalition (GHTC) seeks to engage and inform US decision-makers about policies to accelerate the creation of new tools to address longstanding global health problems in low-resource settings. These tools include new vaccines, drugs, microbicides, diagnostic tests and other products. The coalition advocates for increased and effective use of public resources, incentives to encourage private investment, and improved regulatory systems. The GHTC is housed at PATH and funded by the Bill & Melinda Gates Foundation.

www.ghtcoalition.org

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EXECUTIVE SUMMARY

The United States has long been at the forefront of research and development (R&D) for diseases that affect populations worldwide. Thanks to US investment and innovation, undeniable progress has been made in preventing, diagnosing, and treating conditions such as HIV/AIDS, malaria, tuberculosis, neglected tropical diseases, pneumonia, and diarrheal diseases. For example, the number of children who die before age five has been halved since 1960—from 20 million to less than 9 million each year. The United Nations has estimated that if recent progress against HIV/AIDS and other infectious diseases continues, life expectancy in the poorest countries worldwide will increase from 56 years currently to 69 years in 2050.

Despite this tremendous progress, existing tools in the arsenal against global health diseases are not sufficient to address drug resistance and new infectious disease threats. In addition, no vaccines exist for some of the most intractable diseases, such as malaria and HIV/AIDS, and no treatments are available for some of the tropical diseases that affect one billion people each year. Financial challenges also can inhibit private-sector, nonprofit, academic, and federal agency experts from fully applying their skills to global health R&D, hindering the development of new tools. Even when effective health tools are under development, regulatory challenges at the global, regional, and country level can prevent health products from reaching the people who need them most.

The time is ripe for the United States to address these issues head on. With the release of the US Global Health Initiative (GHI)—President Obama's new six-year, $63 billion plan to address global health issues—the United States has the opportunity to ensure that a commitment to research and innovation for new products and tools is a central part of its efforts to improve health worldwide.

This first annual policy report from the Global Health Technologies Coalition (GHTC)—a group of more than 30 nonprofit organizations working to increase awareness of the urgent need for vaccines, diagnostics, drugs, and other products that save lives in the developing world—provides recommendations for US policymakers on how to accelerate global health innovation and research.

This report examines the financing and regulatory issues that affect global health R&D, highlighting why innovation and product development are critical to the overall US global health strategy. The report also outlines recommendations in three policy areas for Congress and the Administration.

1. To ensure that the United States maximizes its investment in global health and continues its efforts to save lives worldwide, the GHTC urges Congress and the Administration to take the following **public financing** policy actions:
   - Make research and product innovation a central component of the overall US global health strategy, including in the GHI.
   - Increase US funding for and coordination of global health research to develop new tools.
   - Improve documentation of US investments in global health R&D.
2. Strong, coordinated **regulatory systems** are essential to ensuring that safe and effective global health technologies quickly reach people in need. The GHTC recommends that US policymakers consider the following regulatory policy actions:
   - Pursue stronger partnerships between the United States and global regulatory stakeholders, agencies, and product developers.
   - Expand membership in US Food and Drug Administration (FDA) advisory committees to include developing country representatives.
   - Ensure that the FDA carries out recommendations from newly legislated review groups to address neglected diseases in the developing world.
3. **Incentives and innovative financing mechanisms** have the potential to encourage a diverse set of actors with R&D expertise to devote their attention to solving the health challenges of the developing world. In order to guarantee that critical players are engaged in these efforts, the GHTC urges Congress and the Administration to consider the following policy actions to explore these mechanisms:
   - Form a cross-agency working group to explore US participation in a portfolio of incentive and innovative financing mechanisms.
   - Support US engagement with global partners exploring innovative financing.
   - Conduct a vigorous assessment of each incentive mechanism in which the US invests.

US policymakers should make innovation and research central components of US global health efforts. The policy actions outlined in this report provide Congress and the Administration with a solid foundation to boost the research and innovation needed to address global health diseases and to ensure that the most effective tools are available now and in the future.

US leadership in global health R&D

The United States has long been and continues to be the leader in global health research and development (R&D) to benefit populations in the developing world. Thanks to this investment, Americans and millions of people around the world no longer live in fear of diseases such as polio and measles. Millions more, including those receiving drugs that fight HIV/AIDS, live longer and healthier lives.

The history of global health is studded with US-driven success stories. Since 1988, polio cases worldwide have decreased by more than 99 percent in part because of US efforts to eradicate the disease.[1] Between 2000 and 2008—fifty years after a vaccine against measles was first discovered by an American Nobel Prize winner—measles deaths worldwide dropped 78 percent.[2] And 26 countries have reported cutting in half the number of malaria cases and deaths between 2000 and 2007 due in large part to US-driven efforts to prevent and treat the disease.[3]

Research and development of new tools offer the potential to address global health challenges and save millions of lives each year.

How R&D benefits the United States

- Supports US foreign policy goals to increase security, build stronger economies, strengthen US relations worldwide, and reduce infectious diseases.
- Benefits US academic and research institutions through increased funding and by creating jobs. Dr. Francis Collins, director of the National Institutes of Health (NIH), recently stated that "every research dollar generates more than two dollars in goods and services in less than a year."[4]

Building on US R&D successes

Despite these advances, global health problems still threaten whole populations, and more than 30 new infectious diseases have been identified in the last three decades.[5]

- Almost four million people, most in developing countries, die each year from HIV/AIDS, tuberculosis (TB), and malaria. Vaccines to prevent HIV or malaria are still under development, and today's TB drugs, as well as the single available TB vaccine, are outdated.
- One billion people are affected annually by neglected tropical diseases, such as leishmaniasis and African sleeping sickness. Many of these diseases have no effective treatment.
- Millions of children in the developing world are sickened and die each year from pneumonia and diarrhea, diseases that are treatable in the developed world.

Today, we still lack effective tools to combat these and other global health threats. But R&D for new vaccines, drugs, microbicides, diagnostics, and other products offers the potential to solve or slow these diseases and save millions of lives each year. To ensure that effective health solutions are available when we need them, it is critical to invest in global health R&D. The United States has the opportunity to ensure that its commitment to developing global health tools is sustained and elevated with the release of the US Global Health Initiative (GHI)—President Obama's new six-year, $63 billion plan to improve health worldwide.

The US role in R&D

A wide variety of stakeholders participate in creating health products for the developing world. Partners such as the US Government, academic institutions, private industry, nonprofit organizations, and biotechnology groups, as well as innovative collaborations like product development partnerships (PDPs) that leverage private and public sector expertise, each have unique capabilities to offer. Despite the involvement of a spectrum of stakeholders, the development of new global health solutions is not without challenges. Donor investments may be insufficient; there are few incentives for private industry to dedicate resources for products it believes will not generate a profit; and review processes can be complex and cumbersome. These challenges, however, are not insurmountable. US policymakers have the opportunity to advance new technologies by working to:

- Ensure robust and strategic financing by the US Government with sustained coordination among federal agencies.
- Enhance the review and approval processes for new vaccines, drugs, diagnostics, and other health tools.
- Increase engagement with private industry and noncommercial developers through market incentives and innovative financing.

A number of recent announcements—including the GHI[6] and increased prioritization of global health by the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH)—indicate that the time is right to enhance US investment in global health research.

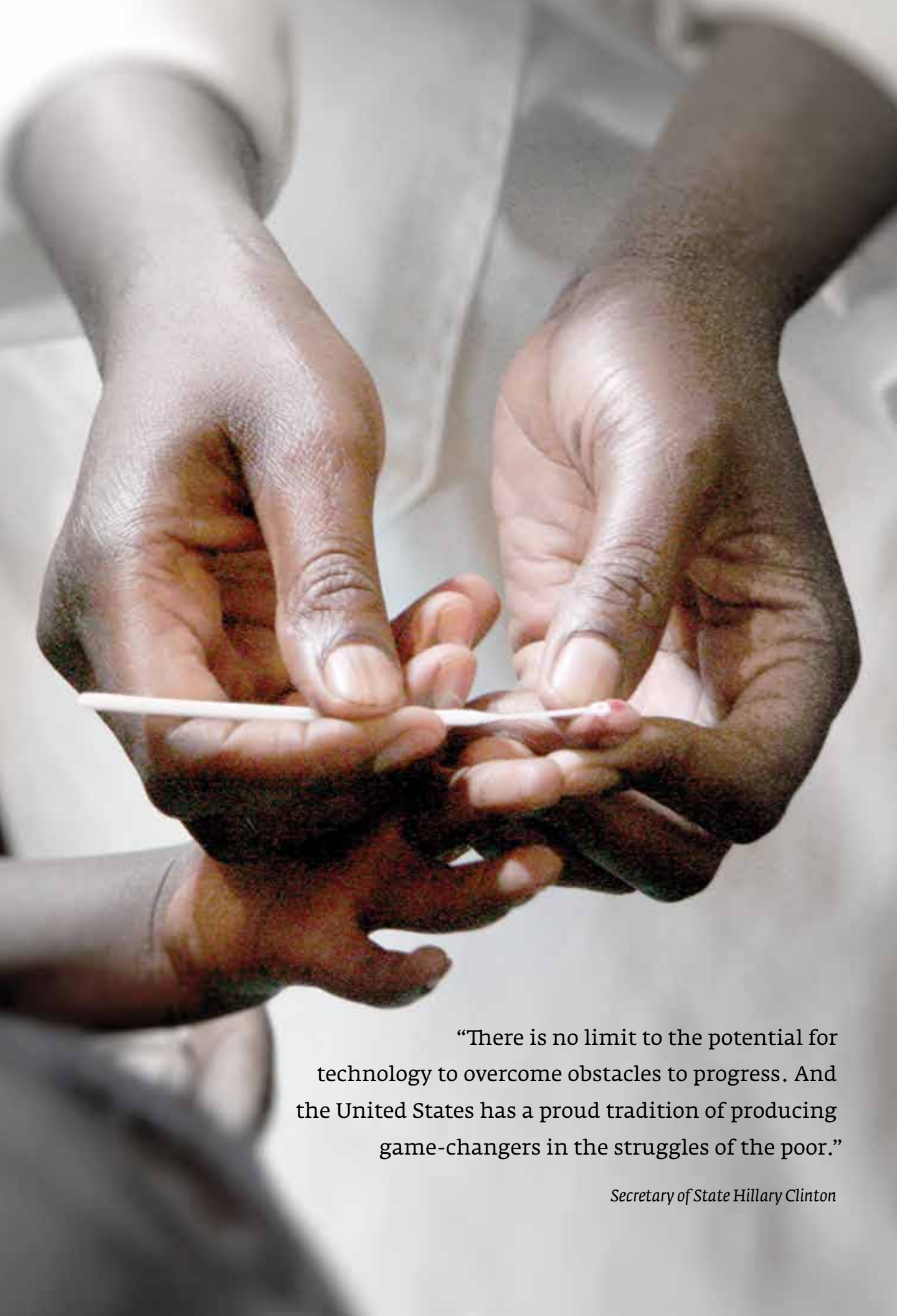
> "There are those who say we cannot afford to invest in science, that support for research is somehow a luxury at moments defined by necessities. I fundamentally disagree. Science is more essential for our prosperity, our security, our health, our environment, and our quality of life than it has ever been before.... I believe it is not in our character, the American character, to follow. It's our character to lead. And it is time for us to lead once again."
>
> *President Obama, April 2009 speech to the National Academy of Sciences*

Health solutions within reach

Within the next decade, support from the US Government can help move many new technology solutions toward completion, including:

- By 2011, a simple finger-prick blood test to measure HIV disease progression.
- By 2016, a new vaccine against tuberculosis.
- Within five years, oral drugs to prevent HIV infection.
- By 2014, new drugs to treat neglected tropical diseases.
- More vaccine candidates against dengue fever.
- By 2015, a new tuberculosis drug regimen.
- By 2012, a malaria vaccine candidate submitted to international organizations for review.

Health tools such as vaccines, diagnostics, and treatments can have an immediate impact and help save infants' lives.



"There is no limit to the potential for technology to overcome obstacles to progress. And the United States has a proud tradition of producing game-changers in the struggles of the poor."

Secretary of State Hillary Clinton

Building on US leadership in global health

Breakthroughs in science and technology are integral to tackling some of the most intractable problems in global health. To continue as a leader in global health, the United States should provide adequate and sustained funding for global health R&D, backed by strong political commitment from Congress and the Administration. Policymakers have the unique opportunity to ensure that the commitment to R&D seen during the Bush Administration continues today by elevating R&D in President Obama's GHI, the new US strategy to improve health worldwide.

The work of US agencies—each of which plays a distinct but complementary role in global health R&D—affords the United States a unique leadership opportunity in conducting a broad range of research, including basic science, clinical development, and applied research. Among the agencies involved in global health research are the CDC, Department of Defense (DoD), Food and Drug Administration (FDA), NIH, and United States Agency for International Development (USAID).

Agency expertise also gives the United States the chance to develop technologies that benefit the health and economies of the developing world. These agencies leverage expertise from a wide range of partners—including public-private partnerships (PPPs), academic and research institutions, and nonprofit organizations—to advance research and innovation. For instance, USAID frequently works in close collaboration with PPPs to leverage private sector expertise in developing new technologies for neglected diseases. Many PPPs conduct research with a focus on access in developing countries, and have added benefits such as bolstering developing world infrastructure to conduct clinical trials. USAID works with PPPs to advance the development of new global health tools, and could leverage these partnerships further for even more impact.

Life-saving contributions from US agencies

In January 2009, a new anti-malarial medicine developed especially for children was among the pediatric treatments to come out of a PDP pipeline supported by USAID.

A six-year collaboration between the Department of Defense and the Government of Thailand resulted in the completion of a large-scale HIV vaccine trial—known as RV144. The trial provided the first evidence of vaccine-induced protection against HIV and led to renewed optimism in the search for an efficacious HIV vaccine.

A trial in Gambia, funded in part by the National Institute of Health's National Institute of Allergy and Infectious Diseases, was the first major clinical trial in 20 years to show that use of a pneumococcal vaccine could substantially reduce death and illness from pneumococcal infections among children in the developing world.

Finding—and funding—solutions

Many of the country's top leaders have expressed support for global health R&D, including the nation's president. President Obama has signaled that innovation and research are priorities of his administration in several speeches and policy decisions over the past year.

In February 2010, the Administration released details about the GHI. The president has included research and innovation as one of the seven GHI principles, a step that further highlights the Administration's acknowledgment of the important role of research in advancing our nation's global health goals. Initial details released about the GHI indicated that while research and innovation are included as one of the initiative's principles, the focus would be primarily on implementation and operations research. As policymakers work to finalize the details of the GHI and implement the program, decision-makers should ensure that the GHI focuses on research, development, and the introduction of new global health tools and technologies to ensure that the fight against global diseases succeeds.

During a speech delivered in early 2009, President Obama expressed a goal of increasing national investment in all R&D, not limited to global health, to more than 3 percent of the US Gross Domestic Product (GDP).[7] In 2007, US spending on all R&D was 2.7 percent of the nation's GDP, making the president's goal a significant, but not insurmountable, one.[8,9] Seizing upon this momentum, the president in February 2010 elevated research in his fiscal year 2011 budget proposal. The proposal would provide more than $32 billion for the NIH, an agency that lists global health research as one of its five priorities for FY 2011. In addition, the Department of State, including USAID, would receive approximately $8.5 billion in global health funding under the president's proposal. All three agencies would receive funding increases under President Obama's proposal compared with FY 2010.

Prevention of diarrhea—which kills an estimated 1.6 million children annually—can be bolstered with new tools such as vaccines, oral rehydration solutions and zinc treatments.

This increase is welcome, and additional impetus is needed to ensure that all agencies involved in global health research receive funding increases.

Accounting for US funding

US contributions to global health R&D are significant, but it has historically been challenging to determine the full breadth of this investment. A review of published data on US financing for global health R&D reveals inconsistent and incomplete estimates. The Institute of Medicine recently found that the US investment in "research relevant to all the health problems of low-income countries cannot be estimated with any meaningful degree of accuracy."[10] In particular, the US Government has not led a full accounting of our nation's R&D expenditures for global health since 1987.[11] One notable exception is the Office of AIDS Research at the NIH, which closely tracks investments in HIV/AIDS research.[12]

A noteworthy recent effort to chart US investment in global health is G-FINDER, an annual survey conducted by the George Institute for Global Health that tracks global investment in R&D for neglected diseases. This comprehensive survey found that while the US Government makes the largest contribution to global health research, its recent contributions remain unchanged and its global share has not kept pace with increased contributions from other countries.[13]

An expanding pipeline in need of support

Historically, efforts to advance products for the developing world have severely lagged behind products for the industrialized world. A recent report puts the number of drugs developed over the 24-year period from 1975 to 1999 for neglected diseases at 33, compared with the more than 1,300 drugs developed in that time for diseases of the industrialized world.[14]

With the advent of new mechanisms to foster the design of products for the developing world, change is slowly coming: between just 2000 and 2007, 106 products for neglected diseases were in development.[15]

While G-FINDER is currently the best source of information on global health R&D, it does not reveal detailed information about the type of research in which the United States has invested. The type of tracking conducted by the Office of AIDS Research should be expanded across all agencies and global health diseases to improve transparency about the US investment in global health research. In addition, the US Government should lead its own examination of its global health R&D spending. Tracking should include how much is allocated, where investments are made, and through which agencies. Accurate and specific data would help to ensure that money is apportioned properly, that research activities are coordinated across federal agencies, and that research gaps are closed. In sum, it would provide policymakers with the critical information they need to make well-informed decisions about future investments.

The United States can also take a more agency-specific approach to tracking funding. For example, in 2006 USAID outlined its five-year health research strategy and has released subsequent annual progress reports.[16] 2010 is the final year of the strategy and the annual documentation that accompanied it. The Obama Administration should request that USAID develop a new six-year research strategy to coincide with the implementation period of the GHI, and that USAID continue to produce an annual report documenting its progress in implementing this strategy.

Robust funding ensures that US agencies can continue their life-saving work in developing new products for global health.

Policy recommendations

To ensure that the United States maximizes its potential impact on global health and continues its efforts to save lives worldwide, the GHTC urges Congress and the Administration to take the following key policy actions:

- **Include research and product innovation as a key component of the overall US global health strategy, including in the GHI.** A commitment to global health research and product innovation should be included as a priority in all US global health efforts and should be seen as complementary to existing programs. In particular, the role of research for new health technologies to meet our nation's global health goals should be sustained and elevated in the president's new GHI as a key component of the administration's focus on innovation.
- **Increase US funding for and coordination of global health research to develop new tools.** Policymakers should ensure that, in line with the Administration's priorities, funding for global health R&D meets the needs of US agencies to carry out product development. Such an increase will help achieve the president's goal of ensuring that at least 3 percent of the national GDP is devoted to R&D. Sufficient funding is needed for agencies such as the CDC, FDA, DoD, NIH, and USAID.
- **Bolster documentation of US investments in global health R&D.** Congress should commission a Congressional Research Service report to examine US Government funding for global health R&D and coordination among federal agencies involved in R&D activities. The Administration also should request that USAID develop a second six-year strategy for R&D and that the agency produce annual reports on the progress of this strategy.

"Neglected diseases claim roughly 500,000 lives each year.... Unfortunately, less than 1 percent of the roughly 1,400 drugs registered between 1975 and 1999 treated such diseases.... Streamlining the FDA review process to treat these diseases is not only in our country's national interest, but it is consistent with our longstanding tradition of caring for those who are less fortunate around the world."

Senator Sam Brownback (R-Kansas)

Assessing new health technologies

To reduce the burden of life-threatening diseases, countries must be able to ensure that only safe, effective health technologies are used by their citizens. Regulatory processes are designed to ensure that products are authentic, safe, and effective before they are widely distributed.

These product review processes come into play during three key stages of technology development—clinical trials, World Health Organization prequalification, and product approval. In addition, after a product is prequalified, approved, licensed, and marketed, it must be monitored to ensure that its benefits match expectations and to detect any safety concerns from use in real-world conditions.

Products must be reviewed and licensed by the national regulatory authority of the country in which they will be marketed and distributed. These authorities decide whether a product is safe for widespread use within that jurisdiction and whether manufacturers can consistently produce high-quality products. For many developing countries without sufficient regulatory capacity, WHO prequalification—while not a regulatory review—is needed to signal product quality, safety, and efficacy.

In the developing world, regulatory processes can range from highly sophisticated to nonexistent. When a country cannot determine the suitability of health technologies—either because it does not have the proper regulatory resources or because a reliance on regulatory review performed in other countries does not address local needs—the health of its people suffers. In the research phases, a lack of regulatory capacity may compromise clinical trials by delaying their progression and jeopardizing the validity of their data. In addition, a lack of clinical trial oversight can mean that the safety of trial volunteers has not been guaranteed. When regulatory review of a final product is not fully functioning, technologies cannot be registered in a timely manner and essential health tools may not reach patients. Finally, inconsistent surveillance can undermine product safety and may lead to a proliferation of unsafe or counterfeit products both within the country and across its borders.

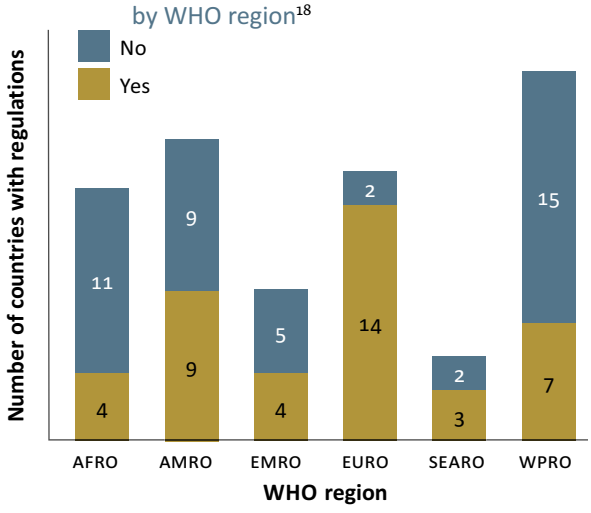
Insufficient capacity among host countries

To properly reflect local health priorities, regulatory review is ideally managed by the government in the country where a product will be registered and used. Developing countries, however, often lack the regulatory capacity needed to bring safe and effective health technologies into use. That capacity requires resources to:

- Review clinical trial applications.
- Oversee the design of, conduct site inspections for, and monitor trials, in accordance with international standards.
- Determine standards for approval and registration of health technologies.
- Conduct inspections of manufacturing facilities and oversee quality assurance over the product supply chain used to test and make the technology.
- Explain to professionals and the public how to use the technologies properly and ensure appropriate labeling.
- Routinely monitor the quality of health products being distributed in the country.

In 2008, the WHO found that only about 20 percent of countries—all of them industrialized—have fully operational regulatory systems for medicines. Among the remaining 80 percent of countries, approximately one-half have varying regulatory capacities and approximately one-third have very limited or no regulation for medicine. According to the WHO, more than two-thirds of people worldwide live in countries with "marginal or inadequate" systems for assuring drug quality, safety, and effectiveness.[17] Figure 1 illustrates this gap in capacity to regulate diagnostic products.

FIGURE 1. Capacity to regulate diagnostic products, by WHO region[18]



AFRO = Regional Office for Africa
AMRO = Regional Office for the Americas
EMRO = Regional Office for the Eastern Mediterranean
EURO = Regional Office for Europe
SEARO = Regional Office for Southeast Asia
WPRO = Regional Office for the Western Pacific

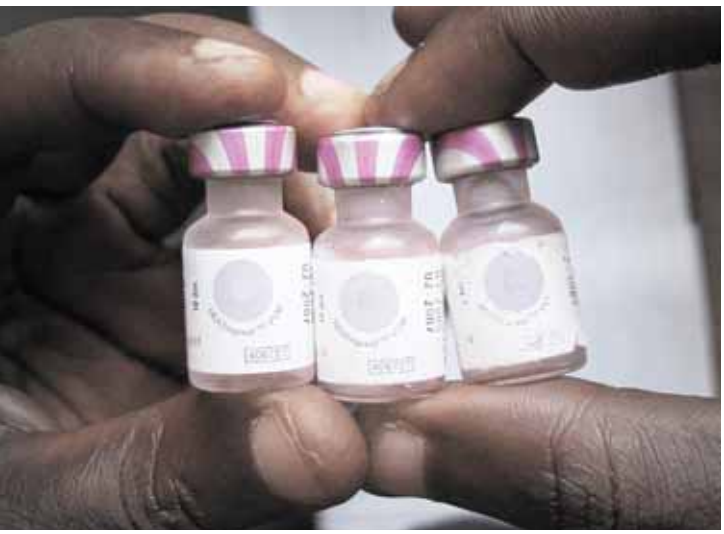
How weak regulatory systems impact health

As many as half of all malaria-fighting artesunate tablets purchased in Southeast Asia are fake. These substandard drugs contain no active ingredient at all, threatening the health of those who purchase them and increasing potential for drug resistance.[19]

Regulatory functions in the industrialized world

The US FDA, the European Medicines Agency, and the WHO each play a unique role in the review and licensure of products intended for the developing world.

The FDA is well known for its role in regulating food and drug safety for US citizens, but it also plays a less visible but important role in protecting the health and safety of populations abroad. In 2004, the FDA announced an initiative to support a goal of the President's Emergency Plan for AIDS Relief (PEPFAR) to improve access to antiretroviral therapy in developing countries. This initiative is designed to ensure that drugs produced by manufacturers all over the world can be reviewed and assessed quickly and efficiently and delivered to patients in need through PEPFAR.[20] In 2008, the FDA issued guidelines on how it would receive and give opinions on applications for vaccines developed for diseases affecting developing countries.[21] These actions signal the agency's willingness to take on review of products specifically intended for use in the developing world.



Even simple technologies, such as this sticker that changes color when a vaccine is exposed to extreme heat, can protect lives in the developing world.

The FDA also supports capacity-building among regulators in developing countries through collaborations with countries and regional regulatory networks.[22] Other US agencies—USAID in particular—also play an important role in building regulatory capacity in the developing world.

The European Medicines Agency—the regulatory body for the European Union—evaluates and supervises medicines for use in the European market. In 2004, the European Medicines Agency established a policy called Article 58, under which it gives a scientific opinion on certain vaccines and drugs intended exclusively for markets outside the European Union. The European Medicines Agency conducts this function in close cooperation with the WHO.

The WHO's Prequalification Programme was established to improve access to medicines and vaccines that meet unified standards. The WHO provides an independent opinion on the quality, safety, and efficacy of drugs and vaccines required for purchase by United Nations procurement agencies, such as UNICEF and others. The WHO also assesses the suitability of the candidate product for the target population and the procurement agency, and ensures continuing compliance with established standards. The WHO is not a regulator, and its decisions do not bind national regulators. However, the prequalification step is an important signal of product quality, safety, and efficacy to developing countries without sufficient regulatory functions. Because of some countries' reliance on WHO prequalification, it is crucial that the FDA collaborate with the WHO when products designed for the developing world are at stake.

The FDA has already entered into confidentiality agreements with the WHO and the European Medicines Agency in an effort to share information and documents about certain health products under evaluation. The agreements aim to streamline the FDA's regulatory activities, the WHO's prequalification actions, and the European Medicines Agency's regulatory duties.[23,24] They also seek to achieve quicker review and approval of health products, as well as allow for information sharing and exchange.

Enhancing US regulatory engagement

By playing a more active role, the United States has the opportunity to make significant improvements in global health and to bolster partnerships with regulatory agencies and other global stakeholders on these issues.

A first step in this direction was recently achieved through an amendment to the Department of Agriculture Fiscal Year 2010 appropriations bill sponsored by Senator Sam Brownback. This language directs the FDA to convene review groups to make recommen-

dations regarding the "appropriate preclinical, trial design, and regulatory paradigms and optimal solutions for the prevention, diagnosis, and treatment" of rare and neglected diseases in the developing world.[25] The recommendations from these groups will provide valuable information on the potential role for the FDA in the future.

In order to maximize improvements in global health, the United States will need to have strong relationships with regulatory stakeholders worldwide. As US agencies enhance their roles in assessing products intended for the developing world and in building regulatory capacity, it is vital to collaborate closely with the WHO and national regulatory authorities. Several mechanisms could achieve this goal, and each should be explored by US policymakers:

- Sabbatical rotations or exchanges between FDA and WHO staff should be established to strengthen partnerships and synergies.
- Parallel review processes by the FDA and WHO should be triggered early in the regulatory process when it becomes clear that a product will be seeking WHO prequalification.
- Financial and political support to the FDA and USAID to offer expert consultation and regulatory assistance to WHO staff and regional and national regulatory bodies should be increased.
- Cross-agency cooperation among the FDA, NIH, CDC, DoD, and USAID, as well as with the WHO, should be encouraged to increase the capacity to conduct clinical trials and implement policy.
- The FDA should be included in existing or future interagency global health committees. The agency should also play a larger role as a technical resource and partner in the joint review of clinical trial applications, alongside nonprofit PDPs, private industry, and civil society.

Simple and appropriate health tools—including prefilled injection devices and syringes, household water purification and new vaccines for malaria—could be used to save the lives of mothers worldwide.

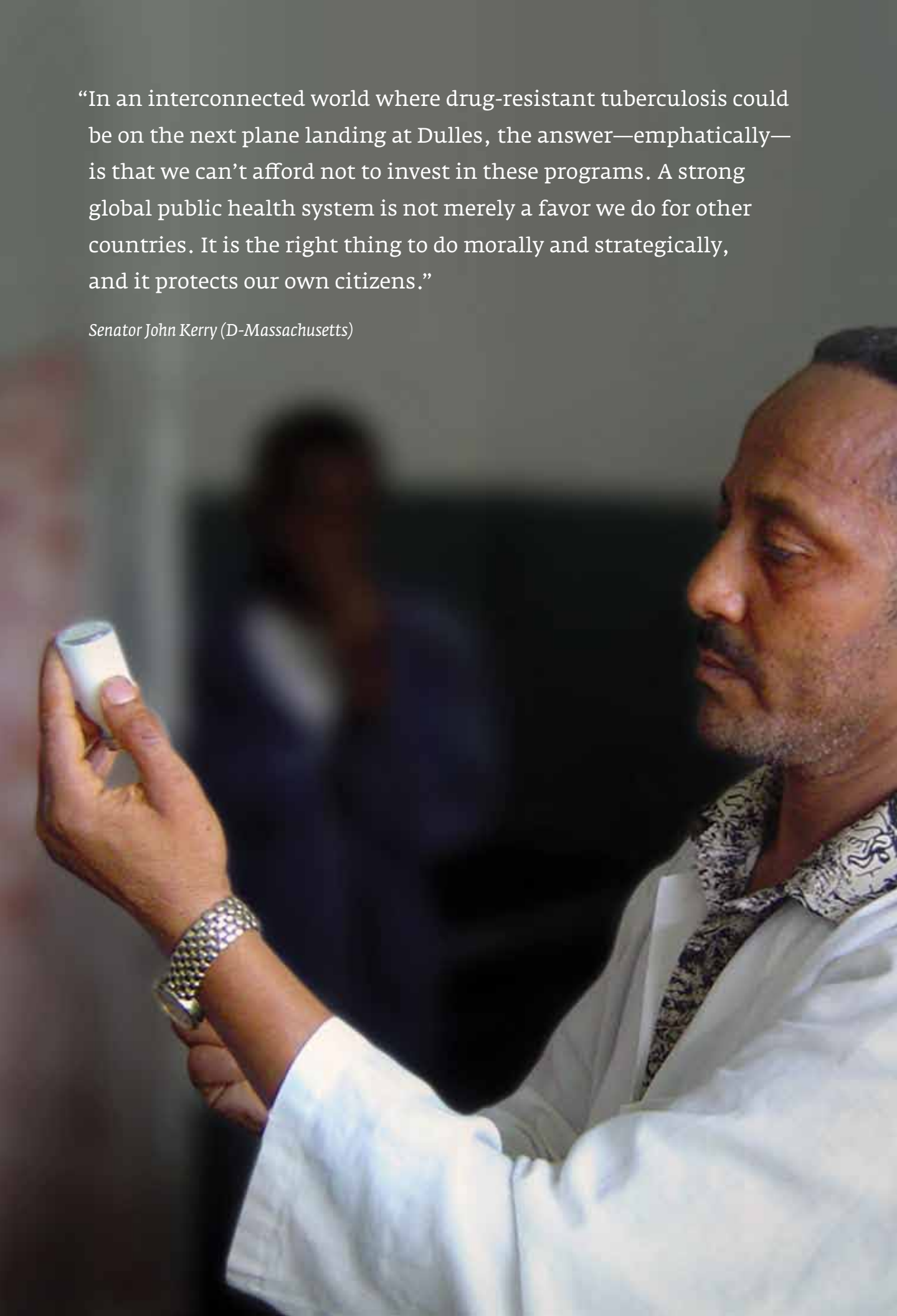
Policy recommendations

Strong, coordinated regulatory systems are essential to ensuring that safe and effective global health technologies quickly reach people in need. In conjunction with other global and regional institutional partners and national regulatory bodies, the United States should play a stronger role in working with global and national regulatory stakeholders to ensure that new products for global diseases are safe and effective. The GHTC recommends that US policymakers consider the following policy actions:

- **Ensure timely implementation of recommendations from new FDA review groups.** Congress should ensure that the congressionally mandated review groups at the FDA are convened in a timely manner; that there is a mechanism for public comment; and that the final recommendations of these groups are submitted within the specified timeframe. Congress also should allocate sufficient resources to the FDA to carry out the recommendations, and require annual progress reports.
- **Pursue stronger partnerships between the United States and global regulatory stakeholders.** The United States should increasingly collaborate with the WHO and national regulatory authorities to accelerate access to global health products. This goal can be achieved by bolstering exchange between FDA and WHO staff; triggering a parallel review process by the FDA and WHO; and giving the FDA and USAID adequate support to offer consultation and regulatory assistance.
- **Strengthen FDA's engagement with other agencies and product developers.** The FDA should increase its collaboration with other US Government agencies that conduct R&D for global health tools. The FDA should be included in existing or future interagency global health committees. It also should partner with other agencies to play a larger role as a technical resource and partner in the joint review of clinical trial applications.
- **Expand membership in FDA advisory committees.** Advisory committees within the FDA provide important expertise and guidance to agency centers on scientific decisions, as well as on safety and efficacy evaluations of new products. Representatives from developing countries should be invited to participate in advisory committees wherever there is relevance to diseases primarily found in the developing world.

"In an interconnected world where drug-resistant tuberculosis could be on the next plane landing at Dulles, the answer—emphatically—is that we can't afford not to invest in these programs. A strong global public health system is not merely a favor we do for other countries. It is the right thing to do morally and strategically, and it protects our own citizens."

Senator John Kerry (D-Massachusetts)



Encouraging investment from a diverse set of actors

Solving the R&D challenges posed by new health technologies for the developing world requires the coordinated expertise and engagement of a wide variety of stakeholders, including private biotechnology and pharmaceutical companies, nonprofit groups such as nonprofit research institutions, academia, and public institutes.

Private companies possess the talent, expertise, and skills essential to advancing health technologies. In fact, private companies discover, develop, and deliver more health technologies than any other sector of the economy,[26] but their investment in products for the developing world remains minimal.[27,28]

PPPs—including PDPs,[29] which leverage public and philanthropic funds to engage private industry, academia, and public agencies in global health R&D—have benefited from donor funding to generate a robust pipeline of potential technologies specifically designed for the developing world. By one estimate, PDPs manage about one-fifth of all funds dedicated to research in neglected diseases.[30] Global health research also benefits from the involvement of other groups—including organized research networks, academic institutions, and public institutes. Among the most crucial contributions from these groups are the basic science breakthroughs that are the first steps in the product development pathway.

Financing challenges, however, often inhibit these groups from applying enough of their skills to global health R&D to rapidly develop critical health products for the developing world. For private industry, products for the developing world are often perceived as offering insufficient or overly risky commercial markets to encourage R&D investment.[31] For nonprofit research institutions and academia, funding is inadequate and often too short-term and unstable to allow for the long-range planning and flexible research programs that product development requires.

For all groups, the current economic crisis has exacerbated the situation and further jeopardized global health R&D efforts. To accelerate global health R&D, analysts have developed multiple proposals, referred to collectively as incentives and innovative financing mechanisms, which aim to overcome these financial obstacles.

Incentive mechanisms generally reduce the risk and uncertainty of developing global commercial markets for health products to encourage industry to invest. Innovative financing mechanisms identify new ways of raising and allocating funds to stimulate and accelerate global health R&D across all sectors. Another important aspect of both mechanisms is that they aim to make more effective use of funds.

Because different incentives and innovative financing mechanisms will be more effective at stimulating certain products or phases of the development pathway, a portfolio or suite of incentives and innovative financing mechanisms is needed to accelerate a range of critical health products for the developing world.

Some incentives and innovative financing mechanisms have already been implemented, while many more are still in conceptual development. These mechanisms may provide critical opportunities to advance global health R&D, and the US Government should become more centrally involved in analyzing, implementing, and supporting these mechanisms as a central strategy in developing essential health products for the developing world.

Incentive mechanisms to spur private investment

Priority review vouchers (**PRVs**) provide companies that develop products for neglected diseases with a voucher to secure faster regulatory review for any future product of their choice. PRVs also can be sold by their holder to other companies.

Advance market commitments (**AMCs**) pool donor funding to guarantee a future market, at a specified price, for companies that can develop a specific product that is demanded by low- and middle-income countries.

Mechanisms to encourage private industry participation in global health R&D

Incentive mechanisms have the potential to advance innovation by stimulating private investment in R&D in the absence of a profitable market. US policymakers have the opportunity to implement incentives to boost private investment in R&D for global health at a time when real progress is possible.

New mechanisms for financing global health research and product development are also needed to supplement investments by traditional donors, in order to accelerate the R&D process. Traditional funding—often given in short-term increments of three to five years—is generally restricted for a specific project or purpose and is highly susceptible to fluctuations in the political and economic environment.

Financing mechanisms to provide additional, stable funding

Several mechanisms that have been proposed and implemented to tap into new sources of funding are being explored as mechanisms to benefit global health research.

For example, the **International Financing Facility for Immunizations** (**IFFIm**) uses donor guarantees to sell bonds on capital markets to frontload spending on providing childhood immunizations worldwide.

Voluntary solidarity contributions are small voluntary donations associated with the purchase of items such as airline tickets to support the procurement of global health products.

A proposed **Currency Transaction Levy** would tax certain financial transactions at a minimal rate, and revenues could be used to support global health and development programs, among other uses.[32]

These factors slow R&D by limiting research actors from developing long-term programs, easily switching between lines of research or product candidates, and rapidly securing funding to pursue emerging promising science. The global economic downturn has also threatened the amount of funding available for global health R&D. Innovative financing mechanisms can help overcome these challenges by providing additional, long-term, predictable, and stable financing to support R&D. Some financing mechanisms raise new funds, often from market-based sources or new taxes, while other mechanisms allocate funding in a different way to accelerate R&D.

Spurring the development and delivery of vaccines, drugs, diagnostics, and other tools can help families around the world.

US engagement in incentive mechanisms

The United States has been engaged in supporting incentive and innovative financing mechanisms, particularly in creating priority review vouchers, offering R&D tax credits, and encouraging small business to conduct innovative R&D through direct grants.

For example, the United States has invested in incentive mechanisms and innovative financing to benefit biodefense, such as the Project BioShield Act of 2004.[33] To encourage the pharmaceutical industry to develop biodefense products, the Act establishes a ten-year, $5.6 billion funding source for the purchase and stockpiling of new vaccines and drugs for use in an emergency. Biodefense measures are critical to US national security, and similar incentives are needed to accelerate the development of global health technologies.

While these initiatives have helped to drive innovation, the United States should be more engaged in analyzing, supporting, and implementing mechanisms specifically designed to spur R&D for health products for the developing world. For example, a pilot Advance Market Commitment (AMC), aimed at developing a new vaccine against pneumococcal disease for developing countries, is underway. It is supported by Italy, the United Kingdom, Canada, Russia, Norway, and the Bill & Melinda Gates Foundation. The Lantos-Hyde Act of 2008 directs the United States to participate in negotiations for future AMCs. Although the first AMC for a pneumococcal vaccine will provide data on the effectiveness of an incentive for a late-stage vaccine, a future AMC may target an early-stage vaccine, such as one for malaria or TB.

To ensure support for future AMCs and other innovative financing and incentive mechanisms, several nations worldwide in 2006 formed the Leading Group on Innovative Financing for Development (the Leading Group). A coalition of 55 member countries and four observer nations, the Leading Group aims to encourage discussion and action on incentives and innovative financing mechanisms.[34] To date, the United States has not participated in the Leading Group, which is rapidly emerging as the primary global venue for discussion and action on these critical issues. Although the Leading Group does not focus solely on health, the work of its members has kept innovative financing alive and relevant. The group's membership is also increasing and includes countries, international agencies and organizations, and nongovernmental organizations.

Policy recommendations

Incentives and innovative financing mechanisms have the potential to encourage a diverse set of actors with R&D expertise to devote their attention to solving the health challenges of the developing world. In order to ensure that critical players are engaged in these efforts, the GHTC urges Congress and the Administration to consider the following key policy actions:

- **Form a cross-agency working group to explore US participation in a portfolio of incentives and innovative financing mechanisms.** To ensure that the United States pursues incentives with the best chance of success, this group should consider adopting a set of criteria to use when evaluating the role of the United States in supporting specific mechanisms, such as those suggested in the box below. These criteria should be applied to the evaluation of multiple mechanisms with the goal of supporting one or two new mechanisms in 2011.
- **Ensure that a vigorous assessment is conducted of each incentive mechanism in which the US invests.** During and following implementation of an incentive mechanism or innovative financing strategy, US policymakers should ensure that a robust assessment takes place to monitor effectiveness and impact of the mechanism. Such an assessment should be incorporated as a key component of US engagement with the mechanism.
- **Support US involvement with the Leading Group on Innovative Financing for Development and other international groups working on financing for health.** US involvement with this group should eventually lead to the nation's participation in future innovative financing mechanisms, such as an AMC. As directed by the Lantos-Hyde Act, the US Government should consider participating in future negotiations for AMCs for new vaccines, as well as other finance mechanisms put forth for consideration by the Leading Group.

Evaluating the potential of new mechanisms

The GHTC suggests that the following criteria be considered by US policymakers when evaluating new financing or incentive mechanisms for global health R&D.

- **Public health impact**. What is the potential of the mechanism to address identified global health needs and to reduce burden caused by global health diseases?
- **Revenue generation.** What is the mechanism's potential to raise or secure a commitment for a quantity of additional funds that is sufficient to stimulate the desired R&D? This would encompass whether funds will be predictably and consistently available to support the R&D process, and flexible or adaptable to suit the needs of the particular R& D effort.
- **Cost-effectiveness**. Does the proposed mechanism offer a cost-effective way of generating sufficient revenue to cover transaction and/or start-up costs, administration costs associated with managing the mechanism, and other operational costs in relation to the potential revenue the mechanism might generate? (Note: This criterion does not evaluate the cost-effectiveness of the product that the mechanism is designed to advance.)
- **Targeted**. What is the mechanism's potential to encourage the interest of the private sector in R&D investments for global health technologies, accelerate efforts to develop new products, and/or create a viable market for new products? This assessment would include the likelihood of attracting skilled product developers at or across different R&D stages, taking into account a variety of products (e.g., vaccines, microbicides, diagnostics, drugs, and other tools), the different stages of R&D, and a spectrum of diseases.
- **Accountability and transparency**. Are the governance, accounting, and public reporting structures for the mechanism and its implementation identified to ensure that both the government and the public can monitor the implementation and track results? The transparency of the mechanism may provide lessons or reduce transaction costs in the adoption of additional mechanisms.
- **Political and/or technical feasibility**. Do any legal, operational, political, or other barriers exist that would preclude adoption or effective implementation of the mechanism? These may include: unique budget or cycle restrictions, political acceptability, or restrictions on international freedom to operate. In applying this criterion, policymakers should also consider ways to remove or modify any restrictive barriers if other criteria demonstrate potential offsetting benefits.

CONCLUSION

The United States should implement and improve policies to advance innovation and stimulate R&D for global health tools. As an established leader in global health, the United States has the opportunity to build on its success and bolster its contribution to developing technologies that can prevent, detect, and treat diseases and save lives worldwide through new initiatives such as the president's GHI.

In order to advance the research critical to developing the most effective health tools, US policymakers should focus on three key areas: public financing, regulatory pathways, and incentives and innovative financing. To ensure that the United States maximizes its impact on global health, the GHTC urges Congress and the Administration to take the following policy actions:

Public financing

- Include research as a key component of the overall US global health strategy.
- Increase US funding for and coordination of global health research to develop new tools.
- Bolster documentation of US investments in global health research.

Regulatory pathways

- Ensure timely implementation of recommendations from new FDA review groups.
- Pursue stronger partnerships between the United States and global regulatory stakeholders.
- Strengthen FDA's engagement with other agencies and product developers.

Incentives and innovative financing

- Form a cross-agency working group to explore US participation in a portfolio of incentives and innovative financing mechanisms.
- Support US involvement with the Leading Group on Innovative Financing for Development.
- Ensure that a vigorous assessment is conducted of each incentive mechanism in which the United States invests.

As the United States embarks on a new global health strategy with the president's GHI, policymakers have a crucial opportunity to ensure that innovation and research are central components of US health efforts worldwide. New leaders at several US agencies—including the CDC, FDA, NIH, and USAID—have stressed the importance of innovation to health efforts both domestically and abroad. By pursuing the policy actions outlined in this report, Congress and the Administration have the chance to boost the critical research and innovation needed to address global health diseases and to ensure that the most effective tools are available both today and tomorrow.

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This report was written in consultation with the following members of the Global Health Technologies Coalition.

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