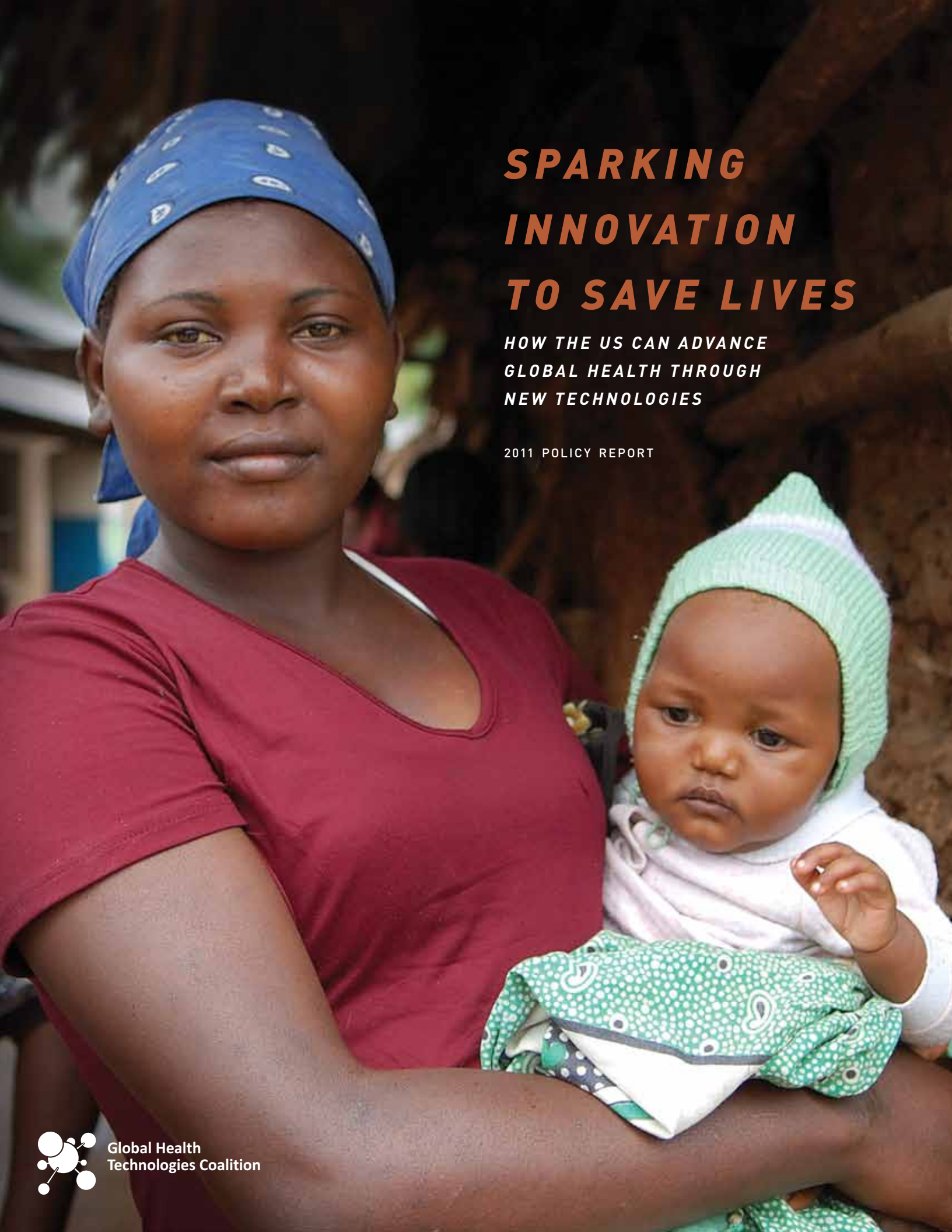

SPARKING INNOVATION TO SAVE LIVES

HOW THE US CAN ADVANCE GLOBAL HEALTH THROUGH NEW TECHNOLOGIES

2011 POLICY REPORT

Global Health Technologies Coalition

CONTENTS

About 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, diagnostics, and other products. The coalition advocates for increased and effective use of public resources, incentives to encourage private sector investment, and streamlined 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 is well-positioned to make significant gains in research and development for diseases and conditions that continue to impose a large burden of death and disability on millions of people each year. Since the release of the first annual policy report from the Global Health Technologies Coalition (GHTC), the administration has expressed a strong commitment to science, technology, and innovation through new international health and development strategies. The US Congress passed legislation that allows federal agencies to award prizes to stimulate innovation. And by advancing several key regulatory initiatives, members of Congress positioned the US Food and Drug Administration to assume stronger authority over the regulation of global health products. Several US agencies developed new partnerships—with the private sector, nonprofit organizations, civil society, academia, and other US agencies—to leverage the expertise and resources needed to accelerate global health research and product development.

Despite these achievements, too many people around the world still suffer or die from HIV/AIDS, tuberculosis, malaria, neglected tropical diseases, diarrheal diseases, and pneumonia. Too many women still succumb to problems related to childbirth. Yet we are closer than ever to developing new vaccines, drugs, diagnostics, and other tools that could prevent these unnecessary deaths, most of which occur in developing countries. The US government is a key partner in accelerating access to new health tools, and now is the time to act.

This second annual policy report from the GHTC—a group of almost 40 nonprofit organizations working to increase awareness of the urgent need for vaccines, diagnostics, drugs, microbicides, and other products that save lives in the developing world—outlines some of the action steps that will help curb unnecessary deaths, extend lives, and secure healthier futures. Serving as a guide for policymakers, the report documents promising policy actions taken over the past year in the areas of US investments in global health and international development, regulatory pathways to ensure the safety and efficacy of health tools, and incentives and innovative financing mechanisms to spur global health product development. This report offers recommendations for how US policymakers can continue to have a lead in improving health worldwide.

US investments in research have contributed to breakthroughs in global health. For example, this nurse in Burkina Faso has a cooler full of lifesaving vaccines that were developed with US support.

INTRODUCTION

Over the past year, the world witnessed remarkable breakthroughs and innovations in global health. For the first time, a proof-of-concept showed that a microbicide can protect women against HIV and herpes.[1] In a landmark announcement in HIV prevention research, a daily antiretroviral combination of tenofovir and emtracitibine showed its ability to reduce infection among some groups at high risk of HIV.[2] A new meningitis vaccine, costing less than 50 cents per dose, was launched in Africa and is expected to prevent disability and death in millions of people. Researchers are closer than ever before to developing new vaccines to prevent malaria, tuberculosis (TB), and dengue fever.

These scientific breakthroughs and advances in global public health did not happen by chance. They resulted from a commitment to research and innovation by many, including governments, public-private partnerships, academic research institutions, nongovernmental organizations (NGOs), and the private sector. The US government plays a unique role in global health research and development, particularly through its experts at agencies such as the Centers for Disease Control and Prevention (CDC), Department of Defense (DoD), Food and Drug Administration (FDA), National Institutes of Health (NIH), and US Agency for International Development (USAID). The administration has invoked science and innovation as central components of its global health and development strategies, and both Democratic and Republican members of the US Congress have taken steps to elevate innovation and research.

Despite these remarkable achievements, there is still much work to be done. Some of the tools needed to achieve major improvements in health and development do not yet exist, and often those that do are outdated or difficult to administer. Neglected tropical diseases, such as sleeping sickness and leishmaniasis, affect more than one billion people annually, and many of these diseases have no effective treatment. There is no vaccine to prevent malaria or HIV infection. Resistance to some TB drugs is increasing worldwide. Although major progress has been made against maternal mortality, almost 400,000 women die every year from pregnancy-related complications—deaths that could be prevented with new tools to address severe bleeding and infections. And two million children still die from pneumonia each year.

This report offers ways for US policymakers to accelerate scientific innovation and facilitate the rapid introduction of safe, effective, and affordable new health technologies. By following the actions outlined in this report, US policymakers can build on the nation's commitment to science and innovation and long tradition of leadership in these areas, helping to ensure that the next generation of global health tools reaches those most in need.

Researchers are closer than ever before to developing groundbreaking health technologies that can have an immediate impact and save lives worldwide.

"Innovation bends the curve of history and makes the impossible possible."

Melinda Gates, Bill & Melinda Gates Foundation

MILESTONES IN GLOBAL HEALTH

Although the first smallpox vaccine was created in 1796, it was not used widely enough to eliminate the disease until the 20th century.

1796

ENSURING WISE US INVESTMENTS

The United States has long been a leader in discovering game-changing scientific breakthroughs, a role that has served as both a source of pride for the American people as well as an economic driver. This is particularly apparent in global health, where US-driven efforts have led to the development of effective tools to prevent, diagnose, and treat illnesses around the world. Many of this past year's advances in global public health are the result of the continued commitment to innovation by the US government, including the CDC, DoD, FDA, NIH, and USAID. Each of these agencies plays a unique yet complementary role in global health research, which taken together complement each other in important ways.

The benefits of a strong US commitment to global health research are also evident domestically, where investments in scientific innovation for global health diseases—some of which affect the US population—propel American job creation and business activity. In California, for example, global health activities in 2007 generated an estimated $50 billion in business. The global health sector supported 350,000 high-quality jobs and $19.7 billion in wages and salaries in the state alone.[3]

Innovation in US international development strategies

During the course of the past year, the administration released three important and related strategies that will guide how the United States approaches international development and global health. All three highlight the vital role of science, technology, and innovation.

The White House reinforced the importance of research and product development to global health when it released new documents about the Global Health Initiative (GHI)—one of the administration's signature development initiatives—in September 2010 and March 2011. An updated version of the administration's GHI strategy document released in March 2011 says that under the initiative, "research will continue to spur innovation for the discovery and development of new biomedical interventions and technologies, such as drugs, diagnostics, and vaccines; medical devices, such as safe syringes; and information and communication technologies, such as mobile telephones and other data-transmitting devices that have the potential to improve people's health."[4] Also in March 2011, the State Department hosted a symposium to highlight the role of innovation in global health, at which US officials emphasized the role of science diplomacy in US foreign policy through programs such as the GHI. Stakeholders at the symposium also emphasized that innovation is central to improving health outcomes and livelihoods of people worldwide.[5]

Recent breakthroughs supported by US agencies

In July, a **USAID**-supported study showed proof-of-concept that a microbicide gel could provide women with protection against HIV and herpes. USAID over the past year has also continued to support research for an experimental drug that could cure malaria in one dose, called OZ439.

The **NIH**'s Therapeutics for Rare and Neglected Diseases program launched five pilot projects in July to spur drug development for diseases including schistosomiasis and hookworm. And in December, the World Health Organization endorsed a novel, rapid, and easy-to-use diagnostic test for TB and drug-resistant TB. Development of this test received critical support from the NIH.

In December, a new meningitis vaccine was distributed for the first time in Africa. Development of the vaccine was supported by the **FDA**, **CDC**, **NIH**, and **USAID**.

In November, the **DoD**'s Walter Reed Army Institute of Research launched the first clinical trials for a vaccine against the most widespread strain of malaria, *Plasmodium vivax*.

For many of these breakthroughs, public-private partnerships—such as product development partnerships—helped to usher these tools through the research and development process. Once fully developed and distributed to people in need, the tools listed here, along with others under development, will significantly improve public health worldwide by making sustained headway against global diseases.

In September 2010, following a year-long review, the administration unveiled the US government's first-ever Presidential Policy Directive (PPD) on global development. When releasing the PPD, President Obama said that the United States is "expanding scientific collaboration with other countries and investing in game-changing science and technology to help spark historic leaps in development."[6] President Obama also stressed the importance of innovation, research, and development in his annual State of the Union address.[7] In December 2010, the US Department of State and USAID released the Quadrennial Diplomacy and Development Review (QDDR), a process to recommend updated approaches to international development, including commitments to invest in science, research, and innovation.[8]

Transparency and coordination of US investments

A range of federal agencies participate in global health research; however, to maximize this US investment, their efforts need to be strategically coordinated. Given the significance of US contributions to global health research, improved documentation and transparency of American investments will be important to aid policymakers to make fully informed budgetary, regulatory, and programmatic decisions. Improved documentation and transparency can also provide American taxpayers with a greater understanding of how these funds are being used.

The administration took an encouraging step toward improving coordination when it convened leading experts to address research activities under the GHI. The committee is led by the NIH director and includes all agencies engaged in global health research. Its mission is to improve coordination of global health-related research and innovation efforts.

US investments in global health research are currently documented in a number of ways. The NIH tracks its activities through its Research Portfolio Online Reporting Tools,[9] and USAID recently launched a Foreign Assistance Dashboard[10] that is beginning to detail US foreign assistance funding. Various efforts have also attempted to show expenditures made by the DoD and the CDC. In 2006, USAID developed a five-year health research strategy and has since released reports documenting its progress in implementing this strategy.[11] To maintain a high level of transparency, Congress should request that USAID and other agencies engaged in global health research develop a five-year research strategy and publicly release annual progress reports.

The National Institutes of Health and global health

The NIH is the largest funder in the US government of global health research, and the agency has recently demonstrated a growing interest in global health issues. In June 2010, the NIH and partners launched the Human Heredity and Health in Africa Project, which aims to build the long-term capacity of African scientists and research institutions to conduct scientific studies on diseases such as HIV/AIDS, TB, and malaria. Additionally, the NIH's Fogarty International Center recently began collaborating with the Department of Health and Human Services' Health Research Services Administration and the State Department's Office of the US Global AIDS Coordinator on the Medical Education Partnership Initiative (MEPI). MEPI supports foreign institutions in sub-Saharan African countries that receive support from the US President's Emergency Plan for AIDS Relief to develop, expand, and enhance models of medical education. This includes enhancing the capacity of local individuals to conduct research on global health diseases.

The NIH also plans to open a new center by October 2011, called the National Center for Advancing Translational Sciences (NCATS). NCATS would establish a focused, integrated, and systematic approach to link basic research with therapeutic development and clinical care. The new center will focus on neglected diseases of the developing world, as well as rare diseases. NIH Director Francis Collins has said that NCATS will impact new technologies for global health, such as new treatments for the parasitic infection schistosomiasis.

Policy recommendations

With a growing determination within the US government to prioritize science and innovation in global health and development strategies, US policymakers are in a position to build on the momentum of recent successes. They should therefore:

Sustain and protect US investments in global health research and product development. Congress and the Obama administration face difficult funding decisions in the current economic climate, and investments must address numerous pressing priorities. US investments in global health research have yielded strong returns, resulting in new health tools with immense public health impact, in addition to fueling American job creation and domestic economic benefits. US global leadership will suffer if the country abandons its commitment to applying American expertise in science to global health challenges. Policymakers should make certain that the agencies carrying out this crucial work—such as the CDC, FDA, DoD, NIH, and USAID—are fully funded to do so.

Develop concrete plans to incorporate research and development as a key priority within US global health and development programs. This year, the administration recognized the importance of science, technology, and innovation as key components of the GHI, the PPD, and the QDDR. The NIH director has also made global health a priority for the agency. Concrete details are needed on how research and innovation for new health products will be incorporated and prioritized within these efforts, and implementation plans need to be completed. USAID and the State Department should lead this effort for the GHI, PPD, and QDDR, and should create metrics to measure progress with support from partners such as the Office of Science and Technology Policy at the White House, the Office of the US Global AIDS Coordinator, the CDC, and the NIH. USAID and the State Department should work with these partners to hold regular consultations with civil society, NGOs, and the private sector when developing these details, implementation plans, and metrics.

Ensure that US investments in global health research are coordinated, efficient, and streamlined. The head of the GHI research committee, along with the GHI principals at USAID, CDC, and the Office of the US Global AIDS Coordinator, should coordinate an effort to document US activities in global health research for greater transparency. The GHI's research committee should be used to foster efficiencies and collaboration across all US federal agencies involved in global health research and innovation. Congress should request that all agencies engaged in global health research develop a five-year strategy and produce publicly available annual progress reports.

> "Republicans and Democrats have long worked together to make a difference in the world through humanitarian efforts, and those investments have paid off."
>
> Former Senate majority leaders Tom Daschle and Bill Frist

STREAMLINING REGULATORY PROCESSES

To prevent, diagnose, and treat global health diseases, regulatory processes in developing countries can help to ensure that the health products reaching their citizens are safe and effective. Regulatory oversight is critical during clinical trials, when health products undergo rigorous testing to measure their safety and efficacy. When clinical trials end and a new health product is ready to be licensed for distribution, the product must be further assessed and approved. Local regulatory authorities play a key role in these processes; for example, local and national authorities monitor clinical trials during development phases, assessing and approving new health tools before licensure, and monitoring the safety of new tools during post-approval phases. These local regulatory authorities are also in the best position to weigh the needs of their citizens against health product characteristics.

However, some countries in the developing world—where life-threatening diseases are widespread—lack the expertise or resources to review and monitor new health tools and clinical trials rigorously and expeditiously.[12] When medical products are unregulated, the health and safety consequences can be damaging, if not deadly.[13] The US government advanced several promising initiatives in the past year that address these urgent regulatory needs, and the Global Health Technologies Coalition (GHTC) strongly encourages US policymakers to sustain and amplify their progress.

Growing momentum in the US Food and Drug Administration

As the US agency charged with protecting the health of American consumers, the FDA is uniquely positioned to help ensure the safety of health tools that could save the lives of millions of people worldwide. For example, in 2004, the FDA launched a program to review and provide tentative approval for generic HIV/AIDS drugs to be delivered in the developing world through the US President's Emergency Plan for AIDS Relief (PEPFAR).[14] As of January 2011, the agency had approved more than 120 HIV/AIDS drugs for distribution through PEPFAR.[15]

Momentum within the agency continues to grow. For instance, the FDA's newly mandated review group for neglected diseases of the developing world, which launched operations this year, was due to make recommendations to Congress early this year. At the time of printing, the recommendations had not been released.[16] A public hearing in September 2010 convened by the group revealed broad support for expanding the FDA's role in international regulatory issues.[17] It is critical that once the review group's recommendations reach Congress, the FDA act quickly to implement them.

The US Food and Drug Administration's progress in global health

In addition to the FDA's review group for neglected diseases making considerable progress over the past year, the agency also made other global health achievements in 2010:

- In February, the FDA and the NIH announced a collaborative initiative to speed medical innovations to the public. Called the Advancing Regulatory Science Initiative, the collaboration aims to build on the achievements of existing programs, such as the FDA's Critical Path Initiative, which has helped to fund TB treatments and vaccines.[18]
- The FDA continues to strengthen its international partnerships. As of April 2010, the agency had established new posts in China, Europe, India, and Latin America, adding to existing posts in Brazil, China, India, and Switzerland.[19]
- The FDA released a Strategic Priorities document, which outlines the goals and priority areas that will guide the agency through the next five years, into 2015. The document recognizes the need to elevate collaborations with a range of stakeholders, including global regulatory partners.[20]
- In March, the FDA helped public- and private-sector partners to significantly accelerate the development of combination treatments for TB through a new collaboration called the Critical Path to TB Drug Regimens.[21]

Renewed energy in Congress

This past year, the US Congress demonstrated a desire to leverage American expertise to address global health regulatory issues. Last June, the Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies of the Senate Committee on Appropriations highlighted the FDA's role in global health when Subcommittee Chair Herb Kohl (D-WI) and Ranking Member Sam Brownback (R-KS) held a hearing to examine the agency's effort to advance new products for neglected tropical and rare diseases.

The Senate heightened the FDA's role in global health when it included important language in a fiscal year 2011 appropriations bill that directed the FDA commissioner to bolster the agency's coordination and interaction with multilateral agencies including regulatory authorities in developing countries. The bill also called on the FDA to report its progress in expanding its global health portfolio and directed the agency to engage more with nontraditional groups developing global health tools, such as product development partnerships (PDPs).[22,23] Though the legislation ultimately did not pass during the 111th Congress, the 112th Congress should incorporate the language in the fiscal year 2012 appropriations bill.

Global regulatory partners

Both the World Health Organization (WHO) and the European Medicines Agency (EMA) lead programs that aim to improve access to global health medicines and vaccines that meet certain standards. Under the WHO's Prequalification Program, the agency provides an independent opinion on the quality, safety, and efficacy of drugs and vaccines required for purchase by United Nations procurement agencies. Although WHO is not a regulator, its Prequalification Program is an important signal of quality, safety, and efficacy to countries without sufficient regulatory capabilities. The process, however, can be lengthy, sometimes taking 18 to 24 months.

The EMA's Article 58 process provides a scientific opinion on certain vaccines and drugs intended exclusively for markets outside of the European Union. The EMA conducts Article 58 evaluations in close cooperation with WHO. The FDA has entered into agreements with WHO and the EMA in an effort to share information and documents about certain health products under evaluation. As the FDA increases its part in global health regulatory issues, the agency should bolster its engagement with these key stakeholders.

"The future is ours to win. . . . The first step in winning the future is encouraging American innovation."

President Barack Obama, January 2011 State of the Union address

A vaccine against diphtheria—a bacterial disease that affects the throat and can cause serious or fatal complications—is developed. The diphtheria vaccine is one of the recommended childhood immunizations, generally required before a child in the United States can start school.

1913

The first latex male condoms are developed.

1919

Policy recommendations

There has been tremendous interest—both within the FDA and Congress—to strengthen the FDA's role in helping to regulate health tools to prevent, diagnose, and treat widespread infectious diseases. To create efficient, streamlined, and transparent mechanisms for bolstering the agency's engagement in global health, the FDA and Congress should consider the following actions:

The FDA should release the recommendations from its neglected diseases review group. The agency should make the recommendations public and include a mechanism for public comment. The agency should also submit annual reports to Congress on its progress, and Congress should make certain that sufficient resources are appropriated to the FDA so that it can fully and effectively implement the recommendations in order to achieve the greatest advances in global health.

The FDA should establish stronger partnerships with other regulatory stakeholders. The agency's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) have engaged in joint inspections and information-sharing with the World Health Organization and the European Medicines Agency, a collaboration governed by a formal agreement between the agencies. The successful model established by CDER and CBER should be extended to other centers in order to leverage this exchange of information, including through joint reviews, across the FDA. The agency should also consider formal arrangements with endemic country regulatory authorities to enable direct information exchange and joint reviews with them. The GHTC made similar recommendations in 2010, and they remain timely and pertinent for the coming year.

The FDA should enhance its internal capacity in neglected diseases. The agency should explore mechanisms to leverage expertise from other US agencies involved in global health, devote sufficient resources to provide training opportunities for existing FDA staff, and hire additional staff with expertise in neglected diseases. Fostering collaboration with other agencies can help create efficiencies and synergies and promote a whole-of-government approach to global health regulatory and research issues. The FDA should also include experts from endemic countries on its advisory boards when products for neglected diseases are reviewed—a recommendation offered by the GHTC in 2010 that remains applicable.

The FDA should bolster its engagement with groups developing global health tools. Nontraditional product developers, such as PDPs, may not have access to staff with expertise in regulatory processes, such as dossier preparation or product registration. Thus, they may benefit from additional support to enable efficient and streamlined product review and approval. To this end, the FDA should establish dedicated review teams for neglected diseases and/or specific points of contact for nontraditional product developers, and create mechanisms to facilitate informal discussions with these product sponsors.

Congress should include appropriations language on the FDA's role in global health and fund the agency accordingly. Congress took a significant step toward improving the FDA's ability to facilitate the introduction of global health tools when it included language on the FDA's role in global health in the fiscal year 2011 appropriations bill. To ensure that this progress is realized, Congress must include this language in next year's appropriations bill and secure the bill's passage. In addition, Congress should fund the FDA fully to allow the agency to carry out its new scope of work in global health.

The first and only tuberculosis vaccine, BCG, is developed. The vaccine is almost 100 years old, and a new one is desperately needed.

1921

STIMULATING RESEARCH AND DEVELOPMENT

Developing and delivering lifesaving global health technologies requires expertise from a wide variety of stakeholders, including private biotechnology and pharmaceutical companies, nonprofit groups such as PDPs, academia, and public research institutes. Because global health products are primarily needed in low-resource countries, where patients and health providers have limited ability to pay for them, commercial incentives are typically insufficient to spur investment by the biotechnology and pharmaceutical industries, which are the traditional drivers of health product development. This market challenge leaves major gaps in the financing and expertise required to develop and deliver essential health technologies for the developing world.

To fill these gaps, global health and economic experts have designed several strategies—including incentives and innovative financing mechanisms—to stimulate and fund global health research and product development. Incentives and innovative financing encourage a variety of stakeholders with requisite expertise to devote their resources to developing and deploying essential health products for low-income countries. When used in conjunction with global health research investments from the United States and other donors, incentives and innovative financing can leverage knowledge and resources from multiple sectors, particularly the biopharmaceutical industry.

Some mechanisms implemented to date include priority review vouchers (PRVs), small business innovation research (SBIR) awards, procurement pools, patent pools, PDPs, tax credits, and advanced market commitments (AMCs). Other mechanisms have been proposed but not yet implemented. Various US agencies have supported these mechanisms. For example, 11 US federal agencies participate in the SBIR program, which since 1982 has provided American small businesses with funding to conduct research and development, including for global health technologies.[24] Incentives and innovative financing mechanisms are essential tools—particularly for governments struggling to allocate increasingly scarce resources—to leverage private-sector investment, to efficiently allocate funding to promising areas of research, and to accelerate the development of game-changing technologies.

Incentives and innovative financing can work

Throughout the past year, there have been several promising advances in the use and impact of incentives and innovative financing mechanisms. For instance, the pilot AMC—an effort currently underway to accelerate the manufacture and delivery of pneumococcal vaccines to millions of children worldwide[25]—enlisted four private-industry partners (GlaxoSmithKline, Pfizer, Panacea Biotec Ltd, and the Serum Institute of India) to provide a long-term supply of pneumococcal vaccine to developing countries at a fraction of their industrialized market price. In December 2010, Nicaragua became the first low-income country with support from the GAVI Alliance to begin immunizing children with a new pneumonia vaccine procured through the AMC. Several other countries, such as Kenya, have followed in 2011 with support from GAVI, representing one of the first times a new vaccine has ever been launched simultaneously in poor and rich countries.[26] Lessons learned from rigorously evaluating the cost-effectiveness and impact of this AMC will inform decisions about whether the mechanism could be replicated for other diseases.

Yellow fever vaccine is developed. Yellow fever occurs in tropical regions of Africa and in parts of South America, and can cause illness in American travelers.

Isoniazid becomes available to treat tuberculosis. The drug is now 50 years old, and there is an urgent need for new TB treatments.

Polio used to be very common in the United States and caused severe illness in thousands of people each year before the polio vaccine was introduced in 1955.

The MMR vaccine against measles, mumps, and rubella is created. Since introduction of its earliest versions in the 1970s, more than 500 million doses have been used in more than 60 countries.

Nifurtimox is developed to treat Chagas disease. 100 million people worldwide are at risk of Chagas, and numbers are growing in non-endemic countries such as the United States.

The first meningococcal vaccine becomes available. The vaccine is recommended for children and adolescents between ages 11 and 18—typically at a routine immunization visit.

1952 1953 1955 1966 1967 1970

Patent pools, which aim to speed the development of new technologies by making licenses for patents and other intellectual property more widely available, have also shown promise over the past year. In October, the NIH became the first patent holder to share intellectual property rights on some HIV/AIDS medicines through a patent pool launched by UNITAID, a system that purchases health products and is funded by a mix of taxes and voluntary contributions on airline tickets.[27] Another licensing pool, the Pool for Open Innovation Against Neglected Tropical Diseases, engaged an influx of new partners, including academic institutions, government agencies, private industry, and nonprofit partners.[28] These diverse partnerships demonstrate that patent pools hold promise for attracting the expertise required to accelerate global health research and product development.

Growing momentum across the US government

The Unites States has played a key role in exploring, supporting, and implementing incentives and innovative financing mechanisms for global health, and several decision-makers in the US government—including those in the US Treasury, USAID, the White House Office of Science and Technology Policy, the NIH, the FDA, and Congress—have demonstrated leadership in this area. During the 111th Congress, former senator Sam Brownback (R-KS) introduced a bill that would expand the FDA's PRV program, which aims to spur research and development by entitling the sponsor of a newly approved drug or biologic that targets a neglected tropical disease to an expedited review of a new drug application.[29] Though the bill did not pass, it did garner bipartisan support (Senators Sherrod Brown [D-OH] and Al Franken [D-MN] were co-sponsors), and the legislation was reintroduced this year.

In December, Congress passed the America COMPETES Act, which gives all federal agencies the broad authority to use prizes and challenges to foster innovation.[30] The America COMPETES Act authorized USAID to launch the Grand Challenges for Development prize-based initiative, which aims to encourage innovative solutions to global development issues. The first challenge, initiated in March 2011, provides grants to foster innovative prevention and treatment approaches for pregnant women and newborns in rural, low-resource settings.[31] USAID also introduced its Development Innovation Ventures program in October 2010, which awards grants to promising projects that have the potential for creating breakthroughs in global development.[32]

The US Patent and Trademark Office (USPTO) is implementing a pilot program to use the patent review system to spark the development and delivery of technologies that address humanitarian needs, including global health diseases.[33] Prize winners will receive a voucher for fast-track patent review that can be transferred on the open market. Key questions remain regarding the implementation of this mechanism, but the USPTO should be recognized for its innovative efforts to stimulate humanitarian technology development.[34]

It is commendable that the US government is helping to leverage incentives and innovative financing to address pressing global health issues. Because these mechanisms are still in their nascent stages, there needs to be further deliberation and evaluation to determine how successful they will be in the long run. The following recommendations should serve as key guidelines for the US government as it assesses these and other incentive mechanisms.

The first antiretroviral drug to treat HIV/AIDS, zidovudine, becomes available. The drug was developed with the support of researchers at the NIH's National Cancer Institute.

The Western blot blood test is developed. The test is used to detect a wide range of diseases, including HIV, Lyme disease, and hepatitis B.

The hepatitis B vaccine becomes available—a required immunization for all children in the United States.

The pneumococcal vaccine is developed. The vaccine is currently recommended for all children in the United States younger than age 5, as well as all adults older than 65.

The first HIV test for screening blood supplies is developed.

The human rotavirus strain is isolated. Rotavirus is the leading cause of severe vomiting and diarrhea among children worldwide. Two different rotavirus vaccines are currently licensed for use in infants in the United States.

1977 1981 1985 1986 1987 1988

Policy recommendations

Early signs indicate that incentives and innovative financing for global health can work. As US policymakers build on the achievements from this past year, they should ensure that incentives and innovative financing mechanisms are effective and feasible, and guarantee comprehensive access to new health technologies. In particular, US policymakers should:

Formally establish a cross-agency working group to explore US investment in incentives and innovative financing mechanisms for global health. Given diverse interests and perspectives across the many US departments and agencies involved, it is essential that the government coordinate around a shared agenda. This working group should be charged with developing recommendations for US leadership in incentives and innovative financing for global health research and development.

Engage with civil society, NGOs, and private industry. This cross-agency working group and all US agencies involved should implement mechanisms to engage civil society groups, NGOs such as PDPs, and the biopharmaceutical industry as key stakeholders to inform priorities and decisions. These consultations, which should occur regularly and involve a broad cross-section of relevant stakeholders, are necessary during each stage of the process—from initial discussions, to developing recommendations for US support, to program evaluation.

Engage with other governments and donors to explore and support incentives and innovative financing. To maximize the impact of US engagement and to leverage additional resources to complement and extend US taxpayer investments, leaders and policymakers should partner and coordinate with other governments and donors. In addition, senior US policymakers and officials should participate in bilateral and multilateral discussions on stimulating investment in research and development for neglected diseases.

Support a portfolio of incentives and financing mechanisms to stimulate needed research and development at all stages of the product development process. Health technologies for different diseases are at various stages of development and face unique scientific obstacles and potential for commercial returns. In addition, many different institutions are engaged in product development, ranging from technology start-ups, to PDPs, to large multinational companies. Given this diversity, no single mechanism is capable of filling all the gaps in the product development pipeline while encouraging the full range of research and development activities needed. The United States should therefore support a portfolio of mechanisms that can address these gaps.

Conduct continuous rigorous assessments of each incentive and financing mechanism that the United States supports. Although a track record exists for some mechanisms, many are new and therefore untested. It will be critical for the US government and its partners to continually assess these mechanisms before and during their implementation. Policymakers should develop a rigorous evaluation framework to predict and monitor performance and impact and invest in independent monitoring and evaluation efforts.[35,36]

New meningitis vaccine created specifically for Africa completes safety trials. The vaccine launches in December 2010 having received critical support from the FDA, CDC, NIH, and USAID.

Miltefosine is developed to treat the neglected tropical disease leishmaniasis. Although effective drugs are available for seven of the most common NTDs, others do not have adequate treatment.

The first HIV/AIDS combination therapy shows efficacy in clinical trials.

Coartem®, the first malaria drug to use artemisinin, is prequalified by the World Health Organization.

Gardasil®, the first vaccine against cervical cancer, is approved by the FDA.

The FDA approves a second-generation female condom.

Results from the first study to show HIV protection from a vaginal gel are released. USAID provided key support for the trial.

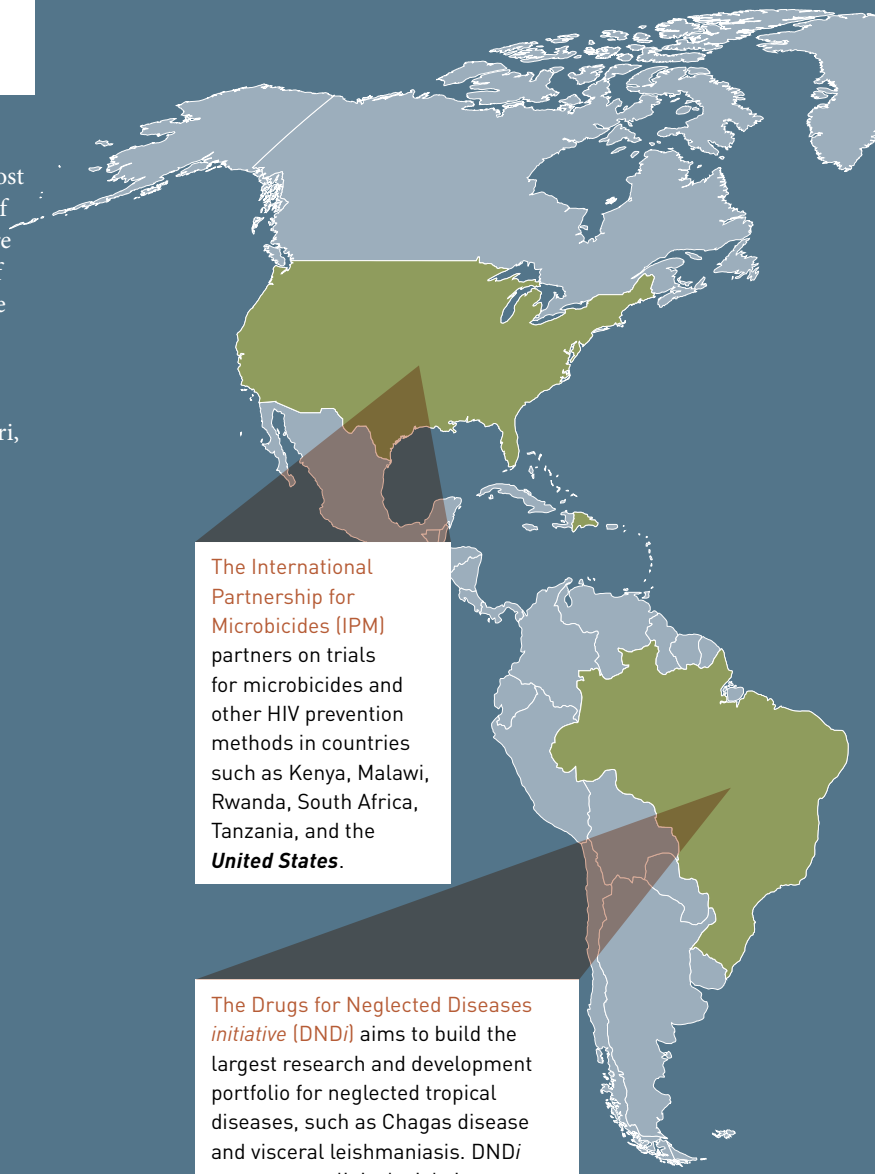
A new study finds that daily antiretroviral drugs offer protection against HIV infection.

A new TB diagnostic is endorsed by the World Health Organization. The test provides an accurate diagnosis for many patients in about 100 minutes, compared with current tests that can take up to three months to obtain results. It received crucial support from the NIH.

1996 2002 2006 2007 2009 2010

GHTC MEMBER RESEARCH SITES

The Global Health Technologies Coalition includes almost 40 nonprofit organizations working to raise the profile of research for new global health tools. GHTC members are involved in clinical trials in 34 countries in all regions of the world, marked here in green. Many of these trials are supported by US agencies—including the CDC, DoD, FDA, NIH, and USAID. Several are conducted in the United States in locations such as California, Illinois, Louisiana, New York, Massachusetts, Maryland, Missouri, North Carolina, Ohio, and Washington state.

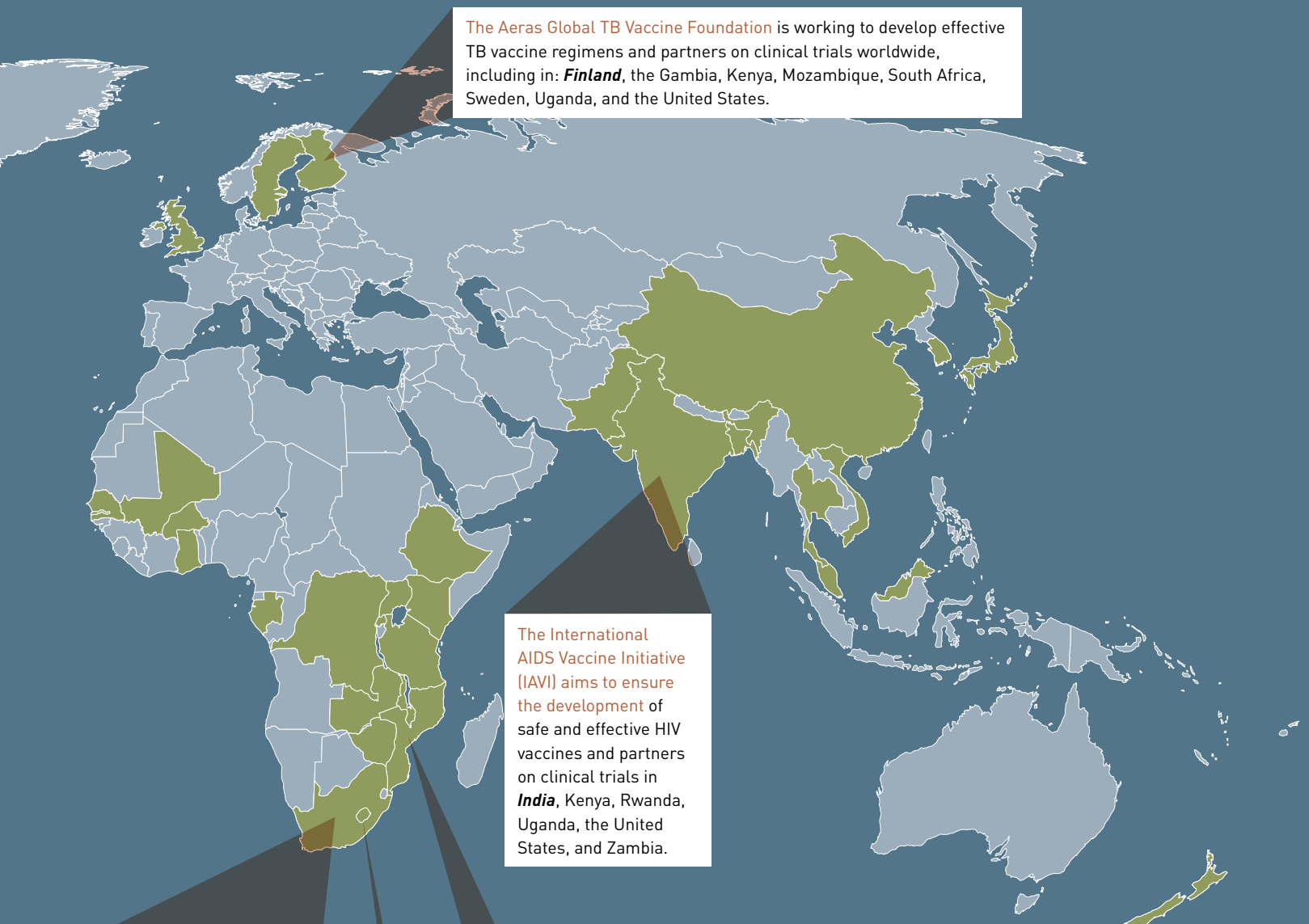


The International Partnership for Microbicides (IPM) partners on trials for microbicides and other HIV prevention methods in countries such as Kenya, Malawi, Rwanda, South Africa, Tanzania, and the ***United States***.

The Drugs for Neglected Diseases *initiative* (DND*i*) aims to build the largest research and development portfolio for neglected tropical diseases, such as Chagas disease and visceral leishmaniasis. DND*i* partners on clinical trials in countries such as ***Brazil***, Democratic Republic of Congo, Ethiopia, India, Japan, Kenya, and Malaysia.

Global Health Technologies Coalition members

Aeras Global TB Vaccine Foundation
AIDS Vaccine Advocacy Coalition
American Society of Tropical Medicine and Hygiene
amfAR
Bill & Melinda Gates Foundation
BIO Ventures for Global Health
CD4 Initiative
CONRAD
Council on Health Research for Development (COHRED)
Dengue Vaccine Initiative
Drugs for Neglected Diseases *initiative* (DND*i*)
Duke Global Health Institute
Elizabeth Glaser Pediatric AIDS Foundation
Family Health International (FHI)
Foundation for Innovative New Diagnostics (FIND)
GAVI Alliance
Global Alliance for TB Drug Development
Global Campaign for Microbicides
Global Health Council
Infectious Disease Research Institute
Infectious Diseases Society of America
Innovative Vector Control Consortium
Institute for OneWorld Health
International AIDS Vaccine Initiative (IAVI)
International Partnership for Microbicides (IPM)
International Vaccine Access Center
International Vaccine Institute
Medicines for Malaria Venture
PATH
PATH Malaria Vaccine Initiative
Population Council
Public Health Institute
Research!America
Results for Development Institute
Sabin Vaccine Institute Global Network for Neglected Tropical Diseases
Seattle Biomedical Research Institute
The Stimson Center
Treatment Action Group
Washington Global Health Alliance



The Aeras Global TB Vaccine Foundation is working to develop effective TB vaccine regimens and partners on clinical trials worldwide, including in: ***Finland***, the Gambia, Kenya, Mozambique, South Africa, Sweden, Uganda, and the United States.

The International AIDS Vaccine Initiative (IAVI) aims to ensure the development of safe and effective HIV vaccines and partners on clinical trials in ***India***, Kenya, Rwanda, Uganda, the United States, and Zambia.

Family Health International (FHI) works to improve the lives of the world's most vulnerable people by conducting research for a range of global health issues, including HIV/AIDS, rotavirus, and reproductive health. It works with partners worldwide to conduct clinical trials, including in Kenya, Tanzania, ***South Africa***, the United States, and Zimbabwe.

The PATH Malaria Vaccine Initiative is partnering on clinical trials for its RTS,S malaria vaccine candidate in seven African countries: Burkina Faso, Gabon, Ghana, Kenya, Malawi, ***Mozambique***, and Tanzania.

The Foundation for Innovative New Diagnostics (FIND) partners on clinical trials for new global health diagnostic tools in countries such as Ethiopia, India, ***Lesotho***, and Uganda.

The Global Alliance for TB Drug Development works to accelerate the discovery and development of faster-acting and affordable TB drugs. It partners on clinical trials in countries ranging from ***New Zealand*** to South Africa and the United States.

CONCLUSION

This past year has been historic for global health, largely because of a commitment from a range of partners to develop and deliver the next generation of health tools—from new vaccines to prevent meningitis, malaria, TB, and dengue fever, to new methods of preventing HIV infection and treating neglected tropical diseases. These successes would not have been possible without support from the US government through its expert agencies, leaders in the US Congress, and the administration. These policymakers seized on a growing desire to prioritize innovation and science to develop global health technologies, and the GHTC calls on Congress and the administration to take the following policy actions to build on this momentum and bridge critical gaps that remain:

Ensure wise US investments

- Sustain and protect US investments in global health research and product development.
- Develop concrete plans to incorporate research and development as a key priority within US global health and development programs.
- Ensure that US investments in global health research are coordinated, efficient, and streamlined.

Streamline regulatory processes

- Ensure that the FDA releases the recommendations from its neglected diseases review group.
- Establish stronger partnerships between the FDA and other regulatory stakeholders.
- Enhance the FDA's internal capacity in neglected diseases.
- Bolster the FDA's engagement with groups developing global health tools.
- Include appropriations language in the US budget on the FDA's role in global health and fund the agency to fulfill this role.

Stimulate research and development

- Formally establish a cross-agency working group to explore US investment in incentives and innovative financing mechanisms for global health.
- Engage with civil society, NGOs, and private industry.
- Engage with other governments and donors to explore and support incentives and innovative financing.
- Support a portfolio of incentives and financing mechanisms to stimulate needed research and development at all stages of the product development process.
- Conduct continuous rigorous assessments of each incentive and financing mechanism that the United States supports.

Global health research will ultimately improve the lives of people around the world, especially those most in need. As this report shows, global health research is also a smart economic investment for the United States. In the current fiscal climate, members of Congress and the administration should set priorities for the nation and fund them accordingly. Investments that help save lives—while also creating jobs and spurring economic growth both here and abroad—should be among the country's highest priorities. Past leadership shows that Congress and the administration understand why support for global health research and the innovation it breeds in global development needs to be sustained and elevated, and US policymakers must continue to protect and elevate this investment in the future.

REFERENCES

1 Study of microbicide gel shows reduced risk of HIV and herpes infection in women [press release]. Durban, South Africa: University of KwaZulu-Natal; July 20, 2010. Available at: http://www.caprisa.org/joomla/Micro/CAPRISA%20004%20Press%20Release%20for%2020%20July%202010.pdf.

2 A study released in November 2010 found that a daily antiretroviral combination of tenofovir (TDF) and emtracitibine (FTC) showed its ability to reduce infection among men who have sex with men and transgender women at high risk for HIV. The results showed that once-daily TDF/FTC reduced risk of HIV infection by an average of 43.8 percent. See http://www.nejm.org/doi/full/10.1056/NEJMoa1011205#t=abstract.

3 The average annual salary of workers in for-profit firms engaged in global health in the domestic market is greater than $71,500. See *The Importance of the Global Health Sector in California: An Evaluation of the Economic Impact* at http://www.ucghi.universityofcalifornia.edu/docs/eir-final.pdf. In Washington State, $4.1 billion in business activity is generated annually from global health activities, and more than 43,000 jobs have been created or supported by global health projects. See Research!America's website for data on Washington State: http://www.researchamerica.org/econ_washington. In North Carolina, the economic impact from global health is roughly $2 billion, supporting more than 7,000 jobs and $508 million in salaries and wages in 2007. See *Why Global Health Matters to North Carolina: The economic impact of the global health sector on North Carolina's economy* at http://globalhealth.duke.edu/policy-docs/NCEcon_Report_Final_March_2010.pdf.

4 September 2010 GHI fact sheets state that the initiative will expand "investments in game-changing innovation by promoting research and development, both in terms of applied science as well as operation and implementation research, to address important questions that are immediately relevant to both GHI and partner country goals and objectives." See http://www.pepfar.gov/documents/organization/136504.pdf and http://www.whitehouse.gov/sites/default/files/Global_Health_Fact_Sheet.pdf.

5 See http://www.state.gov/e/rls/rmk/2011/index.htm.

6 See White House fact sheets on the Presidential Policy Directive (PPD): http://www.whitehouse.gov/the-press-office/2010/09/22/fact-sheet-us-global-development-policy. Also see President Obama's remarks on the PPD: http://www.america.gov/st/texttrans-english/2010/September/20100922172556su0.2969934.html.

7 The text of President Obama's January 25, 2011, State of the Union address is available at http://www.whitehouse.gov/the-press-office/2011/01/25/remarks-president-state-union-address.

8 Among its priorities, the Quadrennial Diplomacy and Development Review aims to bolster the position of development as a core pillar of US foreign policy, as well as strengthen the US Agency for International Development's (USAID) role as the United States' lead international development agency. See *Leading Through Civilian Power: The First Quadrennial Diplomacy and Development Review* at http://www.state.gov/documents/organization/153108.pdf.

9 US National Institutes of Health (NIH) Research Portfolio Online Reporting Tools page. US Department of Health and Human Services website. Available at: http://report.nih.gov/.

10 The Foreign Assistance Dashboard is available at http://foreignassistance.gov/.

11 See *Report to Congress: Health-Related Research and Development Activities at USAID* at http://www.usaid.gov/our_work/global_health/home/Publications/hrit_report.html.

12 In 2008, the World Health Organization (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 WHO, more than two-thirds of people worldwide live in countries with "marginal or inadequate" systems for ensuring drug quality, safety, and effectiveness.

13 A country's inability to effectively regulate and monitor health tools can result in harmful consequences. For instance, in March 2010, the South African HIV Clinicians Society called on the country's drug registration body, the Medicines Control Council (MCC), to fast-track the approval of certain antiretroviral drugs for HIV/AIDS. According to the letter, the single greatest obstacle to obtaining affordable access to medicines appears to be the regulatory registration process, as some applications have been before the MCC for years. This delay in reviewing and approving HIV/AIDS drugs means that millions of people living with the disease in South Africa do not have access to these lifesaving therapies. See: Southern African HIV Clinicians Society. *Delays in Registration of ARVs: Letter by the HIV Clinicians Society*. Pretoria, South Africa; 2010.

14 US Food and Drug Administration (FDA) information on the US President's Emergency Plan for AIDS Relief is available at http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119229.htm.

15 President's Emergency Plan for AIDS Relief: Approved and Tentatively Approved Antiretrovirals in Association with the President's Emergency Plan page. FDA website. Available at: http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119231.htm.

16 This review group was created under legislation sponsored by former senator Sam Brownback (R-KS), which passed as an amendment to the US Department of Agriculture fiscal year 2010 appropriations bill. The bill is available at http://www.rules.house.gov/111/LegText/111_agcr_txt.pdf.

17 Several speakers proposed that the FDA strengthen its engagement with groups and entities such as product development partnerships (PDPs), developing the tools to prevent, diagnose, and treat diseases of the developing world. It is crucial for the FDA to engage with nontraditional product sponsors, including PDPs, at several stages of development so that the agency can serve as a mentor to these groups on regulatory issues. Speakers also called on the FDA to bolster its relationships with global regulatory stakeholders, such as WHO, national regulatory authorities, and regional regulatory networks. See http://www.ghtcoalition.org/headline-051010-critical-public-hearing-highlights-FDA-role-in-global-health.php.

18 NIH and FDA Announce Collaborative Initiative to Fast-track Innovations to the Public [press release]. Washington, DC: National Institutes of Health and US Food and Drug Administration; February 24, 2010. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm201706.htm.

19 FDA's International Posts: Improving the Safety of Imported Food and Medical Products. *FDA Consumer Health Information*. March 2010. Available at: http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM187246.pdf.

20 US Food and Drug Administration. *Strategic Priorities 2011–2015: Responding to the Public Health Challenges of the 21st Century*. September 29, 2010, draft. Available at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/StrategicActionPlan/UCM226907.pdf.

21 Global Partners Join Forces to Speed Development of New TB Drug Combinations [press release]. Washington, DC: Global Alliance for TB Drug Development; March 18, 2010. Available at: http://new.tballiance.org/newscenter/view-brief.php?id=904.

22 Senate Bill S.3606. Available at: http://thomas.gov/cgi-bin/bdquery/D?d111:1:./temp/~bd4VTL:@@@L&summ2=m&|/home/LegislativeData.php|.

23 PDPs are nonprofit organizations with a mandate to research, develop, and support accessibility of new health tools that target diseases disproportionately affecting developing countries. PDPs advance global health goals by accelerating the development of products that may not otherwise be created. See *Innovative Product Development Partnerships: Advancing Global Health and Economic Development Goals* by the International AIDS Vaccine Initiative at http://www.iavi.org/Lists/IAVIPublications/attachments/eb7b4247-6816-4094-9f54-9f2f2b99e95a/IAVI_Innovative_Product_Development_Partnerships_2010_ENG.pdf.

24 More than $16 billion has been awarded through the program to date. See the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs page of the NIH website at http://grants.nih.gov/grants/funding/sbirsttr_programs.htm.

25 Pharmaceutical firms and GAVI Alliance agree to provide long-term affordable supply [press release]. Geneva, CH: GAVI Alliance; March 23, 2010. Available at: http://www.gavialliance.org/media_centre/press_releases/2010_03_23_amc_commitment.php.

26 In addition to Nicaragua, 18 countries are expected to launch the pneumococcal vaccine over the next few years with support from the GAVI Alliance. However, GAVI's challenge to secure the additional financing needed to meet the demand from more than 40 countries for the pneumococcal vaccine over the next four years should be noted. Globally, an additional $3.7 billion will be needed to meet this demand. See *Developing nations begin introducing new vaccine against major killer within a year of its introduction in rich countries* at http://www.gavialliance.org/media_centre/press_releases/nicaragua_pneumococcal.php.

27 US National Institutes of Health (NIH) First to Share Patents with Medicines Patent Pool [press release]. Geneva, CH: UNITAID; September 30, 2010. Available at: http://www.unitaid.eu/fr/resources/actualites/290-us-national-institutes-of-health-nih-first-to-share-patents-with-medicines-patent-pool.html.

28 The pool is administered by the group BIO Ventures for Global Health. See the Pool for Open Innovation website at http://ntdpool.org/.

29 The Creating Hope Act of 2011 would add Chagas disease to the list of eligible diseases, and would also allow for multiple sales and transfers of a voucher once it is awarded. Allowing multiple sales and transfers would make the priority review voucher (PRV) a more attractive option to private industry. See Senate Bill S.606. Legislation at http://www.gpo.gov/fdsys/pkg/BILLS-112s606is/pdf/BILLS-112s606is.pdf.

30 HR 5116. Available at: http://www.govtrack.us/congress/bill.xpd?bill=h111-5116.

31 See press release: http://www.savinglivesatbirth.net/news/11/03/09/saving-lives-birth-press-release.

32 USAID Announces Development Innovation Ventures Program [press release]. Washington, DC: USAID; October 8, 2010. Available at: http://www.usaid.gov/press/releases/2010/pr101008.html.

33 Under the proposed program, patent holders who make their technologies available for humanitarian purposes would be eligible for a voucher for accelerated re-examination of a patent. See *USPTO Launches Effort to Incentivize Humanitarian Technologies* at http://www.uspto.gov/news/pr/2010/10_41.jsp.

34 Public comments on the US Patent and Trademark Office's proposed mechanism are available at http://www.uspto.gov/patents/law/comments/humanitarian.jsp.

35 The Global Health Technologies Coalition has developed a set of criteria that the US government and other partners can use to develop a rigorous evaluation framework. The criteria are available at http://www.ghtcoalition.org/files/IIFfactsheet_10.26.pdf.

36 In 2010, the Results for Development Institute (R4D) released its first policy assessment on accelerating research and development for global health diseases. R4D's Center for Global Health R&D Policy Assessment launched its first assessment, titled "Prizes for Global Health Technologies," which can serve as a resource to US policymakers and other partners when evaluating incentives and innovative financing. R4D's assessment of prizes is the first in a series of policy evaluations to speed research for diseases primarily affecting low-income and developing nations. It is available at http://www.resultsfordevelopment.org/about/newsandevents/r4d%E2%80%99s-rd-policy-prize%E2%80%99s-assessment-open-public-comment.

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

AERAS GLOBAL TB VACCINE FOUNDATION

AVAC

bvgh BIO Ventures for Global Health

The CD4 INITIATIVE

CONRAD LEADERS IN REPRODUCTIVE HEALTH AND HIV PREVENTION

DNDi NORTH AMERICA Drugs for Neglected Diseases *initiative*

ELIZABETH GLASER PEDIATRIC AIDS FOUNDATION

fhi Family Health International

FIND foundation for innovative new diagnostics

GAVI ALLIANCE

TB ALLIANCE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Global Campaign FOR Microbicides

Global Health Council

IDRI *Infectious Disease Research Institute*

IVCC COMBATING INSECT BORNE DISEASE

iWH *Institute for OneWorld Health*

iavi International AIDS Vaccine Initiative
A partner of the Global HIV Vaccine Enterprise

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

IVAC

INTERNATIONAL VACCINE INSTITUTE

Medicines for Malaria Venture

PATH

mvi PATH MALARIA VACCINE INITIATIVE

Population Council

PUBLIC HEALTH INSTITUTE

RESEARCH AMERICA AN ALLIANCE FOR DISCOVERIES IN HEALTH

SABIN VACCINE INSTITUTE

Seattle BioMed

TAG Treatment Action Group

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