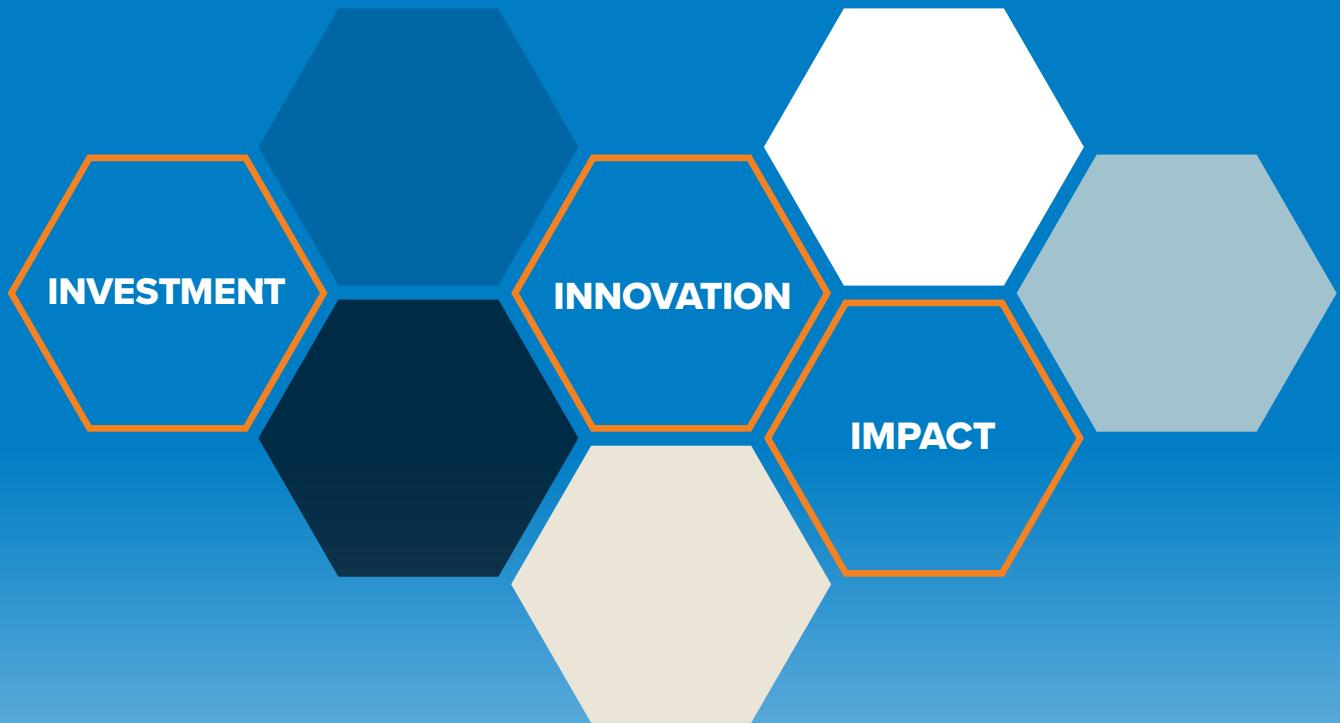


# RETURN ON INNOVATION

Why global health R&D is a smart investment for the United States



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### June 2017

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# RETURN ON INNOVATION

Why global health R&D is a smart investment for the United States

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Contents

## Contents

<b>Key findings</b>	3
<b>Introduction</b>	6
<b>Understanding US government investment in global health R&amp;D</b>	8
How much does the US government invest in global health R&D?	8
What are the US government's global health R&D funding priorities?	9
Which global health challenges is the US addressing?	9
What types of R&D does the US prioritize?	9
Declining US government funding masked by Ebola investments	10
Investing for impact: Emergency funding vs. sustained investment	11
A whole-of-government approach to global health R&D	12
<b>Return on investment: Global health impact from US government investment in R&amp;D</b>	14
New tools that are saving lives	14
An increasingly robust pipeline of global health technologies in development	20
<b>Return on investment: Results for America from US government investment in global health R&amp;D</b>	26
Growing the US economy and creating jobs	27
Leveraging funding from the private sector and other donors	27
Protecting American health	29
Promoting US national security	30
Protecting US global development investments	31
<b>Conclusion</b>	32
<b>Methodology</b>	34
Funding data	34
Registered products and pipeline candidates	34
<b>Registered products table</b>	35
<b>References</b>	38

## Acronyms

<b>AIDS</b>	Acquired Immunodeficiency Syndrome
<b>BARD</b>	Biomedical Advanced Research and Development Authority
<b>BVGH</b>	BIO Ventures for Global Health
<b>CBER</b>	Center for Biologics Evaluation and Research
<b>CDC</b>	Centers for Disease Control and Prevention
<b>DoD</b>	Department of Defense
<b>EIND</b>	Emergency Investigational New Drug
<b>EUA</b>	Emergency Use Authorization
<b>EUAL</b>	Emergency Use Assessment and Listing
<b>FDA</b>	Food and Drug Administration
<b>FDI</b>	Foreign direct investment
<b>GDP</b>	Gross domestic product
<b>HHS</b>	Department of Health and Human Services
<b>HIV</b>	Human Immunodeficiency Virus
<b>MDR-TB</b>	Multidrug-resistant tuberculosis
<b>MMV</b>	Medicines for Malaria Venture
<b>MPT</b>	Multipurpose prevention technology
<b>NDs</b>	Neglected diseases
<b>NIAID</b>	National Institute of Allergy and Infectious Diseases
<b>NIH</b>	National Institutes of Health
<b>NTDs</b>	Neglected tropical diseases
<b>OIP</b>	Office of International Programs
<b>PAHO</b>	Pan-American Health Organization
<b>PEPFAR</b>	President's Emergency Plan for AIDS Relief
<b>PRNDs</b>	Poverty-related and neglected diseases
<b>PRV</b>	Priority Review Voucher
<b>R&amp;D</b>	Research and development
<b>RH</b>	Reproductive health
<b>State</b>	Department of State
<b>TB</b>	Tuberculosis
<b>USAID</b>	US Agency for International Development
<b>VHF</b>	Viral hemorrhagic fevers
<b>WHO</b>	World Health Organization
<b>XDR-TB</b>	Extensively drug-resistant tuberculosis

# Key findings

This report provides an in-depth analysis of US government funding for global health research and development (R&D), as well as analysis of health impact and economic returns from these investments. First, it looks at US government investments in global health R&D over time and outlines funding trends, including implications of emergency R&D investments versus sustainable funding. It also looks at key US agencies fueling research efforts and examines their contributions to novel global health technologies. Next, the report analyzes the health impact of tools supported by US government investments, with case studies highlighting treatments delivered, lives saved, and cost savings. Finally, it considers direct returns to the United States from government investments in global health R&D, including economic growth, job creation, and American health security. We hope this report will inform Congress, Executive Branch, and other key stakeholders as they make policy and budget decisions that affect the future of US leadership in global health R&D.

**US government investments in global health R&D are indispensable to developing new drugs, vaccines, diagnostics, and other tools for poverty-related and neglected diseases and health conditions.**

- Between 2007 and 2015, the US government invested nearly US\$14 billion dollars in R&D for global health.
  - In comparison, in 2015 alone, the US government spent \$1.05 trillion on Medicare and health, \$609 billion on the military, and \$102 billion on education.
- Despite relatively limited investment, US government support was essential in helping advance 42 new technologies approved since 2000 – including 11 new products for malaria, 10 for tuberculosis (TB), and 1 for HIV/AIDS.
- It has also supported 128 promising products in late-stage development – including 103 vaccines, drugs, and diagnostics for neglected diseases; 11 products for Ebola and select viral hemorrhagic fevers (VHFs); and 14 novel technologies for women's health.

**US government investment in global health R&D is critical to respond to market failure. The private sector alone will not fill this gap.**

- There is a market failure for new drugs, vaccines, diagnostics, and other tools for neglected diseases. Because these diseases primarily affect people in some of the world's poorest places, there is little commercial incentive for the private sector to develop these tools.
- US government investment is critical to jumpstart research for urgently-needed health tools and to incentivize private sector engagement by de-risking investment.
- The US government – including the National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), Biological Advanced Research and Development Authority (BARDA), Department of Defense (DoD), and US Agency for International Development (USAID) – also leads the world in scientific and development expertise to effectively conduct global health R&D and demonstrates the best of American innovation.

**The new tools advanced by the United States are saving lives and money by lowering healthcare and treatment costs around the world. US-supported tools in the pipeline hold similar promise.**

- A 50-cent meningitis A vaccine supported by USAID, CDC, NIH, and the Food and Drug Administration has prevented 673,000 cases of meningitis A and 378,000 deaths, and saved 63,000 children from lifelong disability. By 2020, this 50-cent vaccine is predicted to have saved \$9 billion dollars treating meningitis A.
- NIH and USAID helped develop two new pediatric treatments for malaria. For just one of these medicines, over 300 million treatments have been distributed, saving the lives of an estimated 750,000 children.
- A late-stage HIV vaccine candidate supported by NIH and DoD is currently advancing through clinical trials. A 70% effective vaccine is predicted to nearly halve the number of new HIV infections annually in its first decade of use.

**US investments in global health R&D also have direct economic benefits for the US economy, fueling job creation, leveraging private sector funding, and promoting cost savings.**

- In 2015, 89 cents of every US government dollar directed to global health R&D was invested within the United States.
- Between 2007 and 2015, US government investment in global health R&D injected \$12 billion into the American economy – \$1.5 billion in 2015 alone – helping provide jobs for American researchers and supporting US companies.
  - Between 2007 and 2015 this investment is estimated to have created nearly 200,000 new jobs and generated an additional \$33 billion in economic output as it cycled through the economy.
- Every \$1 NIH spends on basic research is estimated to generate an additional \$8.38 of industry investment over the next eight years. This means that by 2023, the US government's 2015 investment in global health basic research alone will spur nearly \$4 billion in additional industry R&D investment for global health that would have not happened independently.
- Forward-thinking investment in R&D has significant cost savings over long-term costs of treatment or emergency investments during a disease outbreak.
  - Twenty-six million dollars invested in polio vaccine R&D resulted in cost savings of \$180 billion on polio treatment in the United States alone since the 1950s.
  - Large-scale global disease pandemics could cost the global economy more than \$60 billion a year, while investing in the R&D needed to protect against these outbreaks would cost only a fraction of that – \$1 billion – each year.

**Despite these results, there is a large and growing gap between increasing global health risks and declining levels of investment in R&D.**

- In 2015, the United States invested just \$1.7 billion in global health R&D – less than one-tenth of one percent (0.0088%) of the nation’s gross domestic product (GDP) for that year.
- US spending on global health R&D has been largely stagnant or declining since peaking in 2009 (excluding emergency investments in Ebola in response to the 2014 outbreak in West Africa).
  - The United States has cut funding to neglected disease R&D in five out of the last six years, despite increasing frequencies of global pandemics, growing antimicrobial resistance, and heightened abilities for diseases to cross borders.
  - Without emergency investments in Ebola, US 2015 investments in global health R&D are the lowest ever since tracking began in 2007. It currently invests a quarter of a billion dollars less than it did in 2012.
- Globally, only 1-2% of health research funding is directed to neglected diseases and health conditions that put millions of lives at risk.

**US investment in global health R&D is also vital for protecting American health and global health security.**

- The recent devastating outbreaks of Ebola and Zika make it clear that diseases know no borders and demonstrate how continued underinvestment in R&D has left America and the world vulnerable, with no tools to prevent, diagnose, or treat these and other diseases that threaten global and American health.
- The 2014 Ebola epidemic in West Africa claimed more than 11,000 lives and cost the United States about \$3 billion in efforts to boost domestic preparedness and contain the outbreak at its source. If an Ebola vaccine had been available, the cost and reach of the epidemic would have been far less.
- Many other debilitating diseases have received far less publicity but also put American health at risk.
  - Chagas’ disease, a debilitating disease endemic in Latin America, currently infects as many as 300,000 people in the United States. Due to limited R&D investment, currently available tools to diagnose, treat, and prevent Chagas’ disease are inadequate. As a result, Chagas’ disease costs the United States economy an estimated \$900 million annually.

**One-time, emergency investments cannot replace sustainable, forward-thinking funding for global health R&D.**

- Emergency investments in R&D during a health crisis can accelerate promising research but have only limited effect in delivering new tools needed during an outbreak.
- Emergency Ebola investments succeeded in accelerating a promising vaccine candidate only because it built on US government investments in research efforts from years earlier – research that was then suspended due to budget cuts. Had those investments been sustained, a vaccine may have been available sooner and could have saved thousands of lives and billions of dollars.
- Sustainable funding for R&D is critical to understand endemic and emerging pathogens, have a strong pipeline of medical countermeasures, and accelerate research to have tools ready when needed to prevent an outbreak from spreading to a deadly pandemic.

# Introduction

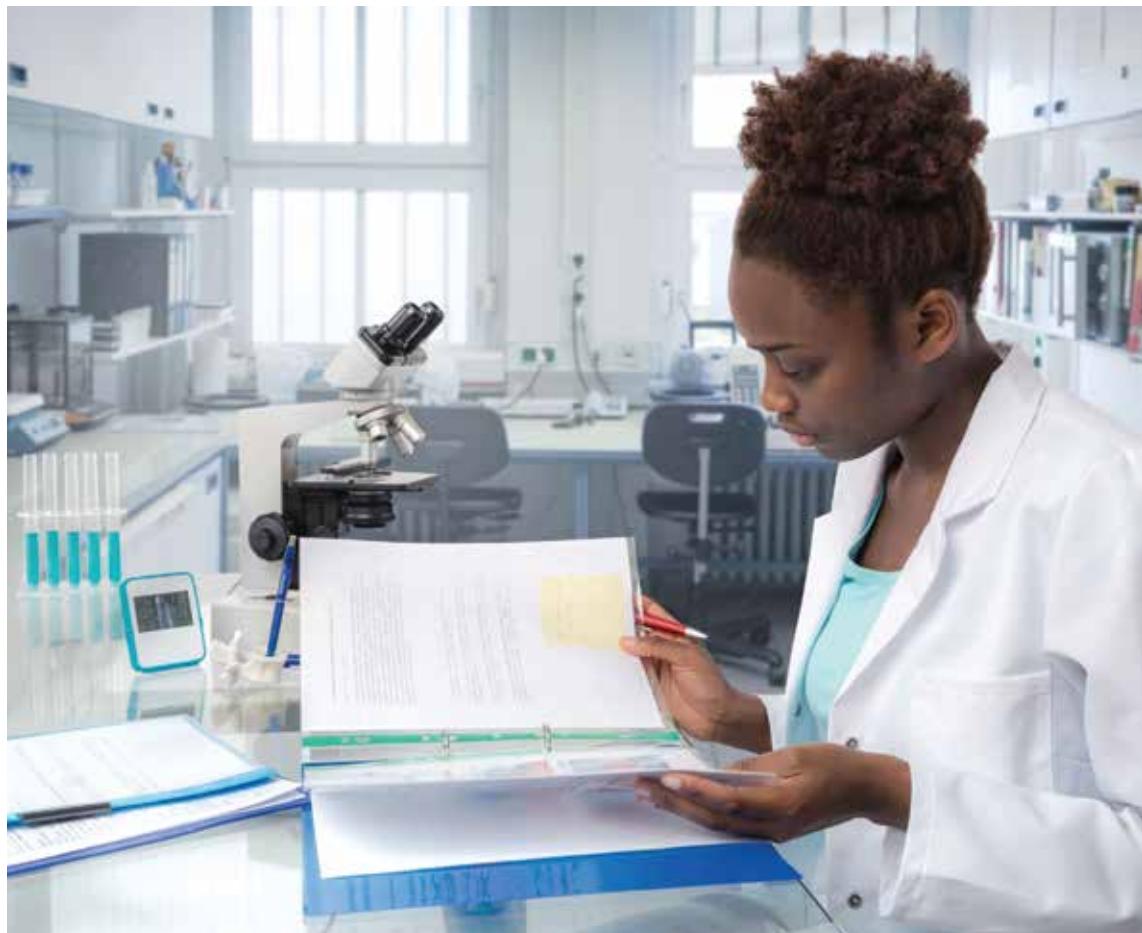
Despite tremendous progress over the past decade, poverty-related and neglected diseases (PRNDs) such as HIV/AIDS, tuberculosis (TB), malaria, and neglected tropical diseases (NTDs) still cause 6.7 million deaths and the loss of 354 million years of healthy and productive life in developing countries every year.<sup>1</sup> Emerging infectious diseases – like Ebola and Zika – compound these statistics. To continue to make progress against both emerging and longstanding global health threats, new drugs, vaccines, diagnostics, and other tools are vitally needed. Not only will these tools help finally end endemic health issues in low-resource settings, but they will also be critical to protecting health worldwide and mitigating the risks of global disease epidemics.



The US government plays an unparalleled role in global health research and development (R&D) – the process of developing new tools for PRNDs. Because these diseases primarily impact people in the world's poorest places, there is little commercial incentive to spur private sector-led research. US government investment is vital to incubating and jumpstarting this research, and de-risking private-sector engagement.

This US investment is strategic and worthwhile. Not only has US investment helped advance technologies that are saving lives and reducing health treatment costs around the globe, but it is also protecting American health through the development of tools for emerging infectious disease threats. Importantly, US government investments in global health R&D also have direct returns for the US economy – spurring job creation, fueling economic growth, and leveraging private sector investment.

This report provides an in-depth analysis of US government funding for global health R&D, as well as analysis of health impact and economic returns from these investments. First, it looks at US government investments in global health R&D over time and outlines funding trends, including implications of emergency R&D investments versus sustainable funding. It also looks at key US agencies fueling research efforts and examines their contributions to novel global health technologies. Next, the report analyzes the health impact of tools supported by US government investments, with case studies highlighting treatments delivered, lives saved, and cost savings. Finally, it considers direct returns to the United States from US government investments in global health R&D, including economic growth, job creation, and American health security. We hope this report will inform Congress, Executive Branch, and other key stakeholders as they make policy and budget decisions that affect the future of US leadership in global health R&D.



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# Understanding US government investment in global health R&D

## How much does the US government invest in global health R&D?

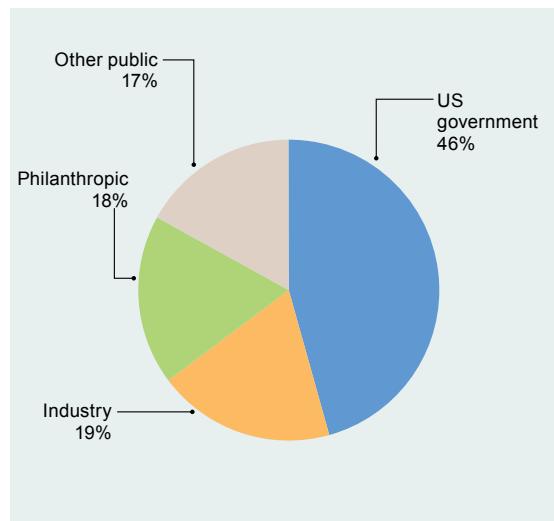
The US government's investment in global health R&D represents less than 0.05% of annual federal spending but is critical to global efforts to develop new drugs, vaccines, diagnostics, and other tools for neglected and emerging infectious diseases and health conditions affecting the most vulnerable populations around the world.

Between 2007 and 2015, the US government invested nearly US\$14 billion dollars in R&D for global health. To put this in context, in 2015 alone, the US government spent \$1.05 trillion on Medicare and health, \$609 billion on the military, and \$102 billion on education. Its 2015 investment of \$1.7 billion in global health R&D represented less than one-tenth of one percent (0.0088%) of the nation's gross domestic product (GDP) for that year. Yet even with this relatively small investment, the US government is a world leader in supporting global health R&D; its 2015 investment accounted for nearly half (46%) of all global funding (including from industry, philanthropic organizations, and other public funders), and three-quarters (74%) of all government funding globally. In comparison, the next largest government funder in 2015 (the European Commission, with \$171 million) contributed 8% of all government funding globally.

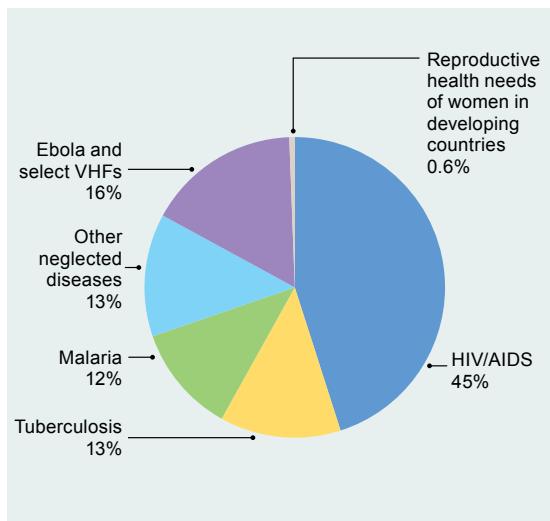
These numbers demonstrate two important points. First, the importance of the United States' scientific and humanitarian leadership in providing financial, technical, and other support for global health R&D. Second, the critical underinvestment globally in R&D to deliver urgently-needed drugs, vaccines, diagnostics, and other tools for neglected diseases and health conditions. Investment in R&D for global health represents just 1-2% of total spending on health R&D each year.



**Figure 1 ● US government share of funding for global health R&D in 2015**



**Figure 2 ● US government funding for global health R&D in 2015 by disease and global health area**



## What are the US government's global health R&D funding priorities?

### Which global health challenges is the US addressing?

US government funding for global health R&D can be divided into three broad categories: neglected diseases, viral hemorrhagic fevers (VHFs), and reproductive health. Of the \$1.7 billion invested in 2015, \$1.4 billion (83%) was for neglected disease R&D; \$276 million (16%) went to R&D for Ebola and select VHFs; and \$10 million (1%) was invested in R&D to address the reproductive health needs of women in developing countries.

Although the high-level breakdown between these three thematic areas is instructive, it is more useful to break this down further to the individual disease or health area level. This shows that the majority of US government funding is concentrated on the ‘big three’ neglected diseases: HIV/AIDS, TB, and malaria. Strong support for HIV/AIDS R&D has been a consistent feature of US government support for global health R&D over the last decade – it has accounted for more than half the US government’s neglected disease R&D funding in every one of the last nine years.

This breakdown also demonstrates the scale and significance of the US government’s response to the 2014 Ebola outbreak: the 16% of total US government global health R&D funding directed to Ebola and select VHFs in 2015 was more than the US government invested in any other single neglected disease except for HIV/AIDS. It was also more than it invested in all other neglected diseases – outside of HIV/AIDS, TB, and malaria – combined. Beyond the ‘big three,’ the US government’s next largest investments in neglected disease R&D were for dengue (\$47 million, 3% of total US government funding for global health R&D), diarrheal diseases (\$46 million, 3%), kinetoplastids (\$39 million, 2%), helminths (\$28 million, 2%) and salmonella infections (\$28 million, 2%). All other neglected diseases received \$44 million, or 3% of all US government global health R&D funding.

### What types of R&D does the US prioritize?

As well as looking at how US government funding is prioritized across diseases, it is also helpful to understand what types of global health technologies the US government is investing in and how this funding is allocated across the spectrum of R&D activity (from basic and early-stage research to late-stage research and advanced product development).

In 2015, more than a quarter (27%) of all US government funding for global health R&D was for basic research (foundational research that is not yet directed at a specific technology). Of the remaining 73% of funding that was for product-specific R&D, more than half was for vaccine development, which accounted for 41% of total US government funding for global health R&D – more than it invested in all other product types combined.

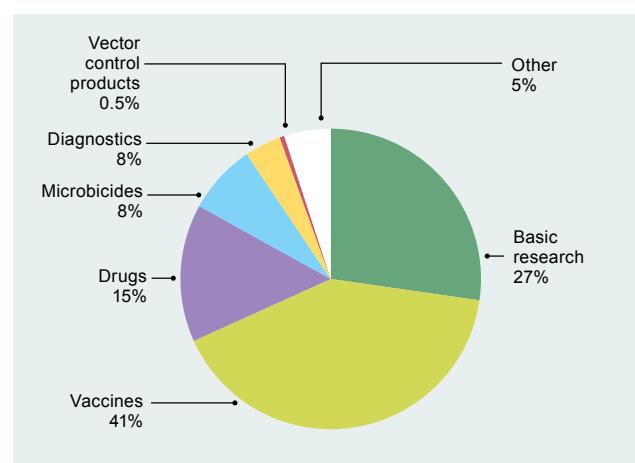
### Declining US government funding masked by Ebola investments

The US government's \$1.7 billion investment in global health R&D in 2015 was its largest ever. However, it is important to recognize that this level of investment was **only due** to an emergency surge in funding for Ebola and select VHF, which hid an ongoing decline in neglected disease R&D funding. Without this Ebola-related investment, US government funding for global health R&D would in fact have fallen in 2015 – like it has every year since 2012.

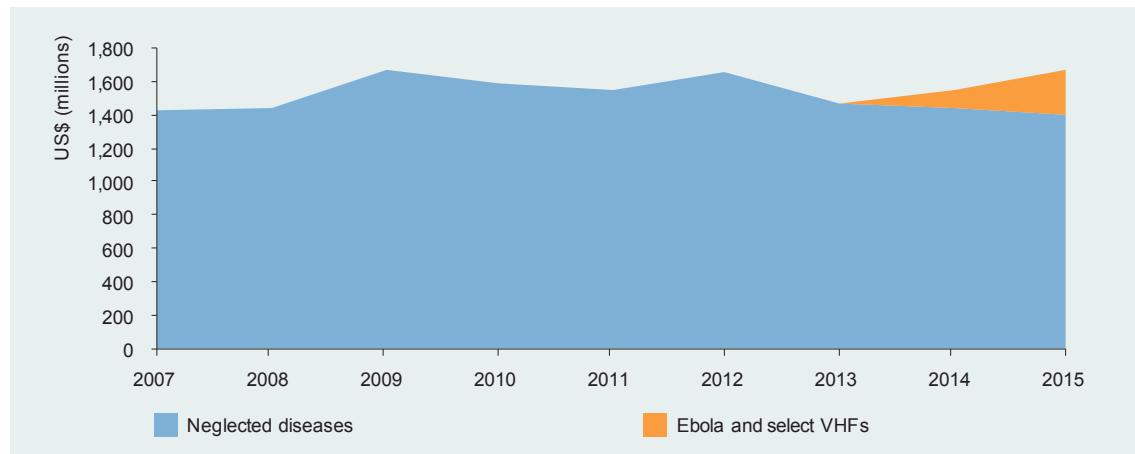
The surge in R&D investment for Ebola and select VHF in 2014 and 2015 reflects the significant US government response to the 2014 epidemic. Prior to the 2014 epidemic in West Africa, funding for Ebola R&D was limited and sporadic. With commitment from Congress and the Administration, in 2015 the US government invested more than a quarter of a billion dollars (\$276 million) in R&D for Ebola and select VHF – more than it invested in R&D for any neglected disease except HIV/AIDS.

At the same time, US government funding for neglected disease R&D hit its lowest point since annual tracking began in 2007: from a peak of \$1.7 billion in 2009, US investment in non-Ebola global health R&D declined to \$1.4 billion in 2015. This finding follows a negative trend: despite increasing frequencies of global pandemics, growing antimicrobial resistance, and heightened abilities for diseases to cross borders, the US government has cut funding to neglected disease R&D in five out of the last six years and currently invests a quarter of a billion dollars less than it did in 2012.

**Figure 3 ● US government funding for global health R&D in 2015 by product type**



**Figure 4 ● US government funding for global health R&D 2007-2015**



## Investing for impact: Emergency funding vs. sustained investment

In the past 3 years, the US government and other donors have mobilized significant emergency R&D funds in response to two major emerging infectious disease outbreaks: Ebola and Zika. While the emergency R&D funding for Zika (which began in fiscal year 2016) is too recent to be included in the funding data analyzed in this report, both examples are useful in examining the role of emergency funding in supporting the development of new vaccines, drugs, diagnostics, and vector control products.

### Emergency funding can be a game-changing intervention

The emergency response to the recent Ebola and Zika epidemics proved that it is possible to rapidly mobilize significant additional funding for global health R&D. It also showed that R&D timeframes can potentially be accelerated under the right circumstances.

The ability of emergency response mechanisms to rapidly provide significant new funding is clear. The US government invested \$276 million in R&D for Ebola and select VHFs in 2015 and at least \$132 million in Zika vaccine R&D in 2016. Combined, the US government's investment in R&D for these two diseases alone approaches its combined R&D investment in all neglected diseases except HIV/AIDS.

The extent to which emergency funding can accelerate product development is less clear. On average, it takes at least 10-15 years to develop a new vaccine. The leading Ebola vaccine candidate (rVSV-ZEBOV) was able to progress from pre-clinical testing to phase III clinical trials in less than two years, and it is likely that the availability of focused (and sufficient) funding for late-stage product development was one of many factors that helped make this possible. But such rapid progress was only possible because previous investments in Ebola R&D by the US and Canadian governments produced a promising vaccine candidate – one that was shelved due to a lack of ongoing funding. Emergency funding reignited this research and picked up where researchers had left off in the past; it did not quickly translate brand new research into a brand new product. This was true for nearly all the most promising drug and vaccine candidates that received emergency Ebola R&D funding in the recent outbreak.

### The downsides of emergency funding

The robust response to recent Ebola and Zika outbreaks was both welcome and productive. But this type of funding also has its downsides. One of

the major concerns with emergency surges of R&D investment during a public health crisis is that even the most accelerated R&D cannot deliver results immediately. Waiting until a crisis has begun before investing in R&D not only guarantees that urgently-needed tools won't be available at its outset – when they have the greatest chance of stopping an outbreak in its tracks – but also makes it highly unlikely that new tools will be available to address the outbreak when it is at its peak. Estimates suggest that 80% of all deaths in Guinea from the recent Ebola outbreak could have been prevented if an Ebola vaccine had been introduced within six weeks of the World Health Organization (WHO) declaring its existence.<sup>2</sup> But even with the advantage of past R&D investments to build on, emergency R&D funding wasn't able to deliver a new vaccine or drug for Ebola before the outbreak had subsided.

A second concern is diverting funds from existing programs to address the emerging threat. By providing genuinely additional funds, emergency funding appropriations can limit the impact that public health emergencies have on existing budgets; without emergency appropriations, these recent outbreaks would undoubtedly have had a much greater impact on funding for neglected disease R&D.

Indeed, funds allocated to existing neglected disease R&D programs were redirected to the emergency response: the Department of Health and Human Services (HHS) transferred at least \$81 million from existing programs to address the Zika outbreak, \$34 million of which was taken from National Institutes of Health (NIH) R&D funds.<sup>3</sup> Even emergency funding itself was re-appropriated: as much as \$589 million earmarked for Ebola was later shifted to the Zika response.<sup>4</sup> Another major concern about emergency funding is its sustainability; in a field where success can take a decade to achieve, funding that disappears after just a few years has the potential to do as much harm as good. If US government funding dries up once the emergency appropriation term ends, many projects will simply be shelved, and the investment that was made in them wasted. And without any certainty around what (and how much) funding will be available in just a few years' time, companies and researchers are likely to be hesitant to invest heavily in new R&D programs.<sup>5</sup>

Emergency funding also carries the pitfalls of anything done in haste; without sufficient time to make strategic funding decisions, it is inevitable that effort will be duplicated, and funding wasted.

Implemented properly, emergency funding can be an extremely useful tool for responding to unexpected emerging disease threats. But it should never be considered a substitute for sustained, ongoing investment in global health R&D.

## A whole-of-government approach to global health R&D

Six key federal agencies lead the US government's efforts to support global health R&D. Five of these agencies – NIH, the US Agency for International Development (USAID), the Department of Defense (DoD), the Centers for Disease Control and Prevention (CDC), and the Biomedical Advanced Research and Development Authority (BARDA) – account for almost all US government funding for global health R&D, while the Food and Drug Administration (FDA) plays an important but largely non-financial role. The various agencies contribute in different but complementary ways, reflecting their unique strengths, priorities, structure, and size.

### Departments and agencies leading the US government's global health R&D efforts

#### **DEPARTMENT OF STATE (State):**

Coordinates the President's Emergency Plan for AIDS Relief (PEPFAR) and sets priorities for US global health assistance.

#### **US AGENCY FOR INTERNATIONAL DEVELOPMENT (USAID):**

Advances the development, introduction, and scale up of affordable and appropriate health technologies to address diseases and conditions impacting low- and middle-income countries, primarily through external funding. Research focus is on late-stage and trials in low-resource settings.

#### **DEPARTMENT OF DEFENSE (DoD):**

Supports R&D for infectious diseases that pose a risk to US troops abroad or to US national security. Research activities span all areas of development, from basic research to late-stage and advanced development.

#### **DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS):**

Oversees NIH, FDA, CDC, and BARDA.

#### **NATIONAL INSTITUTES OF HEALTH (NIH):**

The principal biomedical and public health research agency in the United States. Conducts biomedical research in-house, as well as providing funding externally, with a primary focus on basic and early-stage research.

#### **CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC):**

Protects people in the United States and abroad through disease surveillance, rapid outbreak response, and research to develop health tools and evaluate health interventions.

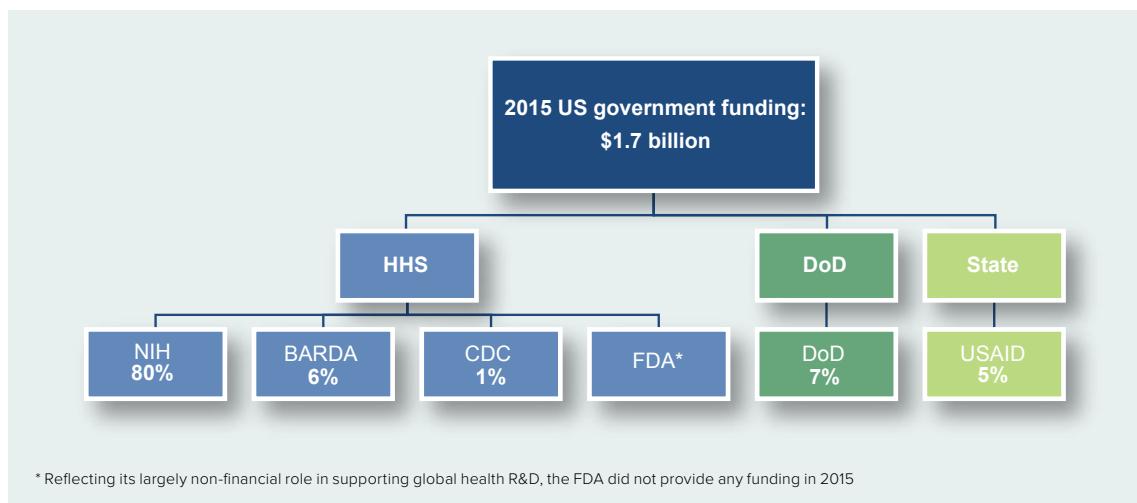
#### **FOOD AND DRUG ADMINISTRATION (FDA):**

Regulates the safety and efficacy of health products marketed in the United States, with its approval serving as a 'gold standard' that can expedite regulatory review in low- and middle-income countries. Also works to strengthen global regulatory capacity and set international standards.

#### **BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY (BARDA):**

Supports development and procurement of medical countermeasures against threats to public health, including emerging infectious diseases and antibiotic resistance. Research focus is on translational and advanced development of products.

**Figure 5 ● Agency share of US government funding for global health R&D in 2015**



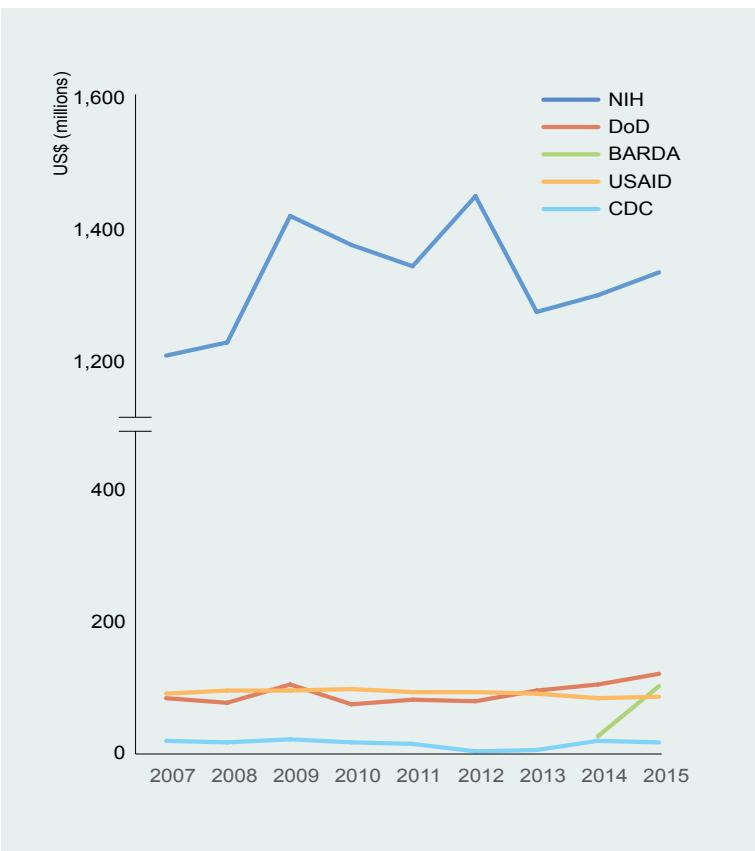
NIH is the largest funder of global health R&D among the US government agencies, investing about twice as much as all the other agencies combined; in 2015, \$1.3 billion (80%) of the US government's \$1.7 billion investment in global health R&D came from NIH. The next most significant agency contribution came from DoD (\$123 million, 7%), closely followed by BARDA (\$104 million, 6%) and USAID (\$87 million, 5%), and finally CDC (\$18 million, 1%).

Looking at the entire period from 2007-2015, the picture is little changed: NIH was still by far the largest funder of global health R&D among the US government agencies, providing \$12 billion (86%) of the \$14 billion the US government has invested in global health R&D since 2007.

The next most significant agency contributions came from USAID (\$836m, 6%) and the DoD (\$830m, 6%), which overtook USAID to become the second largest funding agency in 2014-15, largely due to sharply increased investment in Ebola R&D.

The long-term funding picture also shows the very recent emergence of BARDA as a significant global health R&D funder following the emergency funding response to the Ebola crisis.

**Figure 6 ● Trends in US government funding for global health R&D by agency 2007-2015**



# Return on investment: Global health impact from US government investment in R&D

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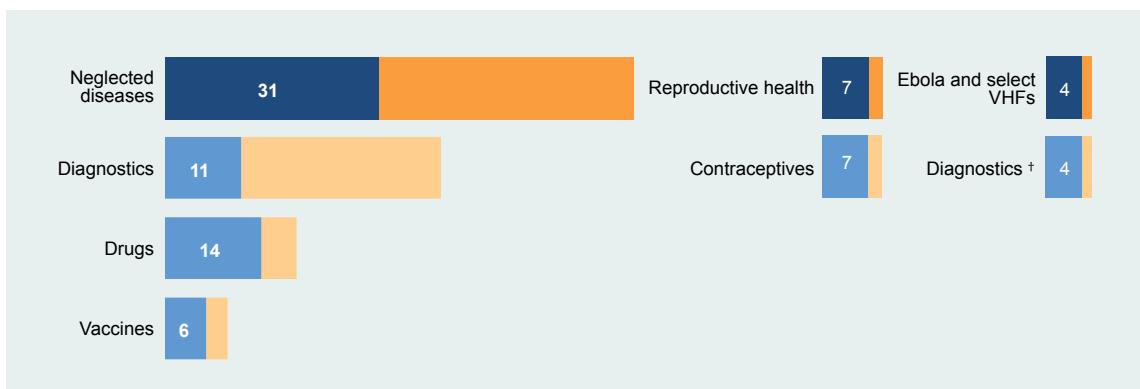
Return on investment: Global health impact from US government investment in R&D

## New tools that are saving lives

Since 2000, 82 new global health technologies have been approved. These new tools – new drugs, vaccines, diagnostics, vector control products, and women's health technologies designed for use in low-resource settings – have helped contribute to the huge improvements in global health outcomes achieved over the last decade and a half, including a 60% reduction in the number of deaths from malaria, a 40% reduction in the number of deaths in children under five, and a 30% reduction in maternal mortality.

The US government supported the development of 42 of these 82 new global health products, including nearly half (31) of the 68 new products for neglected diseases, more than three-quarters (7) of the nine new contraceptives developed specifically for use in resource-limited settings, and four of the five new diagnostic technologies approved for Ebola.\*†

**Figure 7 ● US government support for new global health technologies registered since 2000**



A more granular examination shows that the US government was heavily involved in the successful development of new drugs and vaccines for neglected diseases, supporting nearly three-quarters (14, 74%) of all new neglected disease drugs and two-thirds (6, 67%) of all new neglected disease vaccines developed in the last decade and half. It also supported the development of 11 new neglected disease diagnostic technologies; while proportionately less significant, this is reasonable given that diagnostics are less expensive to develop, and so are less exclusively reliant on public and philanthropic funding.<sup>‡</sup>

More than two-thirds of the 31 new neglected disease products developed with US government support were for either malaria (11, 35%) or TB (10, 32%), reflecting its historical funding focus on HIV/AIDS, malaria, and TB, coupled with the scientific challenges in developing preventive tools against HIV/AIDS. This latter observation is an important reminder of two things: first, that the complexities of science mean that the number of new products developed isn't always proportional to the dollars invested in or hours spent on R&D; and second, that the impact of R&D funding cannot only be measured by the number of products it delivers. Research that doesn't directly lead to a new product – including research into ultimately unsuccessful approaches – helps advance scientific understanding, paving the way for future success.

### How has the US government supported successful new products?

The two largest US government funders of global health R&D—NIH and USAID—were each involved in over half of the 42 new global health technologies delivered since 2000 with US government support. Both of these agencies supported 22 new global health technologies; they were followed by DoD, which supported 13, CDC which supported 6, and FDA which supported 1.

#### NIH

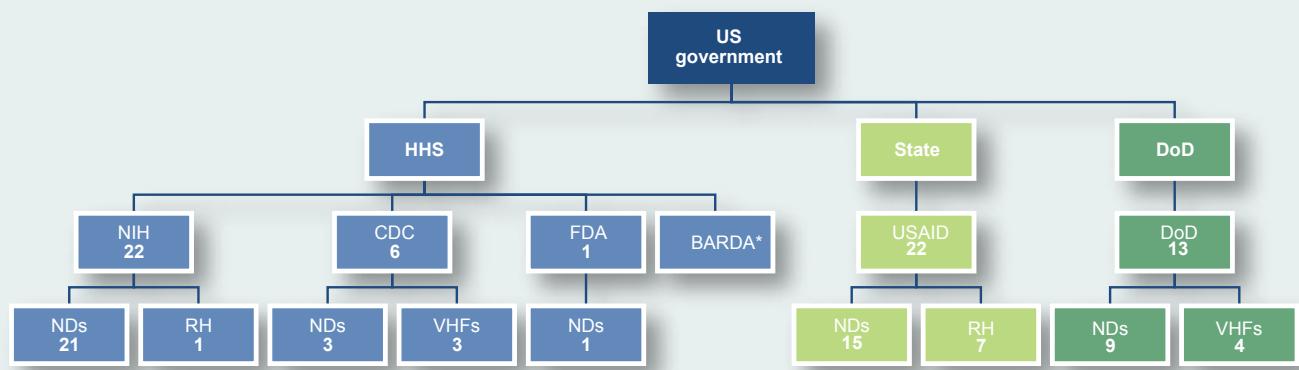
NIH contributed to over half (22) of the 42 new global health technologies developed with US government support. Given that NIH contributes the majority of US government funding for global health R&D, this may not seem surprising. However, as NIH's primary focus is on basic research (which by definition isn't focused on advancing a particular product, but instead lays a scientific foundation)

\* In this report, 'support' includes both direct financial investment and non-financial contributions (active participation in R&D, or the provision of expertise, infrastructure, capacity building, or intellectual property & technology transfer)

† These Ebola diagnostics received emergency approval for use in the recent epidemic. Given the unique nature of the regulatory pathway in pandemic diseases like Ebola, this has been counted as regulatory approval for the purpose of this report. Only novel diagnostic approaches have been counted: the number of individual new Ebola diagnostics approved for use under the FDA Emergency Use Authorization (EUA) or WHO Emergency Use Assessment and Listing (EUAL) mechanisms is higher than the number recognized here.

‡ The high proportion of public involvement in Ebola diagnostics reflects the massive public funding response to the epidemic and Ebola's status as a bioterror threat.

**Figure 8 • US government support for new global health technologies registered since 2000 by agency**



\* As a new player in the field of global health R&D, no BARDA-supported product has yet achieved regulatory approval

and early-stage research (which has only a small chance of translating into an approved product), support for 22 distinct products is notable. Of the 22 new products developed with NIH support, 21 were new products for neglected diseases – with these being relatively evenly spread between drugs (8), diagnostics (7), and vaccines (6). The remaining product was a contraceptive designed for the needs of women in developing countries.

### USAID

Like NIH, USAID also contributed to over half (22) of the 42 new global health technologies developed with US government support. That it was able to do so with a much smaller investment than NIH reflects the different – and complementary – ways these two agencies contribute to global health R&D, with USAID focusing on late-stage (lower risk) product development and a collaborative funding approach (which leverages additional investment from other stakeholders). Just over two-thirds (15) of all USAID-supported products were for neglected diseases (consisting of 12 drugs, 2 vaccines, and 1 diagnostic). The remaining 7 products were for the reproductive health needs of women in developing countries, representing all but 2 of the 9 new reproductive health products developed since 2000 with US government support.

### DoD

The DoD's primary motivation for investing in global health R&D is to protect the well-being of US servicemembers. Accordingly, its focus is on R&D to protect against infectious diseases, as well as manmade and naturally occurring biological threats – both of which can have global health R&D applications. Like NIH, DoD conducts its own research, as well as provides funding externally; in contrast to NIH, its focus extends all the way from basic and early-stage research through to late-stage product development. Since 2000, DoD has played a role in delivering 13 new global health products, or nearly a third of all US government-supported products. Over two-thirds (9) of these 13 products were for neglected diseases (including 5 diagnostics, 3 drugs, and 1 vaccine). The remaining 4 products were all Ebola diagnostics.

### CDC

CDC's principal mandate is to protect US public health, including against both domestic and foreign disease threats (such as the Ebola virus). Accordingly, it plays an important role in R&D to prevent, detect, and respond to infectious disease threats. Since 2000, CDC has helped deliver six new global health technologies, including playing a vital role in developing diagnostic tools for the West African Ebola outbreak: exactly half (3) of the 6 new global health products developed with CDC support were Ebola diagnostics. The remaining 3 products (2 diagnostics and 1 vaccine) were all for neglected diseases.

## The FDA's unique role in global health R&D

The FDA is the largest pharmaceutical regulatory authority in the world, with a principal mandate to protect the public health of US citizens by ensuring the safety, efficacy, and security of the drugs, biological products, and medical devices it approves for use in humans. In addition to this crucial domestic role – and despite the limitations its role as regulator imposes on its ability to directly support product development – the FDA also plays an important role in advancing R&D for global health.

### Capacity building and regulatory harmonization in low- and middle-income countries

Through both its Office of International Programs (OIP) and Center for Biologics Evaluation and Research (CBER), the FDA collaborates with a wide array of international partners to build capacity and improve regulatory systems in the area of global health, helping to ensure that new global health tools are approved by local regulators and ultimately reach people in need.

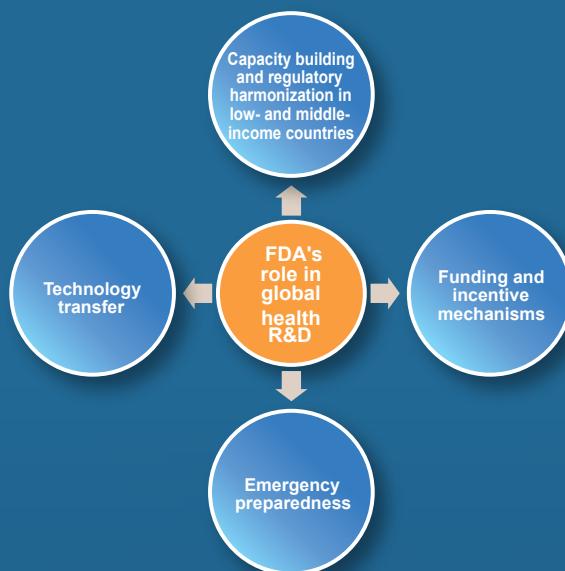
Under PEPFAR, for example, CBER helps train foreign regulators (both in-country and through secondment within FDA), while OIP assists manufacturers and foreign regulators to assure the quality of antiretroviral drugs made available through PEPFAR.

CBER also collaborates with WHO as a Pan-American Health Organization (PAHO)/WHO Collaborating Center for Biological Standardization, providing technical and regulatory expertise to advance development and implementation of WHO international standards in WHO's vaccine prequalification program.

### Technology transfer

Through its technology transfer program, FDA shares in-house discoveries (such as vaccine conjugation technologies) with external organizations. Indeed, it is through this mechanism that the FDA supported one of the 42 new global health products developed with US government support. In-house knowledge on vaccine development technologies developed by FDA was instrumental to the development of the MenAfriVac meningitis vaccine – and in particular to enabling it to be provided for a price of 50 cents per dose, an essential factor in its take-up by developing countries. By 2020, this particular vaccine is predicted to have prevented 100 million cases of meningitis in one of the most impoverished regions of the world.

**Figure 9 • FDA's role in global health R&D**



### Funding and incentive mechanisms

While the FDA rarely funds global health R&D directly, it has done so occasionally – most notably through its Critical Path Initiative, which in 2010 issued a competitive call worth around \$3 million to support the development of new drugs, vaccines, and diagnostics for TB. It also awarded \$3.2 million for Ebola R&D to help provide reference points for the development and evaluation of future Ebola vaccines.<sup>6</sup>

The FDA is also central to one of the key US government incentive mechanisms intended to stimulate global health R&D: the priority review voucher (PRV) scheme for NTDs (recently expanded to include Ebola). Under the PRV scheme, the FDA awards developers of successful new drugs for eligible diseases with a transferrable voucher guaranteeing the expedited review of another pharmaceutical product. The value of a voucher that can speed the approval of a lucrative, blockbuster product – some PRVs have sold for as much as \$350 million – is intended to encourage the development of new drugs and vaccines for neglected diseases.<sup>7,8</sup>

### Emergency preparedness

The FDA also plays a critical role in pandemic response through its Emergency Use Authorization (EUA) and Emergency Investigational New Drug (EIND) schemes, which help promising tools not yet approved by the FDA be used in emergency situations. The EUA mechanism in particular was used to great effect in the recent Ebola and Zika outbreaks, with four of the five new diagnostic tools for Ebola (10 individual tests) approved under the EUA scheme, as well as 14 new Zika tests.

## Real-world impact: US government-supported tools that are saving lives... and dollars

All 42 of the new drugs, diagnostics, vaccines, and reproductive health technologies developed with US government support since 2000 have helped achieve remarkable gains in global health. Four examples below illustrate the real-world impact of just a handful of these new products and detail how US-led global health innovation is saving lives and saving money by lowering healthcare and treatment costs.

### A fifty cent vaccine saving a billion dollars a year

The ‘meningitis belt’ of Africa spans a swath of the continent that stretches from Senegal to Ethiopia. For the last century at least, this region has borne the brunt of regular – and deadly – meningitis outbreaks. In 1996, the worst outbreak of meningitis the region had ever seen resulted in nearly 200,000 infections and more than 20,000 deaths (nearly double the number of deaths from the 2014 Ebola outbreak in West Africa). According to current estimates, close to 350 million people every year are at risk of contracting this potentially lethal disease.<sup>9</sup>

Meningitis vaccines developed using new, more effective technologies had proved to be extremely effective in protecting against infection in high-income geographies. But these new vaccines didn’t protect against meningitis A, the strain historically responsible for almost all outbreaks in the African meningitis belt.<sup>10</sup>

The Meningitis Vaccine Project was established as a partnership between PATH, a US-based global health nonprofit organization, and WHO, with initial funding from the Bill & Melinda Gates Foundation. With support from US government agencies –USAID, CDC, NIH, and FDA – this partnership was able to develop MenAfriVac: the first ever vaccine against meningitis A to be produced using modern technology. Each of the US agencies played a vital role in MenAfriVac’s development, providing funding, clinical trial sites, technical expertise, and technology transfer. In particular, the price of just 50 cents a dose – a fundamental factor in the vaccine’s success – was made possible by vaccine conjugation technology developed by the FDA and transferred to the Serum Institute of India by NIH.

The benefits of US government and other partner engagement in the development of a modern meningitis A vaccine are evident. Since MenAfriVac was first introduced in 2010, 236 million people across the African meningitis belt have been vaccinated. In just seven years, the vaccine has prevented 673,000 cases of meningitis and 378,000 deaths, and saved 63,000 children from lifelong disability. By 2020, this 50 cent vaccine is predicted to have saved nine billion dollars that would otherwise have been spent on treating meningitis.<sup>11,12,13</sup>

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## Malaria drugs designed for children

Along with insecticide-treated bed nets and rapid diagnostic tests, the current gold-standard artemisinin-based anti-malarial drugs have played a key role in dramatically reducing the number of malaria deaths globally in the last decade.

But despite the fact that over 70% of all deaths from malaria are in children under five, until 2009 not a single quality-assured antimalarial drug was tailored to the needs of children.<sup>14</sup> Instead, treating children with malaria meant crushing the adult tablets and mixing with water, then tackling the difficult proposition of getting a child to take the bitter combination by spoon without spitting out or throwing up the medicine.

Two US government agencies – NIH and USAID – funded and collaborated in the development of two new pediatric antimalarial drugs designed to address this critical gap: Coartem Dispersible (artemether-lumefantrine), developed specifically for children as a sweet, cherry-flavored treatment; and Pyramax (pyronaridine-artesunate) granules, a once-a-day treatment approved for use with both *P. vivax* and *P. falciparum* malaria.

Both of these two new treatments were sponsored by the Medicines for Malaria Venture (MMV), a Geneva-based global health nonprofit organization. With funding from NIH and USAID, MMV partnered with the pharmaceutical company Novartis to create a child-friendly version of Novartis' adult anti-malaria drug Coartem. As of 2016, 300 million pediatric treatments of Coartem had been distributed, saving the lives of an estimated 750,000 children.<sup>15,16</sup> Plans for national registration and rollout of Pyramax granules are currently underway.

## Eliminating India's biggest childhood killer

Every year, nearly a quarter of a million children globally – more than 500 children every day – die before their fifth birthday from rotavirus infection. India alone accounts for close to 50,000 of these deaths.<sup>17</sup> Because of the highly contagious and incredibly resilient nature of the virus, rotavirus vaccines provide the only realistic hope of effectively combatting the disease in developing countries.

US government support was crucial to the development of ROTAVAC: the first licensed rotavirus vaccine to be developed using a strain of the virus that was isolated, manufactured, and tested in India. The National Institute of Allergy and Infectious Diseases (NIAID), an institute within NIH, provided funding under the Indo-US Vaccine Action Program for the early-stage development of the vaccine, before transferring the technology to an Indian company, Bharat Biotech in 2000. With the support of additional funding from PATH, a US-based global health nonprofit, NIAID then sponsored clinical trials in India (as well as providing additional expertise) that paved the way for Bharat Biotech to complete development of the vaccine.<sup>18</sup>

In March 2016, ROTAVAC was included in India's national immunization program; following initial rollout in four states, the vaccine will gradually be expanded to cover the entire country. The potential impact for India of introducing this vaccine is significant: preventing more than half a million outpatient visits and nearly 200,000 hospitalizations every year, saving close to \$50 million in direct healthcare costs annually.<sup>19</sup>

## An increasingly robust pipeline of global health technologies in development

The ‘health’ of an R&D pipeline can be measured by the number of potential new health technologies in development at any given time; the larger the pipeline, the greater the chance of successfully developing desperately needed global health tools. And when it can take a decade or more for investments in early-stage R&D to translate into products that are saving lives in the field, the health of the pipeline can itself be an important interim measure of the impact of these investments.

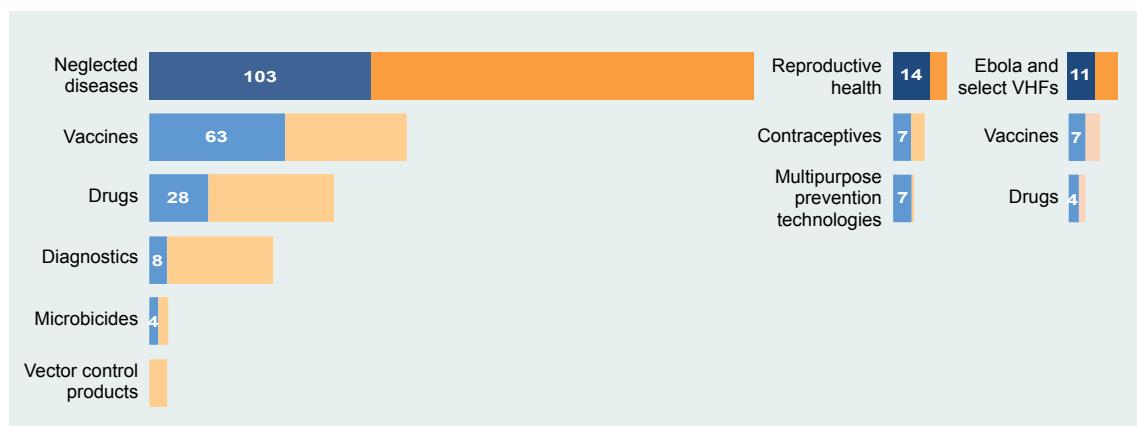
The US government has played an integral role in building an increasingly robust pipeline of global health technologies. It is significant that in 2017, the pipeline of global health products is the largest ever seen. Still, while more robust than in the past, the pipeline does not match the scale of global health need.

At the end of 2016 there were 674 products under development in the global health R&D pipeline, with just under half (321) of these in late-stage development.<sup>◊</sup> The US government directly contributed to 128 (40%) of these 321 late-stage candidates, including 103 products for neglected diseases, 11 products for Ebola and select VHF, and 14 novel technologies for reproductive health.

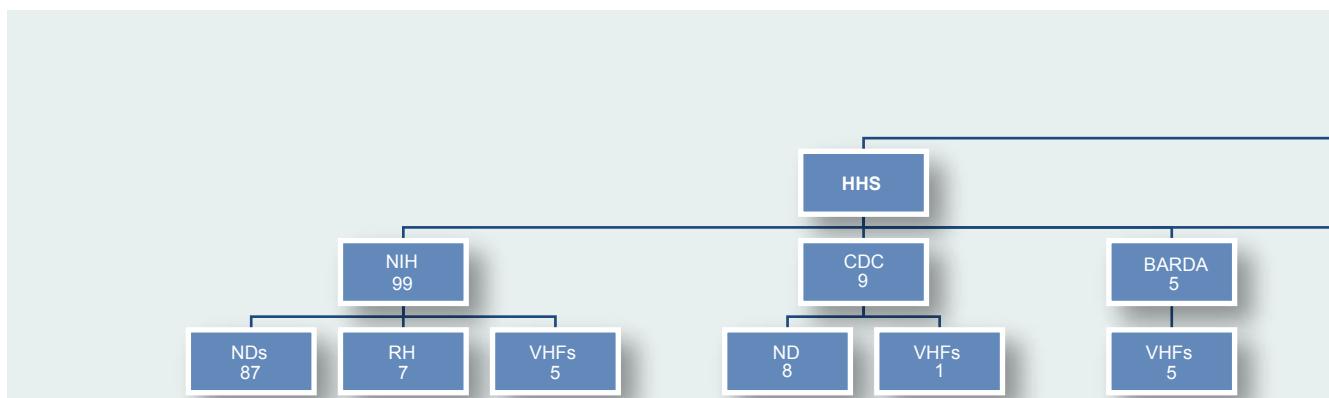
Of particular note is the US government’s leading role in the development of vaccines, microbicides, and contraceptives. US government support contributed to the development of more than half of all

<sup>◊</sup> In the context of this report, ‘late-stage development’ is defined as clinical trials or field evaluation studies.

**Figure 10 • US government support for late-stage global health pipeline candidates**



**Figure 12 • US government support for late-stage global health pipeline candidates by agency**



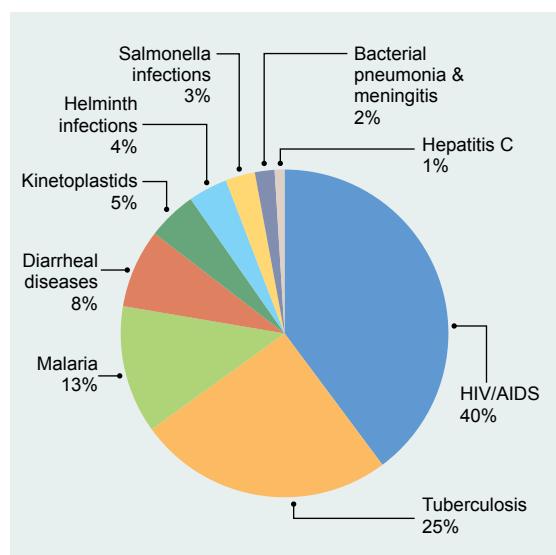
\* As a regulatory body, the FDA does not actively support individual late-stage pipeline candidates

late-stage vaccines (70, 53%) and contraceptives (7, 58%), just under half (4, 44%) of all new microbicides, and all but 1 of the 8 multipurpose prevention technologies (MPTs).

In line with its funding focus, 80% of all US government-supported late-stage pipeline candidates were for neglected diseases, 11% were for Ebola and select VHF, 9% were for the reproductive health needs of developing countries. The US government's historical funding focus on R&D for HIV/AIDS, TB, and malaria is also evident in the pipeline of new technologies it supports.

More than three-quarters of all the late-stage neglected disease pipeline candidates supported by the US government are for either HIV/AIDS (41, 40%), TB (26, 25%), or malaria (13, 13%).

**Figure 11 • Focus of US government support for late-stage neglected disease pipeline candidates**



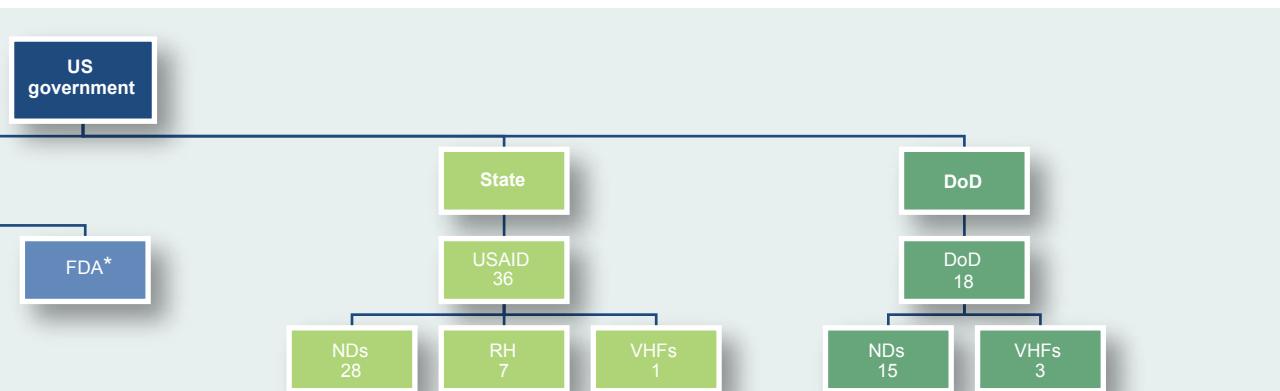
### How has the US government supported the R&D pipeline?

As noted earlier, each agency plays a distinct role as part of a broader whole-of-government approach to supporting global health R&D. The number and type of global health pipeline candidates each agency has supported reflects its unique specialization and value-add, making it difficult to compare agency contributions to global health R&D by the numbers alone.

NIH contributed to more than three-quarters (99, 77%) of all US government-supported late-stage pipeline candidates, and USAID more than a quarter (36, 28%). DoD has contributed to 18 candidates currently in late-stage development (14% of those with US government support), CDC to 9 (7%), and BARDA to 5 (4%).

#### NIH

Just over two thirds of all NIH-supported late-stage pipeline candidates were for either HIV/AIDS (32, 32%), TB (26, 26%), or malaria (9, 9%), while other neglected diseases (20) accounted for a further 20%. The remaining candidates were fairly evenly divided between reproductive health (7, 7%) and Ebola (5, 5%). Vaccines accounted for more than half (56, 57%) of all the late-stage pipeline candidates supported by NIH. Drugs made up a further quarter (26, 26%), followed by diagnostics (8, 8%), contraceptives (5, 5%), MPTs (2, 2%), and diagnostics (2, 2%).



## **USAID**

USAID's primary focus was on HIV/AIDS (10, 28%) and malaria (9, 25%), which together accounted for more than half of all the late-stage pipeline candidates it supported; other neglected diseases made up a further quarter (9, 25%), just one of which was for TB. Although new products for the reproductive health needs of women in developing countries accounted for just under a fifth of USAID's portfolio (7, 19%), this represents half of all the late-stage reproductive health products supported by the US government and a third (35%) of the entire late-stage pipeline globally. USAID also supported one late-stage Ebola pipeline candidate. USAID support was more evenly divided between vaccines (14, 39%) and drugs (11, 31%) than that of NIH; the remainder were either MPTs (5, 14%), microbicides (3, 8%), contraceptives (2, 6%), or diagnostics (1, 3%).

## **DoD**

Like NIH, more than 80% (15, 83%) of the late-stage candidates supported by DoD were for neglected diseases, primarily HIV/AIDS (9, 50%), followed by malaria (4, 22%) and diarrheal diseases (2, 11%). The remaining candidates (3, 17%) were for Ebola and select VHFAs. DoD's focus among late-stage pipeline candidates was overwhelmingly on vaccines (15, 83%), with drugs (3, 17%) accounting for the rest.

## **CDC**

Eight of the 9 late-stage pipeline candidates supported by CDC were for neglected diseases, including 6 TB vaccines, 1 TB diagnostic and 1 HIV/AIDS drug. The only non-neglected disease candidate was an Ebola drug.

## **BARDA**

BARDA is a relatively new player in the field of global health R&D. Its mission is to develop medical countermeasures against diseases that threaten US citizens, and prior to the recent Ebola outbreak, it had primarily focused on pandemic influenza or anthrax. All of the 5 late-stage pipeline candidates supported by BARDA (3 vaccines and 2 drugs) were for Ebola and select VHFAs, and were supported by one-time, emergency investments.



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## Real-world impact: Advancing tools with the power to transform global health and uphold American health and security

From TB to Ebola, the examples below highlight just some of the tools currently being developed with US government support and showcase the ways in which they can transform the future of global health – and uphold American health and security.

### Bringing tuberculosis diagnosis into the 21st century

TB is one of the oldest infectious diseases known to mankind. Yet in 2015, it was still responsible for an estimated 1.1-1.4 million deaths globally – ranking alongside HIV/AIDS as the world's deadliest infectious disease.<sup>1,20</sup> But with fewer than 15,000 of these deaths occurring in high-income countries, developing new tools to combat TB has disappeared from the priorities of most Western countries.

The current TB vaccine is now nearly a century old and offers little or no protection against TB in adults. Current drug regimens are complex, often ineffective, and can require up to two years of treatment, fueling drug resistance and treatment failure. New and affordable diagnostics are also urgently needed: an estimated 4.3 million cases of TB went unreported in 2015, partly due to a lack of appropriate TB diagnostic tools designed for use in low-resource settings.<sup>20</sup> Of the 3.4 million TB cases that were reported, just 30% were tested for resistance to current first-line drugs.<sup>21</sup>

The recent development of a molecular diagnostic test (Xpert MTB/RIF) that can both diagnose infection and test for drug resistance was arguably the most significant advance in TB diagnosis in the last century. In practice, its impact was limited by the cost of the test cartridge and the GeneXpert instrument that runs the test, and its restriction to settings such as hospitals and reference labs, which have a regular electricity supply and trained laboratory staff.

The GeneXpert Omni, currently in the final stages of development, represents a further evolution of this innovative approach to TB diagnosis that could prove revolutionary. Small and simple to use, this new portable instrument aims to be used closer to patients and is expected to increase access to accurate, fast and potentially life-saving diagnosis of TB (as well as other diseases such as HIV, hepatitis C, and Ebola) in even the most remote areas of the world. GeneXpert Omni's development has been supported with funding from NIH, and it will undergo field evaluations in collaboration with the Foundation for Innovative New Diagnostics (FIND), a Geneva-based product development partnership.

Drug-resistant TB is a major and worsening problem. Without accurate, easy-to-use TB diagnostics that can test for drug resistance and are designed for use in the field in resource-limited setting, the goal of global control and eventual elimination of TB is likely to be a pipe-dream.

## Ending the scourge of HIV/AIDS

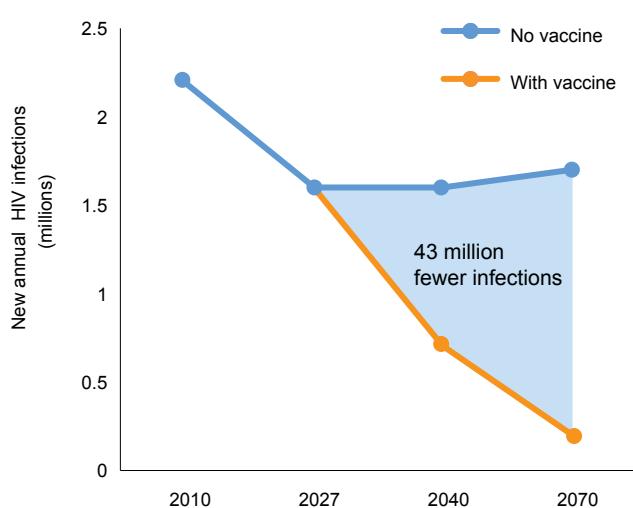
Since its discovery 35 years ago, 78 million people worldwide have contracted HIV, and 35 million have subsequently died from AIDS.<sup>22</sup> In 2015 alone, 2.1 million people contracted HIV, and 1.2 million died from AIDS-related causes – nearly all in low- and middle-income countries.<sup>22</sup>

For the majority of people living in high-income countries, the availability of highly-effective antiretroviral drugs has transformed HIV infection into a chronic manageable condition. But the sheer scale of the HIV epidemic in developing countries, coupled with the cost of providing treatment (and indeed diagnosis) to all who need it, means that the disease remains a death sentence for many across the developing world – and with only current tools, the epidemic is likely to worsen.

HVTN 702 is the first late-stage (phase IIb/III) clinical trial of an HIV vaccine candidate in seven years.<sup>23</sup> Co-funded by NIH and the Bill & Melinda Gates Foundation, sponsored by NIH's NIAID, and conducted by the NIH-funded HIV Vaccine Trials Network, the trial will evaluate a vaccine regimen consisting of modified versions of vaccine candidates previously trialed by the DoD's US Military HIV Research Program.

HIV is a complex virus, and has thus far proven to be an elusive target for a vaccine. But even partial success could save millions of lives and billions of dollars: a 70% effective vaccine\*\* is predicted to nearly halve the number of new HIV infections annually in its first decade of use.<sup>24</sup>

**Figure 13 ● Reduction in new annual HIV infections in low- and middle-income countries following HIV vaccine introduction**



Using WHO cost-effectiveness standards, even a 60% effective HIV vaccine would be highly cost-effective across a wide range of scenarios at a cost of \$20-30 per course, comparing favorably with other recently introduced vaccines.<sup>24</sup>

\*\* This figure assumes HIV vaccine rollout is accompanied with improved funding and implementation of treatment and prevention programs

## Providing protection against Ebola

The 2014 West African Ebola epidemic was the largest Ebola virus outbreak in history. Around 30,000 people became infected, resulting in more than 11,000 deaths – nearly ten times the number of deaths from all previous outbreaks combined.<sup>25</sup> At least another 11,000 individuals are thought to have died from HIV/AIDS, malaria, and TB during the same time period because of the epidemic's impact on access to healthcare services.<sup>26</sup>

One of the key reasons the Ebola outbreak had such a devastating impact was the complete lack of any approved drugs, vaccines, or field-appropriate diagnostics that could have helped contain the epidemic. Following a concerted global effort to rapidly advance Ebola vaccine R&D, at least 13 vaccine candidates entered clinical trials during the recent outbreak.<sup>27</sup> These technologies could be rapidly accelerated because research efforts were already underway. One of these candidates was rVSV-ZEBOV. It is currently the most advanced Ebola vaccine candidate in the R&D pipeline and the only one to have been evaluated in a phase III clinical trial (the final stage of human testing prior to registration) – in which it demonstrated 100% effectiveness.

The US government has contributed to the development of a number of Ebola vaccine candidates through NIH, DoD, and BARDA-supported research. In the case of rVSV-ZEBOV, this contribution came from DoD, who not only funded (and facilitated) late-stage clinical trials of the candidate during the recent epidemic, but had also funded the candidate since the early stages of its development (patented in 2003, the rVSV-ZEBOV candidate was shown to be 100% effective in preventing Ebola in monkeys as early as 2005). Without this prior R&D investment, it would have been impossible to get an Ebola vaccine candidate into phase III trials in the timeframe that was achieved.<sup>28,29</sup>

If a vaccine like rVSV-ZEBOV had been available at the start of the recent epidemic, it would have saved thousands of lives (not just from Ebola, but also from other diseases with heightened mortality during the epidemic, like malaria), as well as the billions of dollars the US government invested in emergency response to improve domestic preparedness and contain the outbreak in Africa.



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# Return on investment: Results for America from US government investment in global health R&D

By investing in global health R&D, the US government isn't only improving global health outcomes and saving lives around the world. When it invests in global health R&D, the US government is also investing in the United States: stimulating the domestic economy; protecting the health of US citizens; improving national security; and safeguarding the nation's international investments.

## Growing the US economy and creating jobs

While one might assume that a dollar invested in improving global health outcomes is a dollar that isn't being invested in the United States, the vast majority of US government funding for global health R&D is actually invested domestically, directly stimulating the US economy. In 2015, 89 cents of every US government dollar directed to global health R&D was invested within the United States. This means that in 2015 alone, US government investment in global health R&D injected \$1.5 billion into the American economy, helping provide jobs for American researchers, supporting US companies, leveraging additional private sector investment, and generating flow-through benefits as it cycles through the economy.

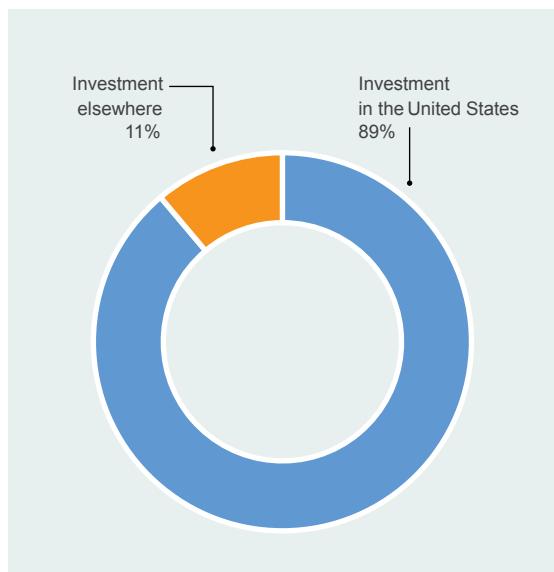
Looking at the longer-term picture, the US government has invested about \$12 billion into the domestic economy since 2007 as a result of its efforts to advance global health R&D. This investment is estimated to have created nearly 200,000 new jobs and generated an additional \$33 billion in economic output as it cycled through the economy.<sup>#‡</sup>

## Leveraging funding from the private sector and other donors

As well as directly stimulating the economy, US government funding for global health R&D also has a multiplier effect and leverages additional investment from the private sector and other donors. For example, every \$1 NIH spends on basic research is estimated to leverage an additional \$8.38 of industry investment over the following eight years.<sup>31</sup> Under this measure, by 2023 almost \$4 billion in additional industry R&D investment would have been generated from the US government's 2015 investment of less than half a billion dollars in basic research for global health.

More directly, in 2015 the US government provided \$192 million to US-based pharmaceutical companies, including both multinational pharmaceutical companies and small pharmaceutical and biotechnology companies, to undertake global health R&D activities. In return, these US-based pharmaceutical companies invested an additional \$294 million in 2015 alone, with the vast majority of this money spent domestically in the United States. In the field of global health – where companies have little to no chance of recouping their R&D costs via product sales – this degree of industry investment would not have happened without supporting investment from the US government.

**Figure 14 • Where does US government funding for global health R&D go?**



**Figure 15 • Leveraging private sector investment: the return on NIH investment in basic research**



<sup>#‡</sup> Based on previous analysis of the economic impact of NIH R&D funding.<sup>30</sup>

Through these and other examples, it is clear that US government investment in global health R&D has a stimulative effect, and that the impact of US government investment in global health R&D is magnified many times over by the additional investment that it attracts. USAID's Saving Lives at Birth Grand Challenge, which aims to identify and accelerate innovations to help women and children during childbirth, has attracted \$110 million in additional funding from other donors and the private sector from an initial US government investment of just \$20 million. BARDA's incentive mechanisms and external funding for product development have also been successful in bringing the private sector to global health R&D, including sustaining and increasing private sector support for Ebola, Zika, and antimicrobial resistance technologies.

## Cost savings from investing in R&D

Investing in R&D for global health brings long-term cost savings when compared to treatment costs for neglected diseases and health conditions, and the costs of emergency response to disease pandemics.

**It cost  
\$50 million**  
to develop MenAfriVac – a low-cost meningitis A vaccine

By 2020, it is predicted to have

**saved  
\$9 billion**

in meningitis A treatment costs

**A \$26 million investment**  
in polio vaccine R&D in the 1950s has

**saved  
\$180 billion**

in treatment costs in the United States alone

The US government spends more than

**\$6.5 billion every year**

combatting HIV/AIDS

Even a 70% effective vaccine would **halve HIV incidence globally** in just 10 years

The US government spent more than

**\$3 billion**

responding to the West African Ebola outbreak Prior to 2014, on average, it invested

**less than  
\$10 million a year**

on Ebola vaccine R&D ... and promising vaccine candidates were shelved because of lack of interest

By 2050, anti-microbial resistance could cause **10 million deaths** and reduce GDP by up to 3.5 percent per year, at a cumulative

**\$100 trillion cost**

to the global economy

Investing **\$2 billion per year**

in R&D could deliver the tools needed to tackle anti-microbial resistance

Large-scale disease pandemics could cost the global economy more than

**\$60 billion a year**

An R&D investment of **\$1 billion per year**

could deliver the tools needed to protect against these outbreaks

## Protecting American health

In addition to improving health in low-and middle-income countries, US government investment in global health R&D also serves to protect and improve the health of US citizens. The recent Ebola and Zika virus outbreaks are a reminder of the intrinsic link between global and domestic health. The Zika virus outbreak in particular showed just how easily a previously-neglected pathogen could transform into an outbreak that directly threatened the United States – and how little could be done to contain the outbreak without any tools to diagnose<sup>††</sup>, treat, or prevent infection.

Nor is it only unpredictable emerging infectious diseases like Zika that pose a threat to US citizens. Other less newsworthy, but similarly neglected, diseases also affect the health of the United States. For example, Chagas' disease is endemic in the tropical and sub-tropical regions of Latin America. But it has also increasingly found a foothold in the United States, with as many as 300,000 people in the United States thought to be infected.

Due to limited R&D investment, currently available tools to diagnose, treat, and prevent Chagas' disease are inadequate. Although 30% of people infected with Chagas' disease will go on to develop severe cardiac or neurological conditions, it is estimated that just 1% of the infected population in the United States is being treated for the disease. As a result, Chagas' costs the US economy an estimated \$900 million every year, including more than \$100 million in direct healthcare spending.<sup>32</sup> Yet in 2015, the US government invested just \$7 million in R&D to develop these missing tools.

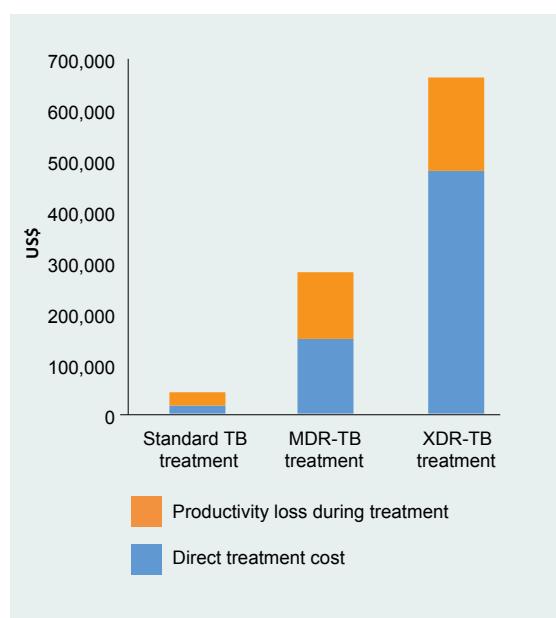
TB is another example. In comparison to Chagas' disease, the prevalence of TB in the United States is extremely low – in 2015, fewer than 10,000 TB cases were reported across the United States. Importantly however, cases of multi-drug resistant (MDR-TB) and extensively drug resistant (XDR-TB) are on the rise, and the lack of effective drugs means that treating MDR-TB and XDR-TB is extremely costly, both in direct treatment costs and in lost productivity.<sup>33</sup>

Treating MDR-TB and XDR-TB is with current tools is a long and expensive process—it takes at least six months of more than 14,000 pills, plus daily injections, to treat MDR-TB,<sup>34</sup> and treating XDR-TB is even more complex. The math is simple: treating MDR-TB in the United

**Figure 16 ● Chagas' disease: annual cost to the US economy vs. current US government R&D investment**



**Figure 17 ● Economic cost of treating one person for TB in the United States**



<sup>††</sup> A number of diagnostic tests have subsequently received FDA emergency use authorization.

States using existing drugs costs nearly ten times as much as treating drug-susceptible TB; and treating XDR-TB costs nearly 30 times as much. The cost of treating just 91 cases of MDR- and XDR-TB in the United States has been nearly \$14 million, a figure that increases to over \$25 million when including productivity losses.<sup>35</sup> The only solution to this problem is developing new, more effective TB drugs—and yet only two new drugs for TB have been approved in the last 50 years.

### Promoting US national security

Funding R&D to develop medical countermeasures against emerging and re-emerging infectious diseases helps protect the nation from pandemic outbreaks and bioterror attacks – critical to protecting US national security. Investments in global health R&D also build strong and effective global health programs, which help build stable societies in partner nations, generate goodwill for the United States, and prevent the deployment of the military.

Without effective countermeasures, safeguarding the health security of the United States in pandemic outbreaks like Ebola becomes immensely challenging, putting the lives – and livelihoods – of US citizens at risk. It is also prohibitively expensive. The US government spent nearly \$600 million to improve domestic preparedness for Ebola within the United States during the recent outbreak, and an additional \$2.4 billion on efforts to combat and contain the Ebola outbreak at its source.<sup>36</sup> If a point-of-care diagnostic and vaccine against Ebola had been available at the start, the 2014 West African Ebola outbreak would never have grown into the global health emergency it became. Not only would thousands of deaths have been prevented, but the US government would also have saved billions of dollars.



Bet\_Noire. iStock

In addition to safeguarding the health security of the United States, investments in global health R&D also help improve national security in other, less obvious ways. By developing game-changing new health technologies to replace ineffective or failing tools, or to fill the gap where these tools simply don't exist, global health R&D helps to improve the effectiveness of US global health programs. In turn, these programs – like PEPFAR – promote US national security by improving perceptions of the United States and reducing political instability and violence in the countries they target.<sup>37</sup>

### **Protecting US global development investments**

The United States currently invests approximately 0.25% of the federal budget in global health programs generally.<sup>38</sup> Even with this limited funding, over the past decade US global health program have made great gains. This makes it imperative to ensure limited funds are being invested strategically, and past investments are protected in order to achieve maximum impact. US investments in global health R&D are one way to ensure investments in global health and development endure, while at the same time upholding strong economic climates for US and foreign direct investment (FDI).

In addition to the US government, US private sector companies also make considerable FDI in low- and middle-income countries, including many of the same countries where the United States implements global health and aid programs. Liberia, for example, has US assistance programs in health, governance, and education, and also has received approximately \$16 billion in FDI since 2003, with the majority of this coming from the United States.<sup>39</sup>

A tangible example of how limited investment in R&D threatened both US government investments in global health and FDI of the private sector is the 2014 West African Ebola epidemic. Because there were no tools to prevent, diagnose, or treat Ebola, the epidemic could not be quickly contained. This had ripple effects in terms of health and economics. Because of reduced access to healthcare during the epidemic, it is estimated that an additional 10,600 lives were lost to HIV, TB, and malaria during the epidemic based on the assumption of an approximate 50% reduction in healthcare services in Guinea, Sierra Leone, and Liberia.<sup>40</sup> It is also estimated that there was a 30% decline in routine childhood vaccination, particularly for polio and TB.<sup>41</sup> All these findings reverse important health gains achieved with the support of US global health investments.

The economic impacts of the health crisis were also severe: reducing GDP by 2.1% in Guinea, 3.4% in Liberia, and 3.3% in Sierra Leone. According to World Bank estimates, a total of \$2.2 billion was lost from the GDP of these three countries in 2015 due to the Ebola outbreak.<sup>36</sup> This loss has a real and tangible impact on both domestic and FDI. In addition, it is also estimated that the Ebola outbreak will collectively cost Guinea, Liberia, and Sierra Leone nearly a billion dollars to rebuild their health system capacity to pre-outbreak levels, reversing the impact of past investments in health system strengthening.

US government investments in global health R&D deliver new health technologies that could prevent the devastating health and economic losses in low- and middle-income countries caused by neglected and emerging infectious diseases – and thereby protect US government and private sector investments in these countries.

# Conclusion

32

Conclusion



The US government's role in global health R&D is vital, and the benefits are clear. Not only does US government investment play an essential and catalytic role in developing new drugs, vaccines, diagnostics, and other urgently-needed tools for neglected diseases and health conditions, but it also delivers tangible economic and security returns for Americans. This is a win-win from a humanitarian and strategic perspective – these investments save and improve lives in vulnerable populations around the world, while at the same time advancing American leadership in science and innovation, creating jobs and economic growth at home, supporting public-private partnerships, and protecting American and health security.

At present, however, the United States' funding commitment to global health R&D doesn't reflect these documented returns. Despite both global health and economic imperatives – in addition to the increasing frequency of global pandemics, growing antimicrobial resistance, and heightened ability for diseases to cross borders – core US government investment in global health R&D continues to decline. In 2015, funding levels for neglected disease R&D reached their lowest point since tracking began in 2007. This must change.

As we search for the most strategic and cost-effective uses of taxpayer resources, global health R&D – which saves lives at home and around the world, leverages private sector capital, and advances US interests – is one of the best buys the United States can make as a nation. By strengthening and sustaining the United States' commitment and financing for global health R&D, Congress and Executive Branch officials have the opportunity to bring us closer to a healthier, safer, more prosperous world.



# Methodology

This report analyses the nature and impact of US government support for global health R&D. There is no single definition of what constitutes ‘global health’ (or even ‘R&D’); the scope of both these terms can vary – entirely justifiably – depending on the context in which they are used.

In the context of this report, global health R&D is defined as basic and product-focused research to develop new health technologies for diseases or reproductive health issues that exclusively or disproportionately affect developing countries, and thus for which no commercial market exists to drive R&D. This is further broken down into three specific categories: neglected diseases; Ebola and select VHFs; and the reproductive health needs of developing countries.

## Funding data

All funding data for this report comes from the G-FINDER survey, conducted annually by Policy Cures Research. The G-FINDER survey has tracked global investment in R&D for neglected diseases since 2007, and for Ebola and select VHFs since 2014. It covers basic research, drugs, vaccines, diagnostics, microbicides, and vector control products, as well as platform technologies (adjuvants, delivery technologies, and diagnostic platforms).

Data on investment in R&D for the reproductive health needs of developing countries for 2013 is from a one-off G-FINDER reproductive health survey conducted in 2014. Investment data for 2014 and 2015 was collected specifically for the purpose of this report from the relevant US government agencies, either directly (in the case of CDC and USAID) or from publicly available databases (for NIH).

Additional in-depth information on the scope and methodology of the G-FINDER reports is available at: <http://www.policycuresresearch.org/g-finder>

## Registered products and pipeline candidates

Data on registered products and pipeline candidates was collected by Policy Cures Research, building on previously-developed comprehensive landscapes of these two categories.

The pipeline information presented here builds on the most recently available comprehensive landscape of the R&D product pipeline for neglected diseases, prepared by Policy Cures<sup>††</sup> in 2015 as an update to the pipeline data used in the 2012 Policy Cures/Global Health Technologies (GHTC) report ‘Saving lives and creating impact: Why investing in global health R&D works’. That work in turn was based on the BIO Ventures for Global Health (BVGH) Global Health Primer. The registered product information presented here builds on the most recently available comprehensive landscape of registered products for global health, also prepared by Policy Cures for the 2012 ‘Saving Lives’ report.

Policy Cures Research undertook additional research to expand the scope of the 2015 pipeline and 2012 registered product lists to match that of the current report, and bring them up to date as at end-2016. This included reviewing and cross-referencing all major sources of available data on registered products and the R&D pipeline for global health. Sources included: the G-FINDER R&D funding database; WHO’s ‘Rainbow Tables’; background documents prepared for WHO’s Product Development for Vaccines Advisory Committee; UNITAID Landscape and Technical Reports; disease-specific pipeline updates prepared by BVGH and the Treatment Action Group; publicly available company and product development partnership R&D portfolios; journal publications; clinical trial registration portals; and university, government, and non-profit organization websites. Both the registered product and pipeline candidate lists were sent to each of the key US government agencies for verification, with CDC, DoD, and USAID all providing input.

<sup>††</sup> In 2016, Policy Cures separated into two independent organizations, with the research and policy team moving across to a new non-profit organization, Policy Cures Research.

# Registered products table

Global health area	Disease or topic	Product type	Product	NIH	DoD	USAID	CDC	FDA
Neglected diseases	Chagas' disease	Diagnostic	Chagas' disease assays					
Neglected diseases	Chagas' disease	Diagnostic	Chagas' disease RDTs					
Neglected diseases	Chagas' disease	Drug	Pediatric benznidazole					
Neglected diseases	Cholera	Diagnostic	Cholera SMART™ / Dipsticks for rapid diagnosis					
Neglected diseases	Cholera	Vaccine	Oral cholera vaccine (Shanchol)					
Neglected diseases	Dengue	Diagnostic	Dengue ELISAs (MAC-ELISA)		R&D			
Neglected diseases	Dengue	Diagnostic	Dengue RDTs					
Neglected diseases	Giardia	Diagnostic	Giardia/Cryptosporidium Quik Chek					
Neglected diseases	HIV/AIDS	Diagnostic	Early infant detection RDTs					
Neglected diseases	HIV/AIDS	Diagnostic	HIV1/2 LFI RDTs					
Neglected diseases	HIV/AIDS	Diagnostic	HIV1/2 p24 ELISA kits					
Neglected diseases	HIV/AIDS	Diagnostic	NAT and non-NAT based viral load technologies		Expertise			
Neglected diseases	HIV/AIDS	Diagnostic	POC CD4 + T-cell counting technologies					
Neglected diseases	Leishmaniasis	Diagnostic	Leishmaniasis RDTs	Funding	Expertise			
Neglected diseases	Leishmaniasis	Drug	Miltefosine	Funding		Funding		
Neglected diseases	Leishmaniasis	Drug	Paromomycin I/M		Expertise Infrastructure			
Neglected diseases	Lymphatic filariasis	Diagnostic	Filariasis RDTs					
Neglected diseases	Malaria	Diagnostic	AtomoRapid™					
Neglected diseases	Malaria	Diagnostic	CareStart™ G6PD RDT and G6PD Biosensor					
Neglected diseases	Malaria	Diagnostic	illumigene®			Funding	Expertise	
Neglected diseases	Malaria	Diagnostic	LoopAmp					
Neglected diseases	Malaria	Diagnostic	Malaria RDTs		Funding			
Neglected diseases	Malaria	Diagnostic	TrueLab™ microPCR platform					
Neglected diseases	Malaria	Diagnostic	Urine Malaria Test™					
Neglected diseases	Malaria	Drug	Artemotil			Funding		
Neglected diseases	Malaria	Drug	Artesunate injection	Funding	R&D	Funding		
Neglected diseases	Malaria	Drug	ASAQ Winthrop®					
Neglected diseases	Malaria	Drug	ASMQ	Funding				

Global health area	Disease or topic	Product type	Product	NIH	DoD	USAID	CDC	FDA
Neglected diseases	Malaria	Drug	Chlorproguanil/dapsone			Funding		
Neglected diseases	Malaria	Drug	Coartem®					
Neglected diseases	Malaria	Drug	Coartem® Dispersible	Funding		Funding		
Neglected diseases	Malaria	Drug	Eurartesim®	Funding		Funding		
Neglected diseases	Malaria	Drug	Pyramax®	Funding	Expertise	Funding		
Neglected diseases	Malaria	Drug	Pyramax® granules	Funding		Funding		
Neglected diseases	Malaria	Drug	SPAQ-CO (sulfadoxine-pyrimethamine/amodiaquine)					
Neglected diseases	Malaria	Drug	Synriam (arterolane maleate/piperazine phosphate)					
Neglected diseases	Malaria	Vaccine	RTSS/AS01E	Funding	Funding R&D Expertise	R&D		
Neglected diseases	Meningitis	Diagnostic	Dipstick RDT					
Neglected diseases	Meningitis	Vaccine	MenAfrivac™	IP & tech transfer		Funding Expertise	Funding R&D	IP & tech transfer
Neglected diseases	Onchocerciasis	Diagnostic	Ov-16 rapid immunochromatographic card test					
Neglected diseases	Pneumonia	Vaccine	Prevnar 13® (PCV13)	Funding				
Neglected diseases	Pneumonia	Vaccine	Synflorix®	Funding				
Neglected diseases	Rotavirus	Vaccine	NIH HRV-BRV (UK) reassortant vaccine	Funding IP& tech transfer				
Neglected diseases	Rotavirus	Vaccine	Rotarix®					
Neglected diseases	Rotavirus	Vaccine	RotaTeq®					
Neglected diseases	Rotavirus	Vaccine	ROTAVAC®	Funding				
Neglected diseases	Schistosomiasis	Diagnostic	SmCTF-RDT					
Neglected diseases	Sleeping sickness	Diagnostic	SD Bioline HAT					
Neglected diseases	Trachoma	Diagnostic	Dipstick immunoassay rapid diagnostic test					
Neglected diseases	Tuberculosis	Diagnostic	Capilia TB	Funding				
Neglected diseases	Tuberculosis	Diagnostic	EasyNAT™					
Neglected diseases	Tuberculosis	Diagnostic	FluroType® MTB					
Neglected diseases	Tuberculosis	Diagnostic	Genedrive®					
Neglected diseases	Tuberculosis	Diagnostic	GenoType® MTBDR and MTBDRplus	Funding				
Neglected diseases	Tuberculosis	Diagnostic	INNO-LiPA Rif.TB					
Neglected diseases	Tuberculosis	Diagnostic	LED fluorescence microscopy	Funding				
Neglected diseases	Tuberculosis	Diagnostic	Liquid culture	Funding				

Global health area	Disease or topic	Product type	Product	NIH	DoD	USAID	CDC	FDA
Neglected diseases	Tuberculosis	Diagnostic	Loopamp - Loop-mediated isothermal amplification (LAMP) of DNA (TB)	Funding				
Neglected diseases	Tuberculosis	Diagnostic	MeltPro TB/INH					
Neglected diseases	Tuberculosis	Diagnostic	NAAT non-automated or case detection screening					
Neglected diseases	Tuberculosis	Diagnostic	Phage-based tests					
Neglected diseases	Tuberculosis	Diagnostic	RealTime MTB/TB MDx m2000					
Neglected diseases	Tuberculosis	Diagnostic	TrueLab™					
Neglected diseases	Tuberculosis	Diagnostic	Xpert® MTB/Rif	Funding Expertise IP & tech transfer	IP & tech transfer		Expertise Infrastructure	
Neglected diseases	Tuberculosis	Drug	Bedaquiline	Funding		Funding		
Neglected diseases	Tuberculosis	Drug	Delamanid			Funding		
Neglected diseases	Tuberculosis	Drug	HR FDC pediatric formulation			Funding		
Neglected diseases	Tuberculosis	Drug	HRZ FDC pediatric formulation			Funding		
Reproductive health	Family planning	Contraceptives	Depo-SubQ Provera 104™ in the Unject™ Injection System			Funding		
Reproductive health	Family planning	Contraceptives	FC2 Female Condom					
Reproductive health	Family planning	Contraceptives	Liletta LNG IUS			Funding		
Reproductive health	Family planning	Contraceptives	NES + EE Vaginal Ring	Funding Infrastructure		Funding Expertise		
Reproductive health	Family planning	Contraceptives	Progering			Funding		
Reproductive health	Family planning	Contraceptives	Sayana Press			Funding		
Reproductive health	Family planning	Contraceptives	SILCS diaphragm (Caya)			Funding		
Reproductive health	Family planning	Contraceptives	Sino-implant 2					
Reproductive health	Family planning	Contraceptives	Woman's Condom			Funding		
Ebola and select VHF	Ebola	Diagnostic	Assay (automated real time RT-PCR)		Funding Expertise			
Ebola and select VHF	Ebola	Diagnostic	Assay multiple strain (non-automated real time RT-PCR)					
Ebola and select VHF	Ebola	Diagnostic	Assay single strain (non-automated real time RT-PCR)		Funding R&D		Funding R&D	
Ebola and select VHF	Ebola	Diagnostic	LFI RDT (multiple strain)		Funding R&D		Funding R&D	
Ebola and select VHF	Ebola	Diagnostic	LFI RDT (single strain)		Funding R&D		Funding R&D	

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## **Global Health Technologies Coalition**

GHTC is a coalition of more than 25 nonprofit organizations advancing policies to accelerate the creation of new drugs, vaccines, diagnostics, and other health tools that bring healthy lives within reach for all people. GHTC works to save and improve lives by advancing solutions to accelerate the development of new health technologies to address neglected global diseases and health conditions.

## **Policy Cures Research**

Policy Cures Research is a non-profit, global health think tank, based in Sydney, Australia. It aims to provide research, information, decision-making tools and strategic analysis to help governments, funders, researchers and civil society organizations with the information they need to make optimal R&D policy and funding decisions for global health.

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