

# CLOSING THE GAP IN TUBERCULOSIS RESEARCH AND DEVELOPMENT FUNDING: ACTIONS FOR U.S. GOVERNMENT EXECUTIVE AGENCIES

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## RECOMMENDED ACTIONS

- Increase U.S. government investment in tuberculosis (TB) research and development (R&D) from \$313.5 million to at least \$444.5 million in FY2020
- Raise the priority of spending on TB R&D because it aligns with multiple other U.S. government research priorities, including HIV/AIDS, antimicrobial resistance (AMR), and global health security
- Ensure coordination of TB research strategies and activities across agencies, including agencies with low current investment in TB R&D

## THE GLOBAL NEED FOR TB R&D

TB remains the number one global infectious disease killer, killing 1.6 million people in 2017, including 300,000 with both TB and HIV/AIDS.<sup>1</sup> Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are threats to U.S. public health, according to the U.S. Centers for Disease Control and Prevention (CDC).<sup>2</sup> In 2017, 558,000 people globally required second-line treatment for MDR-TB, and only approximately 10% were successfully cured, resulting in ongoing risk for outbreaks of drug-resistant TB.

With rising awareness of these dire figures, the global fight against TB is gathering momentum, and U.S. leadership in R&D can bolster the fight. The political declaration adopted by member states at the United Nations High-Level Meeting on TB in September 2018 demonstrates an unprecedented level of global political will to end the global TB epidemic. There is also new scientific opportunity, demonstrated by promising interim results from a phase II vaccine trial and phase II and III new drug regimen trials for the most drug-resistant forms of TB. Continued innovation is needed to develop medical products that rapidly diagnose TB infection



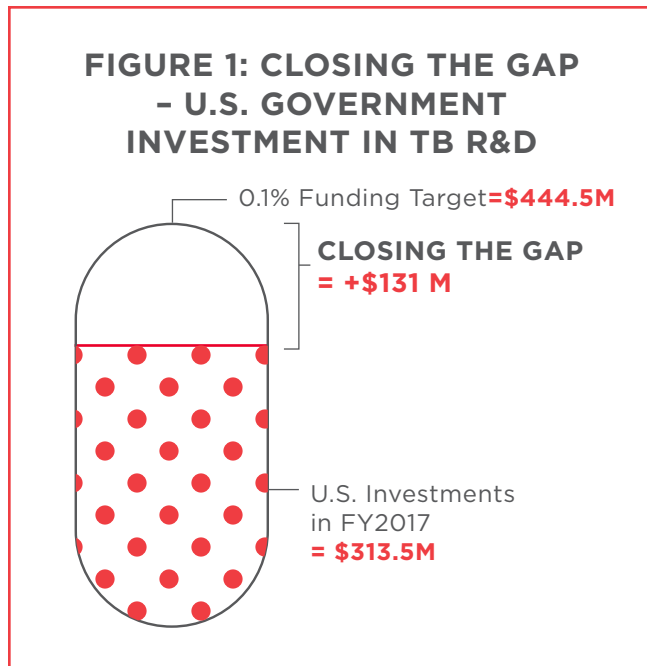
## GLOBAL TB FACTS, 2017

- 10 million people fell ill with TB, including 1 million children
- 1.6 million people with TB died, including 300,000 people with both TB and HIV/AIDS
- 4 million people with TB were not diagnosed, treated, or monitored
- Over half a million people developed drug-resistant TB, and only 10% were cured

and identify resistance to multiple drugs, treat patients with drug-susceptible and drug-resistant TB in weeks rather than months, and prevent TB infection, activation of infection to symptomatic disease, and onward transmission. Now is the time to seize on the momentum and finally turn the corner on this deadly disease.

## U.S. GOVERNMENT COMMITMENT TO COMBATING TB AND OTHER GLOBAL INFECTIOUS DISEASES

By endorsing the political declaration of the UN High-Level Meeting on TB, U.S. government leaders committed to mobilizing “sufficient and sustainable financing with the aim of increasing overall global investments to US\$2 billion, in order to close the estimated US\$1.3 billion gap in funding annually for tuberculosis research, ensuring that all countries contribute appropriately to research and development.”<sup>3</sup> Treatment Action Group has developed a proposal, endorsed by other TB stakeholders, that urges all governments to contribute to TB R&D based on each country’s “fair share” of demonstrated research capacity, as measured by their annual spending on all forms of R&D.<sup>4</sup> If all countries devote at least 0.1% of their annual R&D spending to TB research, they will close the funding gap and position the world to end this deadly epidemic. For the United States, this means increasing annual investment in TB research from \$313.5 million to at least \$444.5 million, a difference of \$131 million (see Figure 1).<sup>5</sup> By committing to greater investment in TB R&D, the United States will demonstrate its global leadership in TB, encourage other governments to contribute their fair share to TB research investments, catalyze investment amplification, and strengthen U.S. priorities in other infectious diseases. U.S. leaders took a significant first step by endorsing the political declaration, and it’s now up to the legislative and executive branches to implement and fully fund the commitment.



Importantly, investing additional funding in TB research will also contribute to other U.S. research priorities in HIV/AIDS, AMR, and global health security. Where agencies have the discretion to do so, they should explore whether appropriations funded under these three strategic research priorities could be applied to TB research in order to fulfill both mandates. First, TB is a leading killer of people living with HIV. To fully benefit from U.S. investments in the global fight against HIV/AIDS through the President’s Emergency Plan for AIDS Relief (PEPFAR), it’s critical that people with both HIV and TB be promptly diagnosed and treated for both infections and that research be conducted to ensure that TB medicines are effective in individuals who are also taking antiretroviral HIV medicines. Second, drug-resistant TB is the leading cause of deaths from AMR, which was declared to be a significant threat to global public health by the United States and the World Health Organization (WHO) in 2015.<sup>6,7</sup> The U.S.

fight against AMR must include efforts against TB, as outlined in the 2015 U.S. National Action Plan to Combat MDR-TB.<sup>8</sup> Finally, the 2018 National Biodefense Strategy validates efforts to improve U.S. preparedness and response efforts for infectious disease outbreaks, including potential outbreaks of MDR-/XDR-TB.<sup>9</sup> Similarly, the Global Health Security Agenda (GHS), an ongoing U.S. priority and global collaborative to build global capacity to withstand infectious disease outbreaks, recognizes AMR as one of its priorities.<sup>10</sup> Combating TB is central to addressing HIV/AIDS, AMR, and global health security, and any strategy to upend the rising threat of TB must include funding science to create the next generation of public health tools.

## U.S. GOVERNMENT LEADERSHIP IN TB R&D

Although global funding for TB R&D reached a new high in 2017, it still fell far short of the \$2 billion in annual R&D spending required to end the global TB epidemic by 2030.<sup>11</sup> The U.S. government through its agencies has long been a global leader in TB R&D investments. In 2017, the U.S. government invested \$313.5 million of the total global investment of \$772 million in TB R&D.<sup>12</sup> Current U.S. government spending on TB R&D is distributed among several agencies that play critical roles along the R&D continuum.

The majority of FY2017 TB research funding (66%) was invested by the National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health (NIH), supporting a broad spectrum of research from basic science to operational research. Other NIH institutes and centers invested 13% of U.S. government TB research investments within their areas of expertise. For example, the Eunice Kennedy Shriver National Institute of Child Health and Human Development partnered with NIAID on pediatric TB research. Funding from the USAID (11%) and the CDC (6%) supported the conduct of clinical trials, operational research, and implementation research – especially in TB-endemic areas. The U.S. Department of Defense (DoD), through its Medical Research and Development Program (MRDP), funded research (2%) for drugs, vaccines, and diagnostics that would benefit troops and families living in TB-endemic areas.

## POTENTIAL AGENCY R&D FUNDING TARGETS

Each of the U.S. government agencies involved in TB research plays an important and unique role across the research continuum and should aim to contribute to its portion of the 0.1% target funding figure, as outlined in Table 1. The \$131 million in additional funding could be applied to priority areas of research including basic sciences, diagnostics, treatments, vaccines, operational research, research infrastructure, and pediatric research.

TABLE 1: TB R&D TARGETS BY AGENCY				
Agency	FY2017 (\$M)	0.1% Target (\$M)	Difference (\$M)	Higher Target (\$M)
<b>NIH/NIAID</b>	206.6	293.4	86.8	440
<b>NIH/Other IC</b>	41.5	57.8	16.3	87
<b>USAID</b>	34	48.9	14.9	73
<b>CDC</b>	18.3	26.7	8.4	40
<b>DoD MRDP</b>	6.1	8.9	2.8	13
<b>NSF</b>	3.4	4.4	1.0	6.7
<b>PEPFAR</b>	1.6	2.2	0.6	3.3
<b>VA</b>	1.2	1.8	0.6	2.7
<b>FDA</b>	1	1.3	0.3	2
<b>Total</b>	<b>\$313.5</b>	<b>\$444.5</b>	<b>+\$131</b>	<b>\$667</b>

Although NIAID funds research across priorities, it is a clear leader in funding basic science that is not funded by the private sector. NIAID released an ambitious five-year “Strategic Plan for Tuberculosis Research” in September 2018 and expressed its intention to help the NIH increase funding to reach \$440 million annually for TB research for the whole NIH. This funding could be directed into the five pillars of the strategic plan, including improving fundamental TB knowledge; accelerating research on TB diagnosis, prevention, and treatment; and developing scientific tools that further enable TB research.

USAID funding increases under both the Senate and House bills and could direct some of the increased funding to support the conduct of clinical trials, operational research, and implementation research, particularly in TB-endemic countries. The CDC should consider augmenting funding for the Tuberculosis Trials Consortium, which will soon be funded for a new term, providing an opportunity for the CDC to implement new strategic directions for the research networks. Both the CDC and USAID should continue to leverage PEPFAR funding for research on HIV/TB co-infection (including operational research and rollout of new interventions) and global health security funding for research on MDR-/XDR-TB.

Other agencies currently contribute minimally to TB research but are in a position to expand TB research activities. The Biomedical Advanced Research and Development Authority (BARDA) supports the conduct of advanced clinical trials and catalyzes the development of medical products against a broad array of public health threats, including AMR. BARDA could direct additional funding to TB R&D, as drug-resistant TB has been prioritized by the U.S. government as an AMR threat.

All agencies should consider expanding collaborations with TB-endemic countries, including the BRICS countries (Brazil, Russia, India, China, and South Africa). Collaborations with BRICS researchers would promote the expansion of research funding by these countries and help to close the TB R&D funding gap.

Lastly, the intention of NIAID to raise its TB research funding to \$440 million annually provides an aspirational but achievable target for other U.S. government agencies over the next few years (Table 1, higher targets). If other agencies follow the ambitious lead of NIAID and raise their TB research funding by a similar proportion, U.S. government investment in TB R&D would surpass the 0.1% funding target by about 50%. Reaching this level of funding would put the United States in good company with three other countries that have surpassed their 0.1% targets: South Africa (by 83%), the Philippines (by 61%), and New Zealand (by 14%).<sup>13</sup> By committing to increased funding for TB R&D, the U.S. government can demonstrate global leadership in closing the TB R&D gap, encourage other governments to contribute their fair share toward TB research, and strengthen U.S. priorities in HIV/AIDS, AMR, and global health security.

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