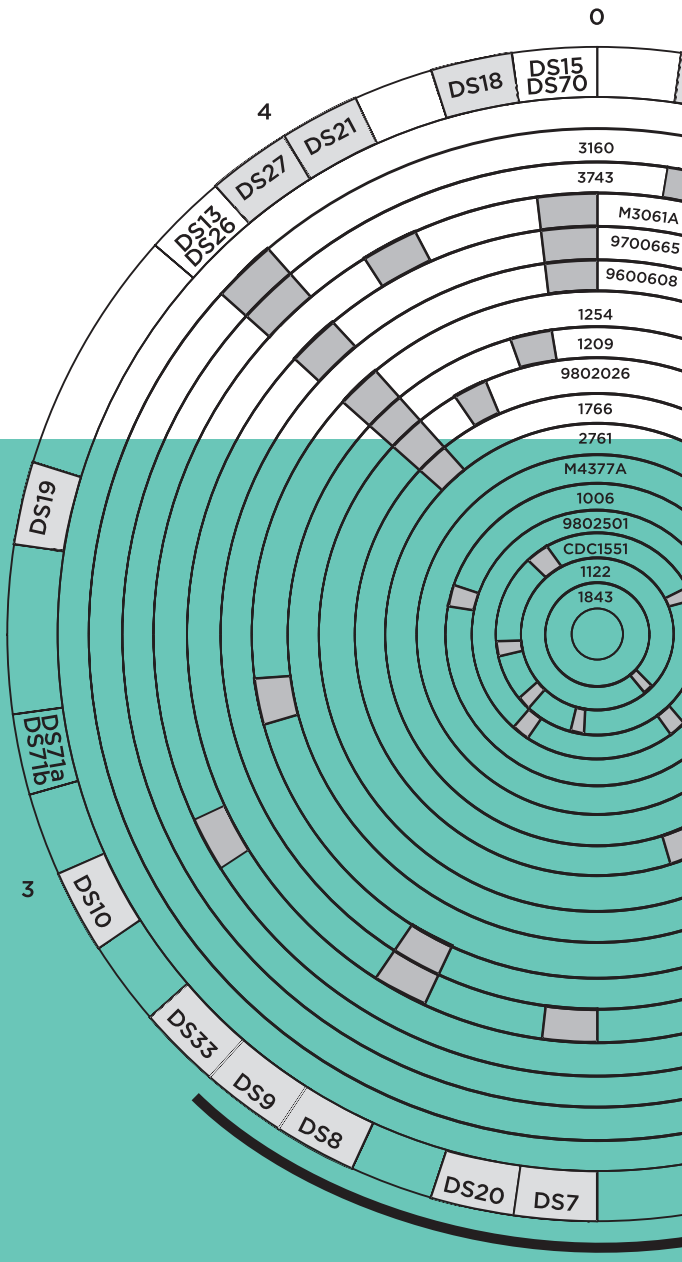
TAG
Treatment Action Group

Stop TB Partnership

TUBERCULOSIS RESEARCH
AND DEVELOPMENT:

2012 Report on Tuberculosis Research Funding Trends, 2005-2011



NOVEMBER 2012

TREATMENT ACTION GROUP

BY ELEONORA JIMÉNEZ-LEVI

ACKNOWLEDGMENTS

TAG is grateful to all the participating TB R&D donors who made this report possible. We would also like to offer special thanks to the Stop TB Partnership and the Bill & Melinda Gates Foundation for supporting TAG's TB/HIV Project.

ABOUT TAG

Treatment Action Group is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS.

TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end AIDS.

TB/HIV PROJECT

Treatment Action Group's TB/HIV Project works to improve research, programs, and policy for people with TB and HIV.

Eleonora Jiménez-Levi is a senior researcher leading Treatment Action Group's resource-tracking efforts on original source funding for tuberculosis and HIV research. She holds a bachelor's degree in political science from Barnard College and a master of science from the Harvard School of Public Health. From 2004 to 2007, Eleonora managed the TB/HIV Monitoring and Advocacy Project at the Open Society Foundations, where she partnered with TAG to help communities affected by TB and HIV advocate for better TB/HIV care and services.

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BY ELEONORA JIMÉNEZ-LEVI

EDITED BY MARK HARRINGTON

THIS REPORT IS DEDICATED TO:

Vedavalli Rangaswamy

(1956-2012)

This year's TB R&D report is dedicated to Vedavalli and Radha Rangaswamy, and all those affected by tuberculosis around the world, who like this family, struggled to find early and accurate diagnosis, and treatment for TB.

Radha, fought for her mother, Vedavalli, to be diagnosed and treated for TB for two years before losing the battle this past October. Radha is a daughter who gave up her studies, took a job to support her mother's treatment, walked out of the family home when the stigma was unbearable, searched for help and reached out to anyone who would listen, has nothing left now but anger and sadness at this tragic and unnecessary loss.

TB is curable; diagnosis and treatment is free, and yet millions die every year. What are we missing? Do we have any answers for Radha? We need to recognize that we have failed Vedavalli and many more like her. We must learn from our mistakes and settle for nothing less than zero TB deaths, zero new TB infections, and zero suffering from TB. The deaths must stop now. Today we must stop TB.

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Executive Summary

Over the last seven years, cumulative investments in tuberculosis (TB) research and development (R&D) totaled $3.6 billion.[I] Yet, each year annual spending toward research for new and improved TB tools falls far from the $2 billion global target defined by the Stop TB Partnership's *Global Plan to Stop TB 2011–2015* (Global Plan).

The *2012 Report on Tuberculosis Research Funding Trends, 2005–2011*, found that out of 132 surveyed institutions, 81 reported investing $649.6 million in TB R&D funding, a paltry 3% increase from 2010's $630.4 million investment.

Of the $649.6 million in TB R&D funding reported for 2011, the top ten donors invested $506.7 million, or 78% of the global total. The largest investments—over $100 million each—originated from the National Institute of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) and the Bill & Melinda Gates Foundation (BMGF), whose combined investments represent 42% of the global total. Two private sector companies in the top ten list invested a total of $96 million in TB drug development, as two new drugs for the treatment of multidrug-resistant TB (MDR-TB) await regulatory review by the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA).

Between 2010 and 2011, the private sector saw the greatest funding increase, growing 13% from $124.2 million to $140.2 million, in support of drug development and diagnostics research. The public sector continued to be the primary funding sector of TB R&D, making only a small increase in investment in 2011, from $376.2 million to $385.3 million. Philanthropic funding was flat at $123.9 million, and multilateral funding declined considerably, from $6 million to $246,064—a figure that was significantly underreported.

In 2011, NIAID remained the top investor in TB R&D, disbursing $157.6 million. Despite the expiration of the American Recovery and Reinvestment Act (ARRA),[II] and the resulting loss of its stimulus funds, investments in TB R&D from NIAID remained stable. The same, however, cannot be said for the National Heart, Lung, and Blood Institute (NHLBI) and the other NIH Institutes and Centers (other NIH ICs), whose investments declined 20% and 23%, respectively, in 2011. Overall, the NIH spent $209 million in global TB R&D—7% less than in 2010.

Nine product development partnerships (PDPs) and research consortia disbursed $110.2 million in support of TB R&D, a 126% increase over 2005 levels, but a 7% decline from 2010.

I. All dollar figures cited in this report are calculated in US dollars.

II. On February 17, 2009, President Obama signed the ARRA to help jump-start a deteriorating U.S. economy. The proposed $787 billion stimulus package targeted key economic sectors including science, engineering, research, and infrastructure. Between 2009 and 2010, the ARRA supported $62.1 million in TB research awards at the NIH.

FIGURE 1

Annual Global Plan Research Funding Targets vs. 2011 Investments

With the exception of basic science[III] and infrastructure/unspecified, whose investments declined 7% and 46%, respectively, funding for the remaining four research areas improved in 2011. Operational research saw the greatest growth at 38%, surpassing the Global Plan's annual funding target of $80 million—the only research category to ever meet and exceed its annual goal. Vaccine development grew 22%, from $78.4 million to $95.4 million, after experiencing a steep decline in 2010. Investments in drug development continued to rise, from $230.5 million to $250 million (a 9% increase). And for a third consecutive year, diagnostics funding increased 14%, from $48.4 million to $55 million.

Figure 1 outlines 2011 investment levels against the funding targets set by the Global Plan. The figure illustrates a somber reality about the world's progress toward eliminating TB as a public health threat. Overall, the annual funding gap is a stark $1.35 billion. New diagnostics, vaccines, and basic science all have enormous spending gaps of approximately $290 million, but TB drug development, which historically receives the largest share of resources, has a $490 million funding gap. In 2011, operational research was the only research category to achieve and surpass its funding target of $80 million. Though praiseworthy, the operational research target itself is probably too low.

III. Referred to as "fundamental science" by the Stop TB Partnership and the World Health Organization.

TABLE 1.1

2011 TB R&D Funders by Rank

2011 Rank	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
1	US National Institute of Allergy and Infectious Diseases (US NIAID, NIH)	P	$157,562,079
2	Bill & Melinda Gates Foundation (BMGF)	F	$112,388,435
3	Otsuka Pharmaceutical	C	$65,124,407
4	US Other NIH Institutes & Centers (US Other NIH ICs)	P	$40,214,119
5	Company X	C	$31,160,854
6	European Commission (EC)	P	$28,287,638
7	UK Department for International Development (DFID)	P-D	$20,745,063
8	United States Agency for International Development (USAID)	P-D	$20,145,652
9	UK Medical Research Council (MRC)	P	$16,850,528
10	US Centers for Disease Control (CDC)	P	$14,174,564
11	AstraZeneca India Private Limited	C	$13,235,259
12	US National Health, Lung, & Blood Institute (US NHLBI, NIH)	P	$10,910,625
13	India (reported)	P	$9,537,034
14	Dutch Ministry of Foreign Affairs-Directorate General of Development Cooperation (DGIS)	P-D	$7,748,586
15	Wellcome Trust	F	$7,266,964
16	Pfizer	C	$6,538,261
17	Canadian Institute for Health Research (CIHR)	P	$6,362,302
18	Emergent Biosolutions	C	$4,568,160
19	German Federal Ministry of Education (BMBF)	P	$4,561,179
20	Company W	C	$4,529,539
21	Sequella	C	$4,500,374
22	Institut Pasteur	P	$4,263,998
23	Sweden (reported)	P	$4,234,028
24	South Africa Department of Science and Technology (SA DST)	P	$4,000,000
25	Australian National Health and Medical Research Council (Australia NHMRC)	P	$3,827,590
26	Company Y	C	$3,800,000
27	US President's Emergency Plan for AIDS Relief (US PEPFAR)	P	$3,478,567
28	UK Health Protection Agency/National Institute for Health Research (UK HPA/ NIHR)	P	$3,409,340
29	Korea (reported)	P	$3,240,538
30	Japan (reported)	P	$3,145,007
31	Company Z	C	$3,129,753
32	Switzerland (reported)	P	$2,913,245
33	Max Planck Institute for Infection Biology (MPIIB)	P	$2,750,000
34	Agence Nationale de Recherche sur la SIDA (ANRS)	P	$2,101,728
35	Bloomberg Philanthropies	F	$2,000,000

P= Public Sector R&D Agency; C = Corporation/Private Sector; M= Multilateral; F=Foundation/Philanthropy;
P-D= Public Sector Development Agency

TABLE 1.2

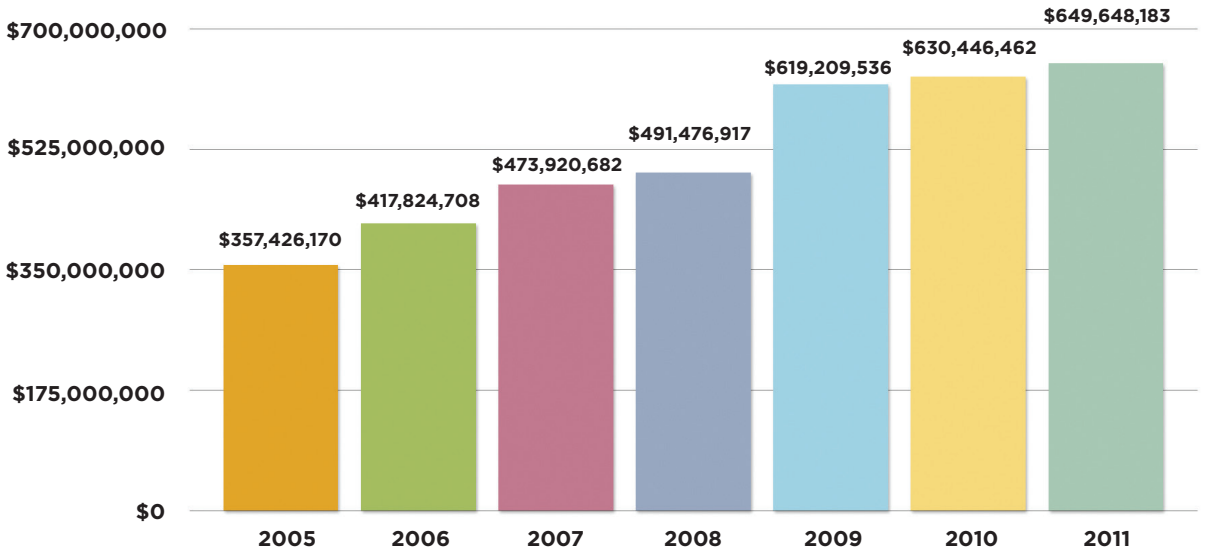
2011 TB R&D Funders by Rank (continued)

2011 Rank	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
36	Norway (reported)	P	$1,958,835
37	Canadian International Development Agency (CIDA)	P-D	$1,853,250
39	UBS Optimus Foundation	F	$1,615,100
40	Eli Lilly and Company	C	$1,500,000
41	Sandoz	C	$1,500,000
42	US Food and Drug Administration (US FDA)	P	$1,452,570
43	Irish Aid - Ireland Development Corporation	P-D	$1,448,690
44	German Research Foundation (DFG)	P	$1,434,203
49	Carlos III Health Institute	P	$783,279
50	Damien Foundation	F	$441,850
51	Danish National Advanced Technology Foundation	P	$392,799
52	Agence Nationale de Recherche (ANR)	P	$357,778
53	Brazilian National TB Program	P	$291,258
54	Australian Research Council	P	$246,514
56	Statens Serum Institut (SSI)	P	$165,062
57	Danish Council for Independent Research | Medical Sciences	P	$140,749
58	Netherlands Organization for Health Research and Development (ZonMw)	P	$139,536
59	GSK Biologicals	C	$129,493
60	World Health Organization (WHO): Stop TB Partnership	M	$125,000
61	Bio Duro, LLC	C	$120,000
63	KNCV Tuberculosis Foundation	F	$89,186
64	FIT BIOTECH	C	$72,435
65	Fondation Merieux	F	$72,435
66	Gulbenkian	F	$72,435
68	Pan American Health Organization (PAHO)	M	$70,000
71	World Health Organization (WHO)	M	$58,543
73	European Centre for Disease Prevention and Control (ECDC)	P	$44,667
78	Colombian Department for Science and Technology (COLCIENCIAS)	C	$12,000
79	Corporate Donors to TB Alliance	C	$5,581
	New Funders Under $500K		$349,523
	Grand Total		**$649,648,183**

P= Public Sector R&D Agency; C = Corporation/Private Sector; M= Multilateral; F=Foundation/Philanthropy; P-D= Public Sector Development Agency

FIGURE 2

Total TB R&D Funding: 2005-2011



1. Introduction

For the seventh year, Treatment Action Group (TAG) publishes the latest investment data and analysis on the state of global tuberculosis (TB) research and development (R&D) funding. The *2012 Report on Tuberculosis Research Funding Trends: 2005–2011* builds on seven years of investment data to report on annual funding trends and gaps among the leading TB R&D donors. The report analyzes current spending levels across six research areas to assess how they compare to the Stop TB Partnership's *Global Plan to Stop TB 2011-2015* (Global Plan) R&D funding targets.

1.1 Rationale

One of the oldest known human pathogens, *Mycobacterium tuberculosis* (*M. tuberculosis*/MTB) continues to pose a global public health threat in the 21st century. The World Health Organization (WHO) reports that MTB—the bacterium that causes TB disease—was responsible for 1.4 million deaths in 2011, including 430,000 among people with HIV. Globally, TB deaths are on track to be 50% lower than 1990 levels—though both Europe and Africa are likely to miss this target.[1] Worldwide, nearly 2 billion individuals are latently infected, and of those 2 billion, an estimated 8.7 million developed active TB disease in 2011. Even more unsettling is the rise in multidrug-resistant (MDR) and extensively drug-resistant (XDR) forms of TB. The WHO estimates 630,000 cases of MDR-TB in 2011,[2] however this figure is likely an underestimate given the limited MDR case-detection capacity currently available.

Current strategies and tools to prevent and control TB are becoming less and less effective. The only vaccine approved for TB, the bacille Calmette-Guérin (BCG), is over 100 years old and protects against two forms of perinatal TB, but cannot offer protection against pulmonary TB, the most common form of TB among adolescents and adults, and cannot be used among HIV-positive infants. The most widely used diagnostic tool—sputum smear microscopy—detects roughly 50% of pulmonary TB cases, and fares far worse among people with immature or compromised immune systems.[3] Solid or liquid cultures are significantly more accurate but take several weeks to confirm diagnosis. Treatment against drug-sensitive (DS) TB involves 6–9 months of first-line drugs, and drug-resistant (DR) TB requires 20 months or more. The lengthy treatment regimen results in suboptimal and at times deadly outcomes because of the difficulty of adhering to treatment as a result of feeling better, drug stock-outs, toxic side effects, treatment costs, and/or incompatibility between TB drugs and antiretroviral medicines for people with HIV.

Promising new tools are being studied, but without political will and adequate funding to support the development of new vaccines, diagnostics, and drugs, the world will not be able to contain the growing problem that DR TB poses, much less eliminate TB as a public-health threat by 2050.

1.2 Background

In 2006, the Stop TB Partnership launched a ten-year strategy for reducing the global TB burden by 2015 and eliminating it altogether as a public-health threat by 2050. The *Global Plan to Stop TB 2006–2015* proposed a global implementation and funding framework for scaling up TB control programs and research for better tools. The original plan called for an annual investment of $890 million to support R&D of new tools to prevent, diagnose, and treat TB. In October 2010, the Stop TB Partnership updated the strategy in the new *Global Plan to Stop TB 2011–2015*, wherein new targets for fundamental science and operational research were introduced and the annual R&D funding target was revised upward to $2 billion.

To measure global progress against the TB R&D funding targets called for in the Global Plan, TAG began tracking annual spending among the leading TB R&D donors, starting with the baseline year of 2005. Since 2006, TAG has accumulated seven years' worth of funding data that informs the TB community about the distribution of R&D resources and the funding needed to accelerate research to end the disease.

Data from the report are used extensively by researchers, advocates, and policy makers—making the report the leading reference source on TB R&D investments. Most recently, the report was cited in the WHO's *Global Tuberculosis Control Report 2012.*

1.3 Methodology

TAG generated original-source funding data for this report using an electronic survey that asked donors to report disbursements supporting TB R&D in 2011 and to categorize those awards using six predefined research categories. The following are descriptions of the areas that make up the TB research agenda for the development of new TB drugs, vaccines, and diagnostics:

- **Basic Science:** Undirected, investigator-initiated research that aims to uncover fundamental knowledge about *Mycobacterium tuberculosis* and closely related organisms (e.g., *M. Africanum, M. bovis*, but not other mycobacterial species).
- **Infrastructure/Unspecified:** Research specific to TB that the donor or funder is unable to further categorize.
- **Diagnostics:** Preclinical or clinical trials of diagnostic technologies and algorithms.
- **Drugs:** Preclinical or clinical research on treatments and treatment strategies for TB disease (including prophylaxis, as well as latent and active TB).
- **Vaccines:** Preclinical or clinical research on TB vaccines.
- **Operational Research:** Research evaluating new and/or existing TB control tools and strategies to guide their effective implementation in program settings. Studies may include randomized trials, surveillance, and epidemiological and observational studies.

In 2011, TAG collected data from 81 out of 132 surveyed institutions. Data from the 81 organizations include nine product development partnerships (PDPs) and research consortia, 14 new donors, and six former TB R&D donors not captured in the 2010 report. Of the 20 new and previously participating donors, seven invested $1 million or more in TB R&D in 2011. However, despite multiple follow-ups, TAG was unable to collect data from 24 previously reporting institutions. While TAG makes every attempt to collect all TB R&D-related data, we prioritized our efforts on the top 30 funders of 2010, who made up 97% of the 2010 TB R&D total. In 2011, TAG secured data from 29 of the 30 top 2010 funders, resulting in a 97% response rate from that sample.

Among the funders included in this report, the U.S. National Institutes of Health (NIH), the European and Developing Countries Clinical Trials Partnerships (EDCTP—a PDP), and the Swiss National Science Foundation (SNF) did not report their 2011 TB R&D disbursements directly to TAG. Instead, TAG accessed their data from publically available online databases.

Funding data reported in non-U.S. currency were converted to U.S. dollars using the July 1, 2011 currency exchange rate provided by the OANDA Corporation at http://www.oanda.com/currency/converter/.[IV]

Results for this report are organized by donor sector, research area, and the top ten funders of 2011. Public-sector investments, including development agency investments, were aggregated for India, Japan, Korea, Norway, Sweden, and Switzerland. New funders who invested $500,000 or less in TB R&D were also combined and labeled "New Funders Under $500,000." To review all the participating TB R&D donors in this year's report, please visit www.treatmentactiongroup.org/tbrd2012.

1.4 Limitations of the Data

Every year TAG strives to collect comprehensive data from leading TB R&D donors to inform the global community on where we stand in meeting the annual $2 billion funding target. The accuracy of our reporting depends largely on our ability to develop and maintain good contacts with donors. However, when organizational restructuring or staffing changes occur, our ability to collect the data is jeopardized.

This was the case for the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), an international financing institution that supports important operational research on TB. Last year, they ranked 30th among 82 donors with a $2.3 million investment in operational research to evaluate TB tools in programmatic settings. Due to the restructuring of GFATM in 2012, TAG was unable to secure any data for 2011.

As evident in this year's report, multilateral spending was at an all-time low of $246,064. This category was affected by the lack of GFATM data and limited funding data from the WHO. TAG predicts the multilateral data is significantly under-reported and as such will make every effort to collect better data for the second edition of this report. TAG works tirelessly to document the most up-to-date investments on TB R&D and encourages new and existing donors not captured here to please share their data and help support the accuracy of this report. Please contact TAG at tbrdtracking@treatmentactiongroup.org if you have information or corrections to share.

IV. All dollar figures cited in this report are calculated in US dollars.

2. Results

2.1 Donor Categories

FIGURE 3

TB R&D Funding by Donor Sector: 2011
Total: 84,140

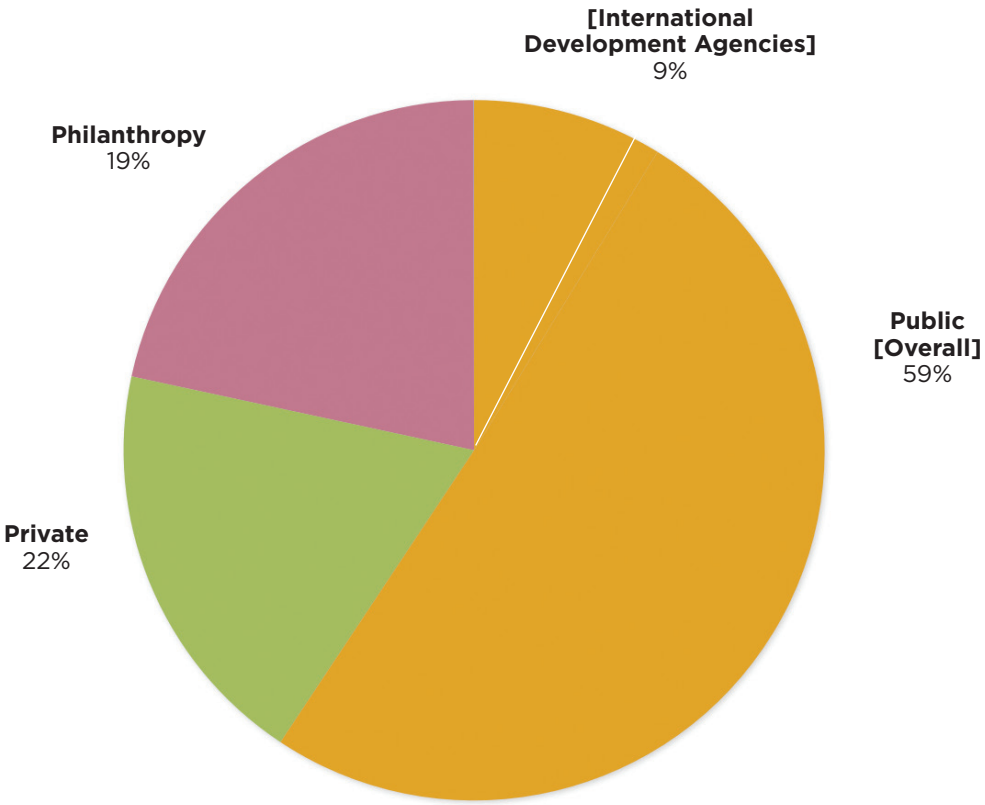
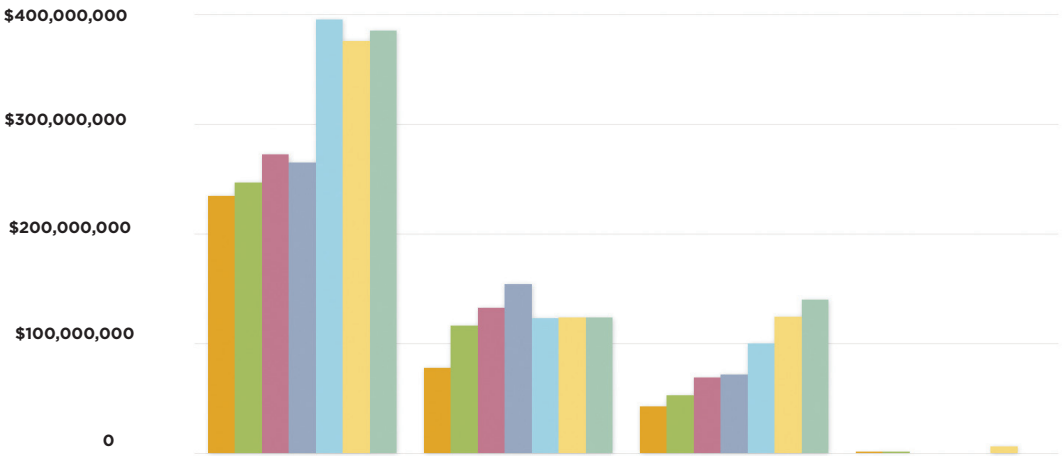


FIGURE 4

Total TB R&D Funding by Donor Sector: 2005-2011



	Public*	Philanthropy	Private	Multilateral
2005	$234,503,645	$78,178,708	$43,095,353	$1,648,083
2006	$246,862,858	$116,289,274	$53,138,347	$1,534,259
2007	$272,404,317	$132,326,981	$69,387,383	N/A
2008	$264,944,215	$154,513,987	$72,018,715	N/A
2009	$395,326,911	$123,383,703	$99,973,537	$525,385
2010	$376,199,816	$123,974,117	$124,249,938	$6,022,590
2011	$385,343,785	$123,889,768	$140,168,565	$246,064

* Includes funding from International Development Agencies.

In 2011, 81 donors reported investing $649.6 million to support TB research and development—a 3% increase from 2010 levels. Despite the $19.2 million in additional resources, 2011's TB R&D investment total represents only 32% of the annual $2 billion funding target set by the Global Plan.

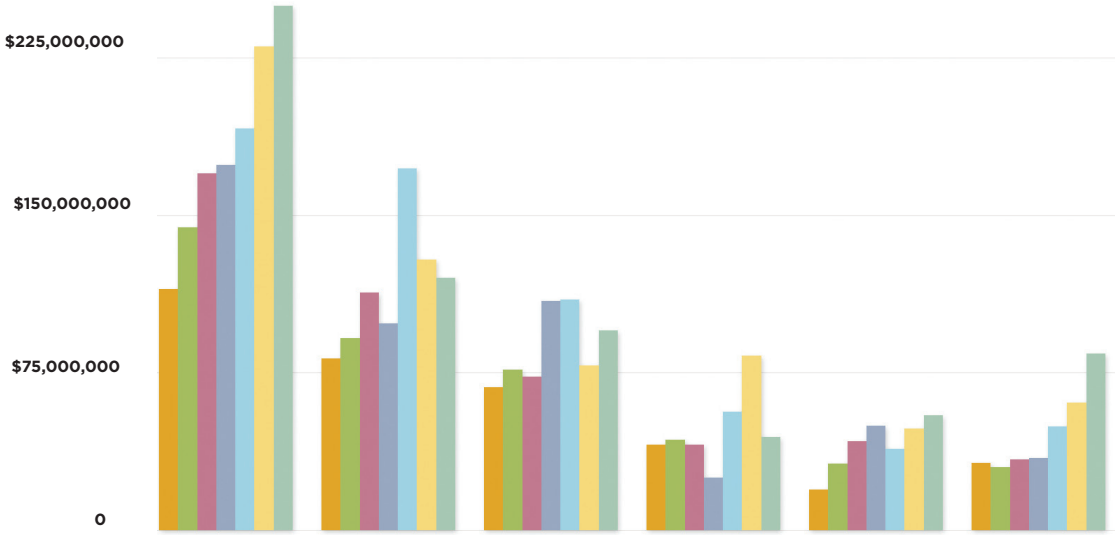
In 2011, private-sector funding grew 13%, from $124.2 million to $140.2 million, in support of drug development and diagnostics research—the largest growth among the four sectors tracked in this report. Public-sector funding remained relatively flat in 2011, growing only 2%, from $376.2 million to $385.3 million. In spite of that small increase, public-sector funding continued to make up the largest share of the global total at 59%.[V] Philanthropic funding was unchanged at $123.9 million, and multilateral funding fell dramatically, from $6 million to $246,064—a research category that was significantly underreported in 2011.[VI]

V. 59% calculation includes international development agency funding (see Figure 3).

VI. TAG suspects there are additional monies from multilateral funding institutions. Please see the *Limitations of the Data* section of this report for further information.

FIGURE 5

Investments in TB R&D by Research Category: 2005-2011



	Drugs	Basic Science	Vaccines	Infrastructure/ Unspecified	Diagnostics	Operational Research
2005	$114,862,738	$81,892,167	$68,351,530	$40,741,527	$19,408,124	$32,170,084
2006	$144,336,532	$91,643,009	$76,555,111	$43,205,600	$31,890,329	$30,194,127
2007	$170,233,497	$113,325,202	$73,225,383	$40,734,199	$42,435,113	$33,967,288
2008	$174,178,052	$98,728,019	$109,337,224	$25,032,930	$49,788,950	$34,411,742
2009	$191,483,304	$172,447,841	$110,133,485	$56,686,918	$38,921,229	$49,536,760
2010	$230,540,443	$129,008,413	$78,446,298	$83,145,063	$48,410,889	$60,895,355
2011	$250,038,877	$120,361,419	$95,446,326	$44,617,845	$55,043,541	$84,140,175

Funding for the six research areas improved in 2011, with the exception of basic science and infrastructure/unspecified, which declined by 7% and 46%, respectively. Operational research showed the greatest growth at 38%, surpassing the Global Plan's annual funding target of $80 million—the only research category to ever meet and exceed its annual goal. Funding for vaccine development grew 22%, from $78.4 million to $95.4 million, after experiencing a steep decline in 2010. Investment in drug development continued to rise, from $230.5 million to $250 million (a 9% increase), as two drug candidates for the treatment of MDR-TB moved closer to regulatory review. And, for a third consecutive year, diagnostics funding increased 14%, from $48.4 million to $55 million.

2.2 Trends in TB Research by Category

FIGURE 6

TB R&D Investments by Research Category: 2011
Total: $649,648,183

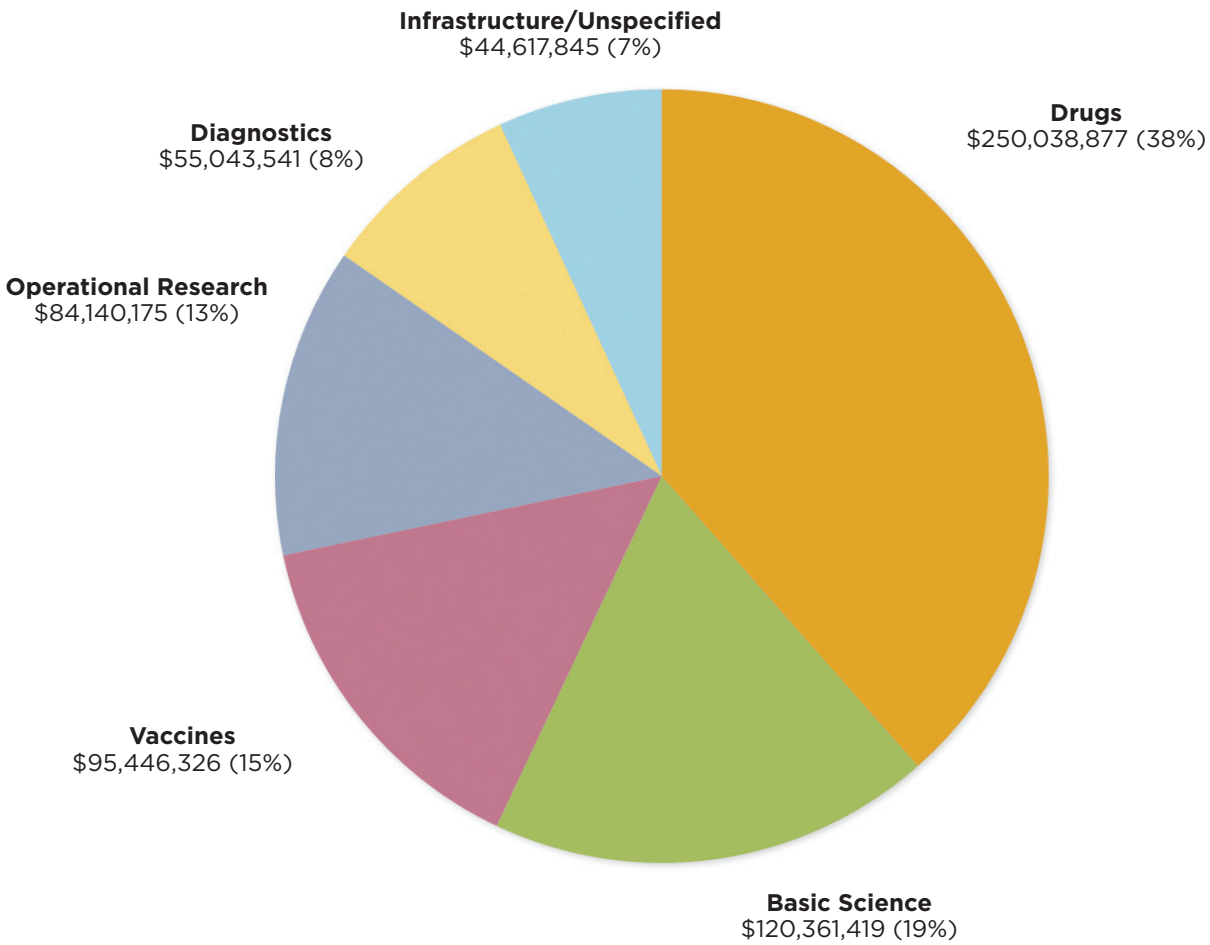
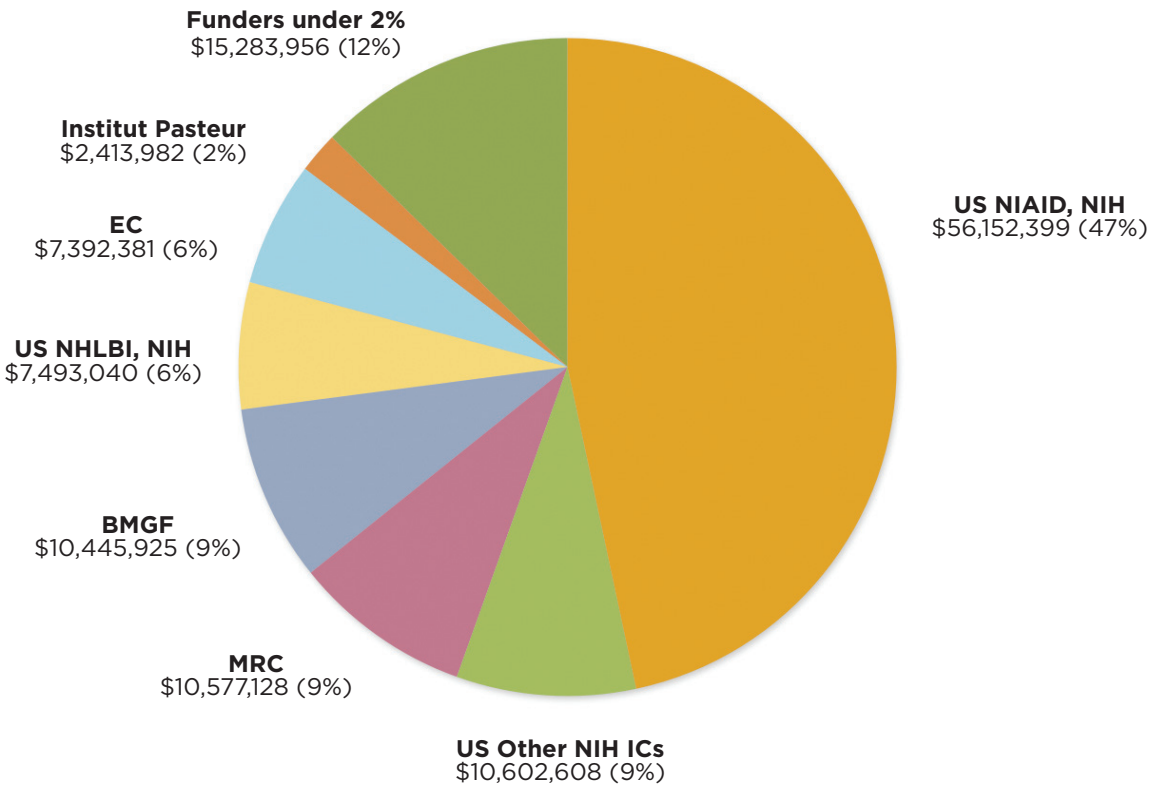


Figure 6 outlines the six research areas and their respective investments for 2011. Once more, drug development represents the greatest share of funding—38% of the global total. Though basic science funding fell, from $129 million to $120.3 million in 2011, it accounted for 19% of global investments. The 46% decline in the infrastructure/unspecified category, from $83.1 million to $44.6 million, moved this category from being the third-most funded research area in 2010 to the least-funded in 2011.

Basic Science

FIGURE 7

Basic Science: $120,361,419



Funders with investments under 2%

Funder	Amount
CIHR	$2,201,100
Sweden (reported)	$2,119,465
Australia NHMRC	$1,529,085
India (reported)	$1,444,088
DFG	$1,434,203
MPIIB	$1,350,000
BMBF	$1,306,175
Wellcome Trust	$1,210,615
Switzerland (reported)	$1,122,678
UK HPA/NIHR	$310,539

Funder	Amount
DGIS	$289,738
Australian Research Council	$246,514
ANR	$232,021
Pfizer	$214,360
ANRS	$110,290
Korea (reported)	$65,100
Carlos III Health Institute	$57,933
New Funders Under $500K	$27,900
COLCIENCIAS	$12,000
Norway (reported)	$153

To design innovative tools to control TB, basic science research[VII] is essential. Basic science research can unveil critical information about the TB pathogen, such as the development of latent to active TB infection, and host-pathogen interactions. Understanding the underlying mechanisms of TB can also drive biomarker discovery, which is urgently needed in drug and vaccine development to reduce the cost and length of clinical trials, and in diagnostics research for a breakthrough discovery of a point-of-care (POC) test.

While the number of donors supporting basic science research grew 23%, from 22 to 27 donors, in 2011, overall funding in fact fell 7%, from $129 million to $120.4 million. The National Institute of Allergy and Infectious Diseases (NIAID), the leading funder in basic science for seven consecutive years, kept post-ARRA (American Recovery and Reinvestment Act)[VIII] investments consistent with 2010 levels at $56.1 million. The second-largest investment was also from the NIH, specifically from the other NIH Institutes and Centers (other NIH ICs). Funding from the other NIH ICs fell 35%, from $16.2 million to $10.6 million. TAG attributes this funding decline largely to the expiration of ARRA in 2011, since the stimulus funding accounted for 34% of their basic science resources in 2010. The last NIH center, the National Heart, Lung, and Blood Institute (NHLBI)—the third leading global funder in 2010—invested $7.5 million in 2011—nearly $3 million less than the United Kingdom's Medical Research Council (MRC) and the Bill & Melinda Gates Foundation (BMGF), which made the third and fourth largest contributions to basic science in 2011. Overall, the NIH supported $74.2 million, or 62%, of the world's funding dedicated to basic science on TB.

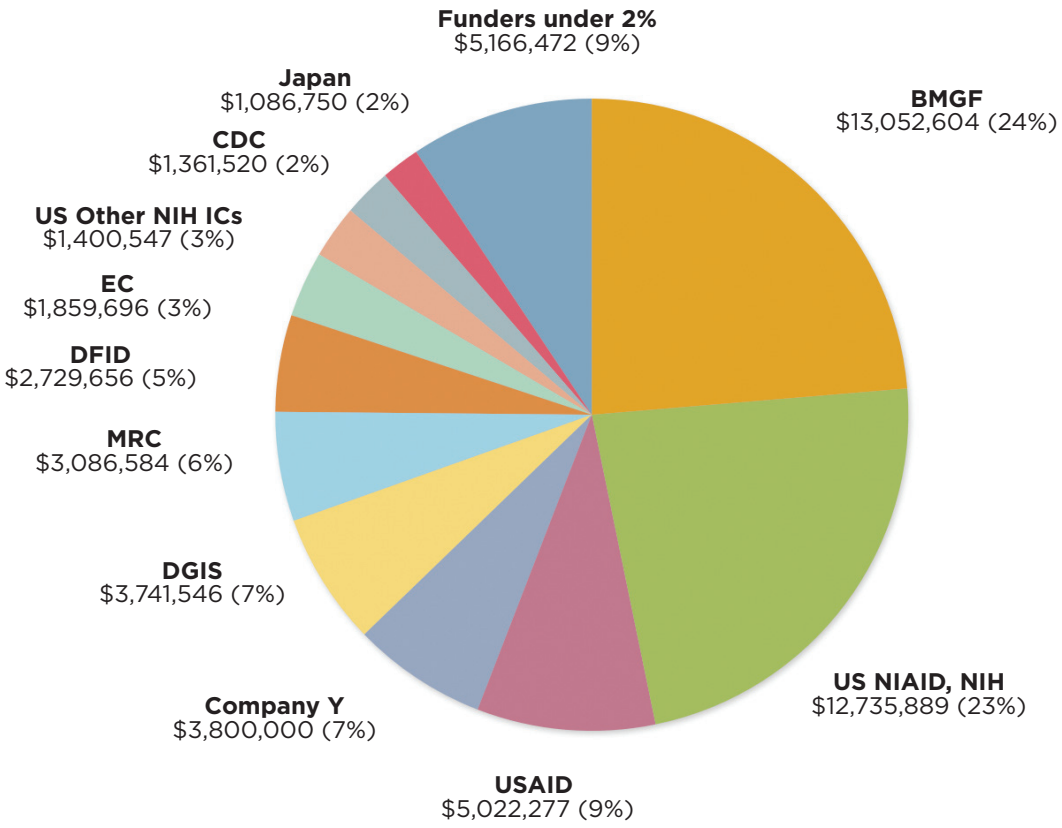
After reducing their investments in 2010, the MRC and BMGF bounced back in 2011. The MRC invested $10.6 million and the BMGF invested $10.4 million, a 13% and 136% increase, respectively. Both funders emphasized the value of improved scientific understanding of TB and believed it could lead to major advances if well funded. According to the Global Plan, $420 million is needed annually to support basic science research. This means an additional $300 million for 2011 alone is needed to effectively support this research area.

VII. Referred to as "fundamental science" by the Stop TB Partnership and the World Health Organization.
VIII. On February 17th, 2009, President Obama signed the ARRA to help jumpstart a deteriorating U.S. economy. The proposed $787 billion stimulus package targeted key economic sectors including science, engineering research and infrastructure. Between 2009 and 2010, the ARRA supported $62.1 million in TB research awards at the NIH.

TB Diagnostics

FIGURE 8

TB Diagnostics: $55,043,541



Funders with investments under 2%

Funder	Amount
Norway (reported)	$987,580
ANRS	$833,989
UBS Optimus Foundation	$717,822
Korea (reported)	$559,398
Institut Pasteur	$433,891
BMBF	$370,691
Company X	$290,000
Australia NHMRC	$210,603

Funder	Amount
Sweden (reported)	$189,732
US NHLBI, NIH	$152,446
ZonMw	$139,536
Sequella	$87,509
Damien Foundation	$84,024
CIHR	$62,069
Carlos III Health Institute	$47,181

Compared to other global infectious diseases, such as HIV and malaria, TB is the only major killer without a quick, low-cost, and effective POC test.[4] Current TB diagnostics tests have varying degrees of effectiveness, determined by any number of obstacles including costs, distance/access to sophisticated laboratories, electricity, human resources, and/or a long wait time to secure results. For HIV and pediatric populations, TB diagnosis comes with additional complexities. All of these challenges must be addressed by a POC test, however, insufficient funding and lack of biomarker discovery research is impeding its development.

In 2011, 26 donors invested $55 million in TB diagnostics research—a 14% annual increase and the greatest investment ever made to diagnostics research since TAG began this resource tracking exercise in 2006. Nevertheless, the $55 million contribution represents only 16% of what is needed annually to meet the Global Plan's $340 million target.

The BMGF, which was the second leading investor in diagnostics research in 2010, became the leading investor in 2011, spending $13 million. NIAID, ranked second here, spent $12.7 million. While BMGF and NIAID reduced their investments in 2011, by 11% and 20%, respectively, together they made up 47% of the global total on diagnostics research.

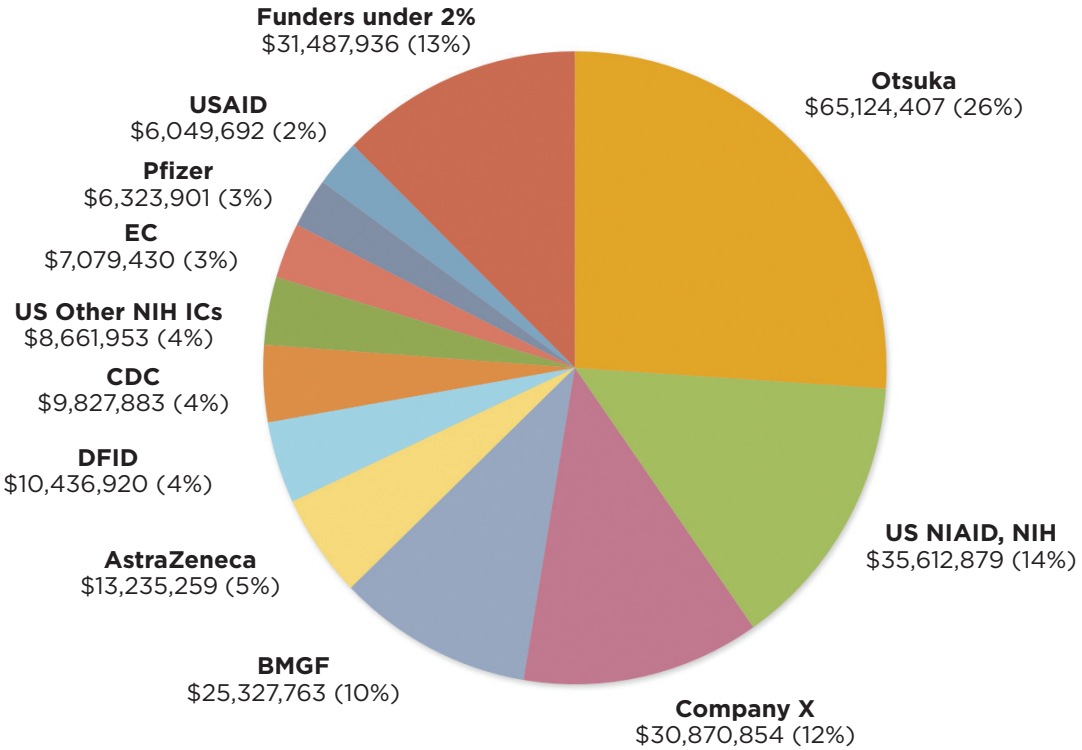
Increased investments were observed among the top ten global R&D donors, such as the United States Agency for International Development (USAID), the MRC, the United Kingdom's Department for International Development (DFID), and the European Commission (EC), ranging from $1.4 million to $3.2 million, compared to 2010 levels. More investments, particularly from middle-income countries, will be essential to fill the funding gap in diagnostics research.

The rollout and evaluation of the latest WHO-approved TB diagnostic technology, Cepheid's GeneXpert MTB/RIF test, continued in 2011. Numerous operational research studies focused on assessing its efficacy in programmatic settings, and one of the major obstacles standing in the way of its increased uptake were the prohibitive costs of the machine and cartridges. To alleviate this financial burden, in August 2012, the U.S. government, UNITAID, and the BMGF stepped in and made an $11.1 million up-front payment to the manufacturer, Cepheid, to reduce the price of cartridges by 40%, from $16.86 to $9.98, for low- and middle-income countries with high-burdens of TB.[5]

TB Drugs

FIGURE 9

TB Drugs: $250,038,877



Funders with investments under 2%

Funder	Amount
Company W	$4,529,539
Sequella	$4,412,865
SA DST	$4,000,000
MRC	$2,842,988
CIHR	$2,134,045
Sandoz	$1,500,000
Eli Lilly	$1,500,000
US FDA	$1,452,570
Irish Aid	$1,448,690
Wellcome Trust	$1,261,286
ANRS	$1,099,708
Institut Pasteur	$1,066,726
Korea (reported)	$1,029,022
BMBF	$968,834

Funder	Amount
UK HPA/NIHR	$559,419
Australia NHMRC	$545,557
US NHLBI, NIH	$230,944
Damien Foundation	$198,471
ANR	$125,756
WHO Stop TB Partnership	$125,000
Bio Duro	$120,000
KNCV	$89,186
DGIS	$85,230
New Funders Under $500K	$58,741
Sweden (reported)	$47,433
Japan (reported)	$27,500
Carlos III Health Institute	$22,846
Corporate Donors to TB Alliance	$5,581

This is the most exciting period in TB drug development since the 1960s. There are 11 new or repurposed drug compounds in the clinical pipeline for treatment of DS- and DR-TB—the most robust pipeline in over 40 years. Two companies with drug compounds in phase III filed for regulatory approval from the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) in 2012. If approved, both drugs will be used to treat MDR-TB.

Study results from a new approach testing multiple TB drug candidates at once, pioneered by the TB Alliance, showed the promise of a new drug regimen that might be able to cure both DS- and DR-TB in four months.[6] Findings from the New Combination 1 (NC001) trial also validated the appropriateness of using colony-forming units and time-to-MGIT-culture-positivity as study endpoints. These findings have significant implications for future combination studies since they eliminate the need to conduct expensive and lengthy clinical trials, reducing the clinical research timeline from decades to years.

As the most well-funded research area, TB drug development made up 38% of the total global spend. In 2011, 28 donors invested $250 million in TB drug development—a 9% increase from 2010 levels. Otsuka Pharmaceuticals continued to be the lead investor in 2011, keeping disbursement levels stable at $65.1 million, or 26% of the global TB drug total, to develop a new compound, delamanid, to treat MDR-TB. NIAID decreased its spending on drug development for a second consecutive year, from $41.9 million to $35.6 million, a 15% decline.

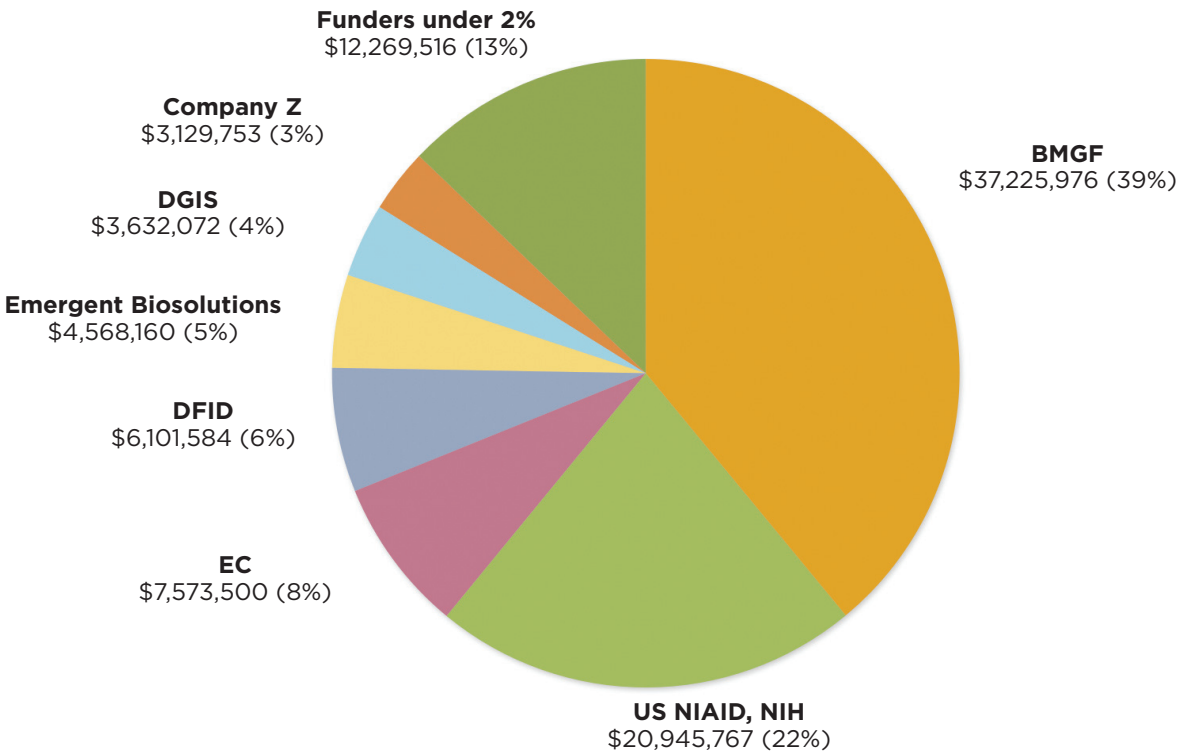
Company X invested 50% more in TB drug development compared to 2010 levels, with a total investment of $31.2 million, making it the third leading TB drug investor. The BMGF increased its investments by 22%, from $20.7 million to $25.3 million, with 84%, or $21.4 million, of that funding disbursed to the TB Alliance as part of a five-year award.

To continue supporting groundbreaking developments that deliver shorter and simpler TB treatment regimens (that also address the needs of pediatric and HIV-positive populations), the world must invest at least $740 million annually to see these drugs come to fruition. The latest spending data, however, show investments in TB drug development account for only 34% of the annual funding target defined by the Global Plan. More resources and new donors are urgently needed to fill the $490 million funding gap.

TB Vaccines

FIGURE 10

TB Vaccines: $95,446,326



Funders with investments under 2%

Funder	Amount
US Other NIH ICs	$1,667,539
BMBF	$1,665,994
MPIIB	$1,400,000
Wellcome Trust	$1,192,170
UK HPA/NIHR	$926,638
CIHR	$732,010
Carlos III Health Institute	$655,319
Norway (reported)	$591,321
Korea (reported)	$534,099
US NHLBI, NIH	$409,823
Danish National Advanced Technology Foundation	$392,799

Funder	Amount
Institut Pasteur	$349,400
Australia NHMRC	$326,158
MRC	$324,949
Sweden (reported)	$284,598
SSI	$165,062
New Funders Under $500K	$164,091
Danish Council for Independent Research | Medical Sciences	$140,749
GSK Biologicals	$129,493
Gulbenkian	$72,435
Fondation Merieux	$72,435
FIT BIOTECH	$72,435

In 2011–2012, TB vaccine R&D reached a turning point. After a decade's worth of research toward the discovery of novel approaches, the pipeline now has 12 vaccine candidates in clinical trials. The two candidates furthest along are MVA85A/AERAS-485 and AERAS-402/Crucell Ad35. Both in phase IIb, the vaccines are being developed as "booster" vaccines for people who received the BCG vaccine at infancy or were exposed to TB naturally.[7] The goal of these vaccines is to extend protection against the most common form of TB—pulmonary TB—for children, adolescents, and adults.

In 2011, TB vaccine funding grew 22%, from $78.4 million to $95.4 million. After reducing their investments in 2010, the BMGF and NIAID's vaccine spending rose 22% and 62%, respectively. The BMGF's $37.2 million investment made up 39%, and NIAID's $20.9 million investment represented 22% of the global vaccine total.

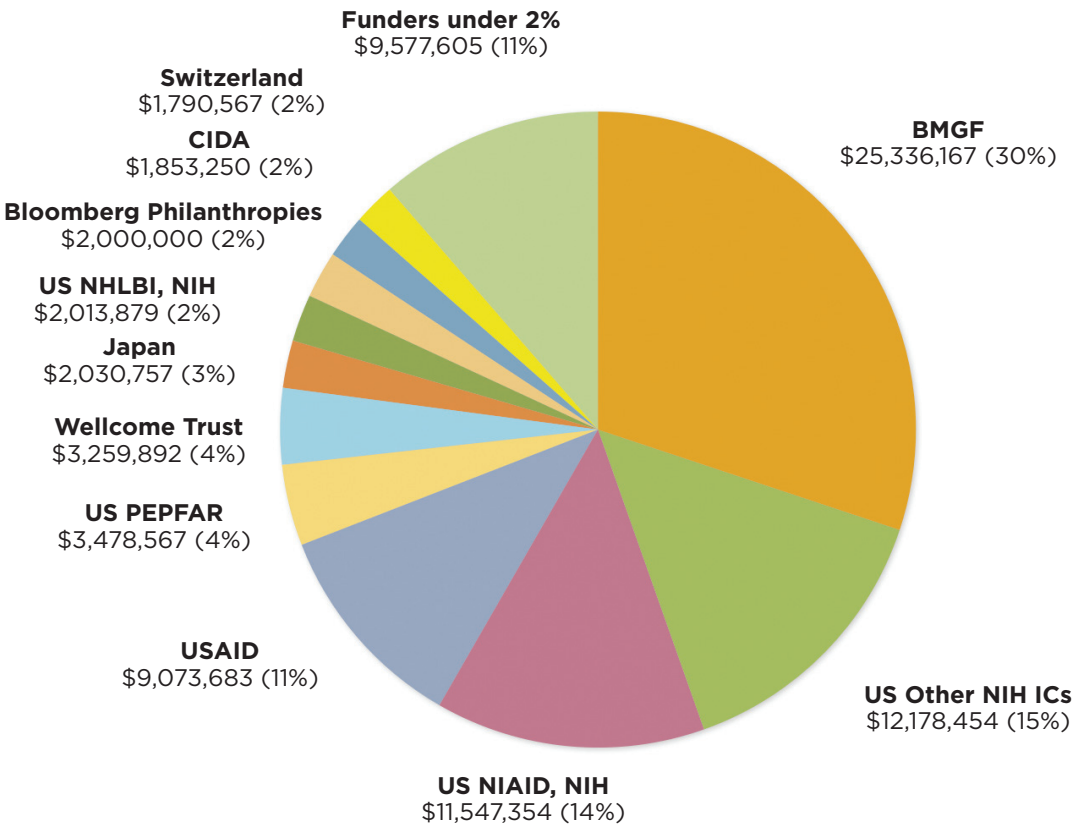
Without a novel vaccine that is effective in all populations and protects against all forms of TB, the world will not be able to achieve TB elimination. The Global Plan recommends $1.9 billion, or an annual investment of $380 million over five years, to accelerate TB vaccine development. The 2011 TB vaccine total of $95.4 million represents only 25% of that $380 million target—an investment that cannot adequately support clinical vaccine development.

In March 2012, the Stop TB Partnership's Working Group on New TB Vaccines released *Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade*, a comprehensive plan designed to reinvigorate TB vaccine research and spotlight five critical areas that require intensified research and funding to fulfill the discovery, approval, and distribution of new TB vaccines. The strategy acknowledges the important role leading vaccine funders have played in getting the pipeline up and running, but stresses that without additional funding from new donors, particularly from middle-income countries, the full costs of global TB vaccine development will not be met.[8]

Operational Research

FIGURE 11

Operational Research: $84,140,175



Funders with investments under 2%

Funder	Amount
UK HPA/NIHR	$1,612,745
DFID	$1,476,903
Sweden (reported)	$1,472,637
Australia NHMRC	$1,216,186
UBS Optimus Foundation	$897,278
CIHR	$773,064
Korea (reported)	$651,929
CDC	$432,147
Norway (reported)	$379,781

Funder	Amount
Brazilian National TB Program	$189,730
Damien Foundation	$159,356
India (reported)	$71,509
PAHO	$70,000
ANRS	$50,497
WHO	$44,579
New Funders Under $500K	$32,550
BMBF	$27,837
MRC	$18,878

Operational research is an instrumental part of the TB R&D agenda because it provides important information on the efficacy, efficiency, and applicability of new tools and programs designed to control TB in programmatic settings. The evidence gathered from operational research studies informs researchers and program managers overseeing TB control initiatives about the best strategies to introduce and scale up access to new tools.

In 2011, operational research funding rose 38%, from $60.8 million to $84.1 million—the first time that investments in operational research exceeded the Global Plan's annual target of $80 million. The $84.1 million total, however, does not include data from GFATM—an important sponsor of operational research on TB. In 2010, GFATM disbursed $2.3 million in research funding to evaluate TB tools in programmatic settings. But due to that organization's restructuring in 2012, TAG was unable to secure any 2011 data despite knowing that GFATM recommends grantees spend 5–10% of their funding awards on monitoring and evaluation.[9]

After ranking third in 2010, the BMGF invested $25.3 million in operational research—a 169% increase from 2010's investment—making it once more the leading funder in this research area. The second leading funder, other NIH ICs, decreased its investment by 18%, from $14.8 million to $12.2 million. Among the top ten donors that traditionally support operational research (i.e., public-sector and international development agencies), only the BMGF and NIAID invested additional monies to operational research; the remaining donors reduced their investments.

The 38% increase in operational research funding is therefore largely attributable to BMGF and NIAID's combined $19 million investment, in addition to new investments from Bloomberg Philanthropies ($2 million) and the Canadian International Development Agency (CIDA) ($1.9 million). For the first time, TAG was able to document investments from CIDA to TB REACH, an initiative of the Stop TB Partnership that funds innovative approaches for early and increased TB case detection.[10]

2.3 Product Development Partnerships and Research Consortia

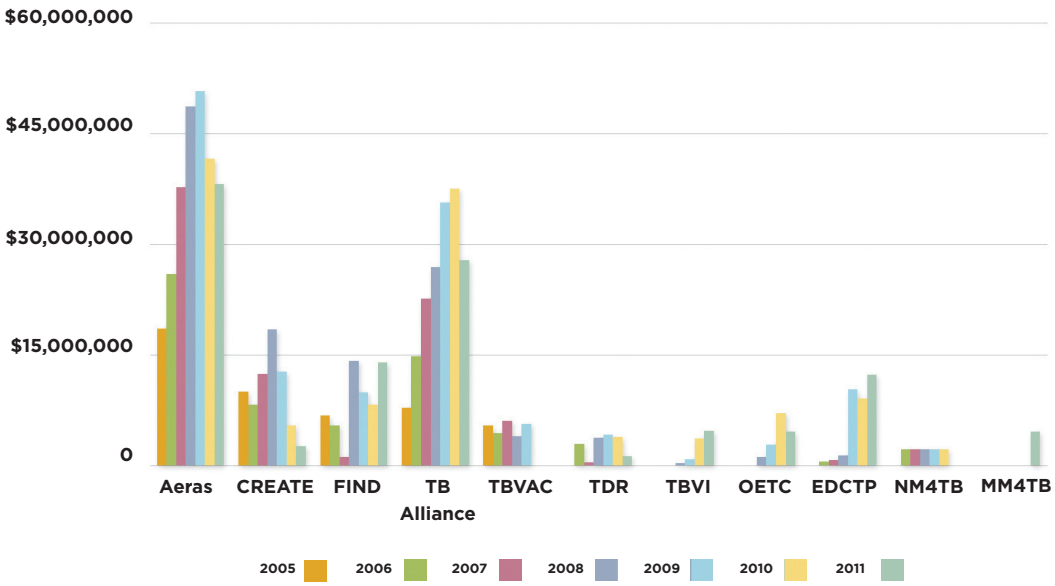
In 2011, nine PDPs and research consortia disbursed $110.2 million in support of TB R&D, a 126% increase over 2005 levels, but a 7% decline from 2010.

This year, TAG began tracking a new research consortium made up of 25 academic, pharmaceutical, and public research institutions. More Medicines for TB (MM4TB) is an EC Seventh Framework Programme–funded initiative that builds on the work of its predecessor, New Medicines for TB (NM4TB). NM4TB was an $11 million five-year Sixth Framework Programme–funded consortium made up of European academic institutions, one major pharmaceutical company, AstraZeneca, and other small-to-medium-sized enterprises to develop novel drug therapies.[IX] The consortium was funded through January 2011, and the outcome of its research resulted in the discovery of a new drug candidate, benzothiazinone (BTZ043), which is now in preclinical development.[11] MM4TB has expanded the number of collaborators and funders, with the EC supporting $17 million, or 72% of the $23.5 million five-year project.[12]

IX. In past reports, NM4TB disbursements were not tracked. New data from this PDP are now included in this year's report and reflected in the 2006–2010 PDP totals.

FIGURE 12

TB R&D PDPs and Research Consortia: 2005-2011



	Aeras	CREATE	FIND	TB Alliance	TBVAC	TDR	TBVI	OETC	EDCTP	NM4TB	MM4TB
2005	$18,580,139	$10,000,000	$6,778,239	$7,874,983	$5,445,450	N/A	N/A	N/A	N/A	N/A	N/A
2006	$25,923,809	$8,298,826	$5,492,942	$14,808,362	$4,451,895	$2,995,748	N/A	N/A	$580,039	$2,214,000	N/A
2007	$37,704,051	$12,375,000	$1,145,409	$22,624,182	$6,091,335	$453,382	N/A	N/A	$805,625	$2,214,000	N/A
2008	$48,679,266	$18,493,585	$14,177,202	$26,885,734	$3,944,425	$3,817,352	$339,741	$1,196,000	$1,416,064	$2,214,000	N/A
2009	$50,792,515	$12,786,985	$9,975,320	$35,643,490	$5,634,040	$4,243,264	$841,333	$2,851,000	$10,343,479	$2,214,000	N/A
2010	$41,572,980	$5,410,545	$8,212,896	$37,538,794	Concluded	$3,900,000	$3,700,914	$7,142,159	$9,081,799	$2,214,000	N/A
2011	$38,166,117	$2,657,411	$13,938,587	$27,824,033	Concluded	$1,315,700	$4,731,422	$4,568,160	$12,313,115	Concluded	$4,644,099

PDPs and research consortia play an important role in accelerating the development of new TB drugs, diagnostics, and vaccines. As nonprofit institutions, PDPs receive funding and other in-kind services from private, public, and philanthropic organizations to maximize research knowledge and resources. Since PDPs are funding recipients rather than original-source funders, their disbursements are tracked separately from the global total to avoid double counting.

2.4 Top 10 Funders in TB R&D in 2011

Of the $649.6 million global R&D total documented in this year's report, the top ten donors spent $506.7 million, or 78% of the global share. The largest investments—over $100 million each—originated from NIAID and the BMGF, whose combined investments represent 42% of the global total. Two drug companies invested a total of $96 million in TB drug development, as two new drugs for the treatment of MDR-TB await regulatory review. International development agencies also played a critical funding role in 2011, disbursing $40.9 million.

1. The National Institute of Allergy and Infectious Diseases (NIAID)

Despite the expiration of ARRA stimulus funding at the end of 2010, NIAID's investments in TB R&D remained consistent with 2010 levels at $157.6 million. The steady investment by NIAID is likely due to the high scientific quality of applications and strong institutional support for TB R&D. Additional NIAID support in the form of the AIDS clinical trials networks such as the ACTG and IMPAACT networks—which are now undertaking innovative TB drug, diagnostic, and vaccine studies—are not likely to be fully captured in the NIAID total. We urge NIAID to work with the disease-categorization specialists at the NIH to more accurately capture and quantify this important and growing new element in the global struggle against TB.

In 2011, NIAID issued 297 awards[X] to accelerate TB research, with 36% of its investment directed to basic science research, for which funding remained stable at $56.1 million. For diagnostics—an area where NIAID has traditionally played a leading funding role—spending declined 20%, from $15.8 million to $12.7 million, placing it second to the BMGF, which invested $300,000 more to become the leading diagnostics funder in 2011. Although investments for drug development fell 15%, from $41.9 million to $35.6 million, NIAID continued to be the second-largest investor in TB drug development.

Lamentably, vaccine and operational research were the only two areas to see increased funding from NIAID. In 2011, vaccine funding increased 62%, from $12.9 million to $20.9 million, which accounted for 22% of the global vaccine total. Operational funding also rose 42%, from $8.1 million to $11.5 million.

Viewed in its entirety, the NIH invested 7% less in 2011 compared to 2010, when investments in TB research peaked at $224 million—the largest NIH investment ever dedicated to TB since 2005 (see Table 2).

X. The NIH's Research, Condition, and Disease Categorization database listed a total of 298 awards for TB research from NIAID in 2011. However, after careful review, TAG excluded one grant (titled "Improving the Diagnosis of Histoplasmosis in an Endemic Region," worth $387,954, to the Johns Hopkins University) considering it a non-TB-related award.

2005-2011 NIH Funding for Select Infectious Diseases (in millions)

Table 2

	2005	2006	2007	2008	2009*	2010*	2011
HIV/AIDS	$2,921	$2,902	$2,906	$2,928	$3,338	$3,407	$3,059
Smallpox	$187	$149	$142	$94	$98	$97	$41
Anthrax	$183	$150	$160	$134	$115	$130	$87
Tuberculosis	$158	$150	$188	$142	$216	$224	$209
Malaria	$104	$98	$112	$142	$121	$148	$145

* Includes ARRA stimulus funds

NIH Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)
Accessed 10 October 2012 on http://report.nih.gov/categorical_spending.aspx

2. The Bill & Melinda Gates Foundation (BMGF)

In 2011, the BMGF invested $112.4 million in TB R&D—3% less than the previous year. Despite this small decline, funding levels remained stable, helping the foundation retain its position as the second-largest global funder of TB research for a third consecutive year.

The foundation invests significantly across all the TB research areas. Current investments are predominantly aimed at developing new short-course TB drug regimens and diagnostic tools that can be used closer to the point of care. Research evaluating the efficacy of new tools and service-delivery models are also among their short-term priority areas.

With regard to the foundation's long-term vision, the BMGF will continue to invest in research to develop more effective vaccines and an accurate and affordable POC diagnostic test.

Between 2010 and 2011, investments in drug and vaccine development increased 22%. Operational research and basic science witnessed the largest year-to-year growth, increasing by 168% and 136%, respectively. Diagnostics research funding fell slightly, by 11%, but the greatest decline was seen in infrastructure/unspecified—a research area that received $35.5 million in 2010 but only $1 million in 2011.

The BMGF is a significant contributor to the important work performed by PDPs and research consortia. In 2011, the foundation's two largest investments were disbursed to Aeras, which received $36.4 million for vaccine development, and to the TB Alliance, which received $21.4 million to accelerate the development of anti-TB regimens.

3. Otsuka Pharmaceutical Company

Otsuka is a private pharmaceutical company developing a new drug for the treatment of MDR-TB. Delamanid (OPC-67683), a nitroimidazole, is part of a new class of TB drugs under investigation for people with confirmed MDR-TB. The phase III compound was the first of the new generation of TB drugs to be submitted for regulatory approval—to the EMA, late in 2011. A decision is expected sometime in the first quarter of 2013.

In 2011, Otsuka invested $65.1 million to support all necessary clinical trial developments and to prepare regulatory filings for delamanid. This investment was the third-largest global contribution to TB research, and the leading investment from a private-sector company. In addition to developing and rolling out delamanid, Otsuka will continue to look at ways to enhance treatment outcomes for all TB patients through a comprehensive TB management strategy that combines new therapies, diagnostics, improved models of patient care and support, and sound public policies to minimize resistance to new drugs.[13]

Delamanid—or its competitor, Janssen's drug bedaquiline (TMC207)—are likely to be the first new drugs approved for TB since rifampin was approved by the FDA back in 1963.

4. Other NIH Institutes and Centers (Other NIH ICs)

The NIH is a U.S. public-sector research agency consisting of 27 different research centers and institutes. Since 2006, TAG has tracked TB R&D research investments by the NIH across three institutional categories: NIAID, NHLBI, and other NIH ICs, which represents the remaining 25 research centers.

Although the other NIH ICs invested 23% less than in 2010, spending $40.2 million in TB R&D, they were still the fourth-largest funder of TB R&D. Five out of six research areas witnessed a funding decline in 2011, with the exception of TB drugs, which grew 64%, from $5.2 million to $8.6 million. As TAG predicted in 2010, after the expiration of ARRA stimulus funding, research funding for TB from the NIH declined.

5. Company X

Company X is a private company carrying out TB drug development. In 2011, the company invested $31.2 million in TB R&D—a 51% increase from 2010 levels.

6. The European Commission (EC)

The EC is the European Union's executive body that oversees the work and common funds of the Union's member states. The EC has several funding schemes to support global health research programs, including the Sixth and Seventh Framework Programmes, the Directorate-General's Research and Innovation Division, and the European Research Council.

In 2011, the EC invested $28.3 million to TB R&D, a 9% increase from 2010. Its investments support the full spectrum of TB research, from basic molecular research to preclinical tests and proof-of-principle studies. Between 2010 and 2011, funding for basic science

grew 64%, and diagnostics research soared 352%. Though vaccine research funding fell 28% in 2011, it still constitutes the EC's largest investment, at $7.6 million.

The EC recognizes the urgency of the MDR-TB crisis and is especially interested in funding research that addresses the treatment needs of MDR-TB patients and the development of new diagnostics to detect cases early and accurately.

7. The United Kingdom Department for International Development (DFID)

After investing $3.8 million in additional funding, the DFID moved from ninth to seventh place, making its largest investment to date—$20.7 million in TB research. Consistent with its long-term strategy to improve disease control and access to effective interventions, TB drug and vaccine research continued to receive the largest shares of funding, at $10.4 million and $6.1 million, respectively in 2011. Diagnostics funding grew 264%—the most among the funded research areas—from $700,000 to $2.7 million, an investment that confirms the agency's new interest in supporting diagnostics research that addresses the needs of people with HIV.

8. The United States Agency for International Development (USAID)

After increasing investments by 28% in 2010, USAID kept funding levels constant at $20 million in 2011 and held on to the eighth spot among the top ten donors. The largest share of USAID funding, $9 million, was directed to operational research—a 13% decline from 2010. Funding fell 14% for TB drug development, from $7 million to $6 million. Diagnostics research was the only research area to grow considerably in 2011, from $1.8 million to $5 million, a 179% increase.

While operational research and drug development are USAID's traditional funding areas, the agency expressed that if more research funds were available, it would be interested in backing vaccine development if a viable and promising candidate is identified.[14]

9. The United Kingdom Medical Research Council (MRC)

MRC is the UK's leading government funded research agency. A long-time TB R&D donor, the agency funded the first-ever randomized controlled study evaluating streptomycin for the treatment of TB in the 1940s, and a large-scale trial of BCG vaccination in school children in the 1950s.[15]

After ranking 12th in 2010, the MRC disbursed 24% more in 2011, from $13.6 million to $16.9 million, placing it among the top ten funders in 2011. Basic science research made up the greatest share of MRC funding, $10.6 million, followed by TB diagnostics, which saw a sizeable increase, from $.1 million to $3.1 million, and TB drug development, which grew 31%, from $2.2 million to $2.8 million. Vaccine and operational research fell 82% and 85%, respectively, compared to 2010 levels.

Today, the MRC operates in response mode to issues around global health. While the research council does not have a specific strategy to combat TB, it anticipates future investment on TB research will remain relatively stable.[16]

10. The United States Centers for Disease Control and Prevention (CDC)

Since TAG first began this resource-tracking exercise in 2006, the CDC has made annual contributions to TB R&D worth $17 million or more, and always placed among the top ten funders. In 2011, the CDC narrowly missed the top ten list, as a result of its 29% funding drop, from $19.9 million to $14.2 million—the smallest investment ever documented for the CDC.

The TB Trials Consortium and the TB Epidemiological Studies Consortium are two ten-year research contracts that make up the majority of the agency's TB portfolio. The consortia support international and national operational research on the diagnosis, clinical management, and prevention of TB, as well as scientific capacity-building.[17, 18]

The $5.7 million funding decline in 2011 affected all the research areas funded by the CDC. Operational research funding fell 86%, from $3.2 million to $400,000. Infrastructure/unspecified declined 37%, and diagnostics 20%. TB drug development, which receives the greatest share of institutional funding, fell only 10%, to $9.8 million.

3. Conclusion and Recommendations

3.1 Conclusion

In 2011, 81 donors invested $649.6 million in TB R&D, an 82% increase from the baseline year of 2005, but only a 3% increase over 2010 funding. The top ten donors disbursed $506.7 million of the $649.6 million total, or 78% of the global share. While the 2011 global investment figure is the largest total ever recorded, it continues to fall $1.35 billion short of the annual $2 billion funding target recommended by the Global Plan.

Table 3

Summary of Changes in TB R&D Investment, 2005-2011

Year	Total TB R&D Investment	Change over Previous Year ($)	Change over Previous Year (%)	Change over 2005 ($)	Change over 2005 (%)
2005	$357,426,121				
2006	$417,824,708	$60,398,587	16.9%	$60,398,587	16.9%
2007	$473,920,682	$56,095,974	13.4%	$116,494,561	32.6%
2008	$491,476,917	$17,556,235	3.7%	$134,050,796	37.5%
2009	$619,209,536	$127,732,619	26.0%	$261,783,415	73.2%
2010	$630,446,462	$11,236,926	1.8%	$273,020,341	76.4%
2011	$649,648,183	$19,201,721	3.0%	$292,222,062	81.8%

Between 2010 and 2011, the private sector saw the greatest funding increase, growing 13%, from $124.2 million to $140.2 million, in support of drug development and diagnostics research. The public sector continued to be the leading funder of TB R&D, despite making only a small increase in investment in 2011, from $376.2 million to $385.3 million. Philanthropic funding was flat at $123.9 million, and multilateral funding declined significantly, from $6 million to $246,064—a figure that was significantly underreported in 2011.

Of the six research areas tracked in this report, TB drug development continued to receive the largest share of global R&D investments. Compared to the Global Plan target, however, the $250 million TB drug figure represents only 34% of the $740 million annual target. Conversely, funding for operational research exceeded the Global Plan's target in 2011 by $4.1 million. The $84.1 million operational research investment is the first time a TB-related research area has met and surpassed its funding goal. Should TAG be able to collect additional data from the GFATM for the second edition of this report, the operational research total for 2011 will be even greater.

In 2011, NIAID remained the top investor in TB R&D, disbursing $157.6 million. Though ARRA stimulus funding expired at the end of 2010, funding from NIAID remained stable. For the other NIH ICs and the NHLBI, funding levels declined 23% and 20%, respectively, in 2011. Overall, the NIH spent $209 million on global TB R&D—7% less than in 2010. Keeping TB a priority will be a challenge given the state of the global economy, the upcoming threat of drastic across-the-board U.S. budget cuts if sequestration occurs, and other competing priorities. A strong case needs to be made to ensure the NIH and other U.S. agencies involved in global TB control are adequately funded to accelerate much-needed research.

In June 2012, the Congressional Research Service issued a report to congress on the epidemiological state of TB worldwide. The report provided an overview of the government's funding mechanisms and programs designed to respond to the global epidemic, and outlined three key areas the 112th Congress should consider when deliberating the United States' TB control strategy and budget. The first recommendation describes the challenge TB/HIV coinfection poses on TB *and* HIV control programs, the need for more joint TB/HIV services and establishing of targets; the second highlights the growing concern of MDR- and XDR-TB and how their rapid development could erode all the gains made in TB control over the last two decades. Lastly, the report calls attention to the archaic tools used to control TB and the need for more R&D funding to develop innovative and affordable tools.[19]

We hope these recommendations result in additional funding to the CDC, the NIH, PEPFAR, and USAID—research and implementing agencies that are in great need of resources to help the world control and ultimately eliminate TB.

3.2 Recommendations

Research to accelerate global TB R&D is gravely underfunded. The scientific gains achieved in the last decade for drug, vaccine, and diagnostics development means more resources are needed to see these new tools actually come to fruition.

To achieve this, additional resources are considered necessary in:

- Biomarker discovery to modernize TB drug and vaccine development by demonstrating the progress and effects of treatment or immunity early on, which in turn radically reduces the time and costs of the clinical trials;

- Biomarker discovery for the development of a POC diagnostic test that can identify people with latent TB at risk of developing active TB, as well as biomarkers associated with infection, treatment response, cure, and drug susceptibility or resistance;[20]

- TB sample banks that support biomarker discovery with well-characterized specimens;

- Late-stage drug and vaccine clinical trials, many of which will take place in high-burden countries with limited laboratory capacity or infrastructure that meet Good Clinical Practice standards; and

- Basic science research to enhance our scientific understanding of TB disease and the *M. tuberculosis* pathogen.

The global TB community should also give further consideration to establishing access plans to optimize the rational use of, and to prevent the emergence of resistance to, new TB drugs and regimens when they become available; developing pediatric investigational plans to ensure child-friendly formulations are available as quickly as possible; conducting drug-drug interaction studies for novel TB drug regimens; providing compassionate use and expanded access, which are particularly important for people with MDR- and XDR-TB who have limited treatment options; and modernizing TB regulatory guidelines and streamlining regulatory requirements across and within regions.

All of these recommendations and more can be accomplished through a concerted effort if policy makers, researchers, activists, clinicians, donors, implementers, and people affected by TB pledge their commitment to achieve zero TB deaths, zero new TB infections, and zero suffering from TB. *The Zero Declaration*, created by a worldwide group of TB stakeholders who met in Cambridge, Massachusetts, in June 2012, is a new strategy that calls on the international community to embrace a "new global attitude in the fight against TB…and mobilize sufficient political will and resources to prevent needless transmission, sickness, and death."[21] The goal of the campaign is to organize and inspire people to work toward eliminating TB as a public health threat with greater urgency, more political will, and increased investments.

To learn more about the *Zero Declaration* and join the global movement, please visit: http://www.treatmentactiongroup.org/tb/advocacy/zero-declaration.

Appendix 1

Table 4.1

2011 and 2010 Top Reporting TB R&D Funders

2011 Rank	2010 Rank	Funding Organization	Funder Type	Total
1	1	US National Institute of Allergy and Infectious Diseases (US NIAID, NIH)	P	$157,562,079
2	2	Bill & Melinda Gates Foundation (BMGF)	F	$112,388,435
3	3	Otsuka Pharmaceutical	C	$65,124,407
4	4	US Other NIH Institutes & Centers (US Other NIH ICs)	P	$40,214,119
5	6	Company X	C	$31,160,854
6	5	European Commission (EC)	P	$28,287,638
7	9	UK Department for International Development (DFID)	P-D	$20,745,063
8	8	United States Agency for International Development (USAID)	P-D	$20,145,652
9	12	UK Medical Research Council (MRC)	P	$16,850,528
10	7	US Centers for Disease Control (CDC)	P	$14,174,564
11	10	AstraZeneca India Private Limited	C	$13,235,259
12	11	US National Health, Lung, & Blood Institute (US NHLBI, NIH)	P	$10,910,625
13	32	India (reported)	P	$9,537,034
14	17	Dutch Ministry of Foreign Affairs-Directorate General of Development Cooperation (DGIS)	P-D	$7,748,586
15	14	Wellcome Trust	F	$7,266,964
16	23	Pfizer	C	$6,538,261
17	16	Canadian Institute for Health Research (CIHR)	P	$6,362,302
18	28	Emergent Biosolutions	C	$4,568,160
19	18	German Federal Ministry of Education (BMBF)	P	$4,561,179
20	15	Company W	C	$4,529,539
21	22	Sequella	C	$4,500,374
22	13	Institut Pasteur	P	$4,263,998
23	31	Sweden (reported)	P	$4,234,028
24	41	South Africa Department of Science and Technology (SA DST)	P	$4,000,000
25	29	Australian National Health and Medical Research Council (Australia NHMRC)	P	$3,827,590
26	19	Company Y	C	$3,800,000
27	21	US President's Emergency Plan for AIDS Relief (PEPFAR)	P	$3,478,567

* New TB R&D Funder
** Previous TB R&D Funder who did not report funding in 2010

Basic Science	Infrastructure/ Unspecified	Diagnostics	Drugs	Vaccines	Operational Research
$56,152,399	$20,567,791	$12,735,889	$35,612,879	$20,945,767	$11,547,354
$10,445,925	$1,000,000	$13,052,604	$25,327,763	$37,225,976	$25,336,167
$0	$0	$0	$65,124,407	$0	$0
$10,602,608	$5,703,018	$1,400,547	$8,661,953	$1,667,539	$12,178,454
$0	$0	$290,000	$30,870,854	$0	$0
$7,392,381	$4,382,631	$1,859,696	$7,079,430	$7,573,500	$0
$0	$0	$2,729,656	$10,436,920	$6,101,584	$1,476,903
$0	$0	$5,022,277	$6,049,692	$0	$9,073,683
$10,577,128	$0	$3,086,584	$2,842,988	$324,949	$18,878
$0	$2,553,014	$1,361,520	$9,827,883	$0	$432,147
$0	$0	$0	$13,235,259	$0	$0
$7,493,040	$610,493	$152,446	$230,944	$409,823	$2,013,879
$1,444,088	$8,021,437	$0	$0	$0	$71,509
$289,738	$0	$3,741,546	$85,230	$3,632,072	$0
$1,210,615	$343,000	$0	$1,261,286	$1,192,170	$3,259,892
$214,360	$0	$0	$6,323,901	$0	$0
$2,201,100	$460,013	$62,069	$2,134,045	$732,010	$773,064
$0	$0	$0	$0	$4,568,160	$0
$1,306,175	$221,650	$370,691	$968,834	$1,665,994	$27,837
$0	$0	$0	$4,529,539	$0	$0
$0	$0	$87,509	$4,412,865	$0	$0
$2,413,982	$0	$433,891	$1,066,726	$349,400	$0
$2,119,465	$120,164	$189,732	$47,433	$284,598	$1,472,637
$0	$0	$0	$4,000,000	$0	$0
$1,529,085	$0	$210,603	$545,557	$326,158	$1,216,186
$0	$0	$3,800,000	$0	$0	$0
$0	$0	$0	$0	$0	$3,478,567

P = Public Sector R&D Agency P-D = Public Sector Development Agency F = Foundation/Philanthropy
C = Corporation/Private Sector M = Multilateral

Appendix 1

Table 4.2

2011 and 2010 Top Reporting TB R&D Funders (continued)

2011 Rank	2010 Rank	Funding Organization	Funder Type	Total
27	21	US President's Emergency Plan for AIDS Relief (PEPFAR)	P	$3,478,567
28	25	UK Health Protection Agency/National Institute for Health Research (UK HPA/NIHR)	P	$3,409,340
29	40	Korea (reported)	P	$3,240,538
30	36	Japan (reported)	P	$3,145,007
31	*	Company Z	C	$3,129,753
32	39	Switzerland (reported)	P	$2,913,245
33	26	Max Planck Institute for Infection Biology (MPIIB)	P	$2,750,000
34	42	Agence Nationale de Recherche sur la SIDA (ANRS)	P	$2,101,728
35	*	Bloomberg Philanthropies	F	$2,000,000
36	43	Norway (reported)	P	$1,958,835
37	*	Canadian International Development Agency (CIDA)	P-D	$1,853,250
39	33	UBS Optimus Foundation	F	$1,615,100
40	34	Eli Lilly and Company	C	$1,500,000
41	27	Sandoz	C	$1,500,000
42	47	US Food and Drug Administration (US FDA)	P	$1,452,570
43	37	Irish Aid - Ireland Development Corporation	P-D	$1,448,690
44	**	German Research Foundation (DFG)	P	$1,434,203
49	46	Carlos III Health Institute	P	$783,279
50	45	Damien Foundation	F	$441,850
51	53	Danish National Advanced Technology Foundation	P	$392,799
52	48	Agence Nationale de Recherche (ANR)	P	$357,778
53	44	Brazilian National TB Program	P	$291,258
54	57	Australian Research Council	P	$246,514

* New TB R&D Funder
** Previous TB R&D Funder who did not report funding in 2010

Basic Science	Infrastructure/ Unspecified	Diagnostics	Drugs	Vaccines	Operational Research
$0	$0	$0	$0	$0	$3,478,567
$310,539	$0	$0	$559,419	$926,638	$1,612,745
$65,100	$400,990	$559,398	$1,029,022	$534,099	$651,929
$0	$0	$1,086,750	$27,500	$0	$2,030,757
$0	$0	$0	$0	$3,129,753	$0
$1,122,678	$0	$0	$0	$0	$1,790,567
$1,350,000	$0	$0	$0	$1,400,000	$0
$110,290	$7,243	$833,989	$1,099,708	$0	$50,497
$0	$0	$0	$0	$0	$2,000,000
$153	$0	$987,580	$0	$591,321	$379,781
$0	$0	$0	$0	$0	$1,853,250
$0	$0	$717,822	$0	$0	$897,278
$0	$0	$0	$1,500,000	$0	$0
$0	$0	$0	$1,500,000	$0	$0
$0	$0	$0	$1,452,570	$0	$0
$0	$0	$0	$1,448,690	$0	$0
$1,434,203	$0	$0	$0	$0	$0
$57,933	$0	$47,181	$22,846	$655,319	$0
$0	$0	$84,024	$198,471	$0	$159,356
$0	$0	$0	$0	$392,799	$0
$232,021	$0	$0	$125,756	$0	$0
$0	$101,528	$0	$0	$0	$189,730
$246,514	$0	$0	$0	$0	$0

P = Public Sector R&D Agency P-D = Public Sector Development Agency F = Foundation/Philanthropy
C = Corporation/Private Sector M = Multilateral

Appendix 1

Table 4.3

2011 and 2010 Top Reporting TB R&D Funders (continued)

2011 Rank	2010 Rank	Funding Organization	Funder Type	Total
56	24	Statens Serum Institut (SSI)	P	$165,062
57	50	Danish Council for Independent Research | Medical Sciences	P	$140,749
58	51	Netherlands Organization for Health Research and Development (ZonMw)	P	$139,536
59	62	GSK Biologicals	C	$129,493
60	63	World Health Organization (WHO): Stop TB Partnership	M	$125,000
61	54	Bio Duro, LLC	C	$120,000
63	**	KNCV Tuberculosis Foundation	F	$89,186
64	64	FIT BIOTECH	C	$72,435
65	65	Fondation Merieux	F	$72,435
66	59	Gulbenkian	F	$72,435
68	**	Pan American Health Organization (PAHO)	M	$70,000
71	20	World Health Organization (WHO)	M	$58,543
73	67	European Centre for Disease Prevention and Control (ECDC)	P	$44,667
78	**	Colombian Department for Science and Technology (COLCIENCIAS)	C	$12,000
79	55	Corporate Donors to TB Alliance	C	$5,581
		New Funders Under $500K		$349,523
		Grand Total		**$649,648,183**

* New TB R&D Funder
** Previous TB R&D Funder who did not report funding in 2010

Basic Science	Infrastructure/ Unspecified	Diagnostics	Drugs	Vaccines	Operational Research
$0	$0	$0	$0	$165,062	$0
$0	$0	$0	$0	$140,749	$0
$0	$0	$139,536	$0	$0	$0
$0	$0	$0	$0	$129,493	$0
$0	$0	$0	$125,000	$0	$0
$0	$0	$0	$120,000	$0	$0
$0	$0	$0	$89,186	$0	$0
$0	$0	$0	$0	$72,435	$0
$0	$0	$0	$0	$72,435	$0
$0	$0	$0	$0	$72,435	$0
$0	$0	$0	$0	$0	$70,000
$0	$13,964	$0	$0	$0	$44,579
$0	$44,667	$0	$0	$0	$0
$12,000	$0	$0	$0	$0	$0
$0	$0	$0	$5,581	$0	$0
$27,900	$66,242	$0	$58,741	$164,091	$32,550
$120,361,419	**$44,617,845**	**$55,043,541**	**$250,038,877**	**$95,446,326**	**$84,140,175**

P = Public Sector R&D Agency P-D = Public Sector Development Agency F = Foundation/Philanthropy
C = Corporation/Private Sector M = Multilateral

Appendix 2

FIGURE 13

TB R&D Funders Ranked 1-12 That Invested Above $500,000 USD & Funders That TAG Has Tracked in Previous Years: 2005-2011

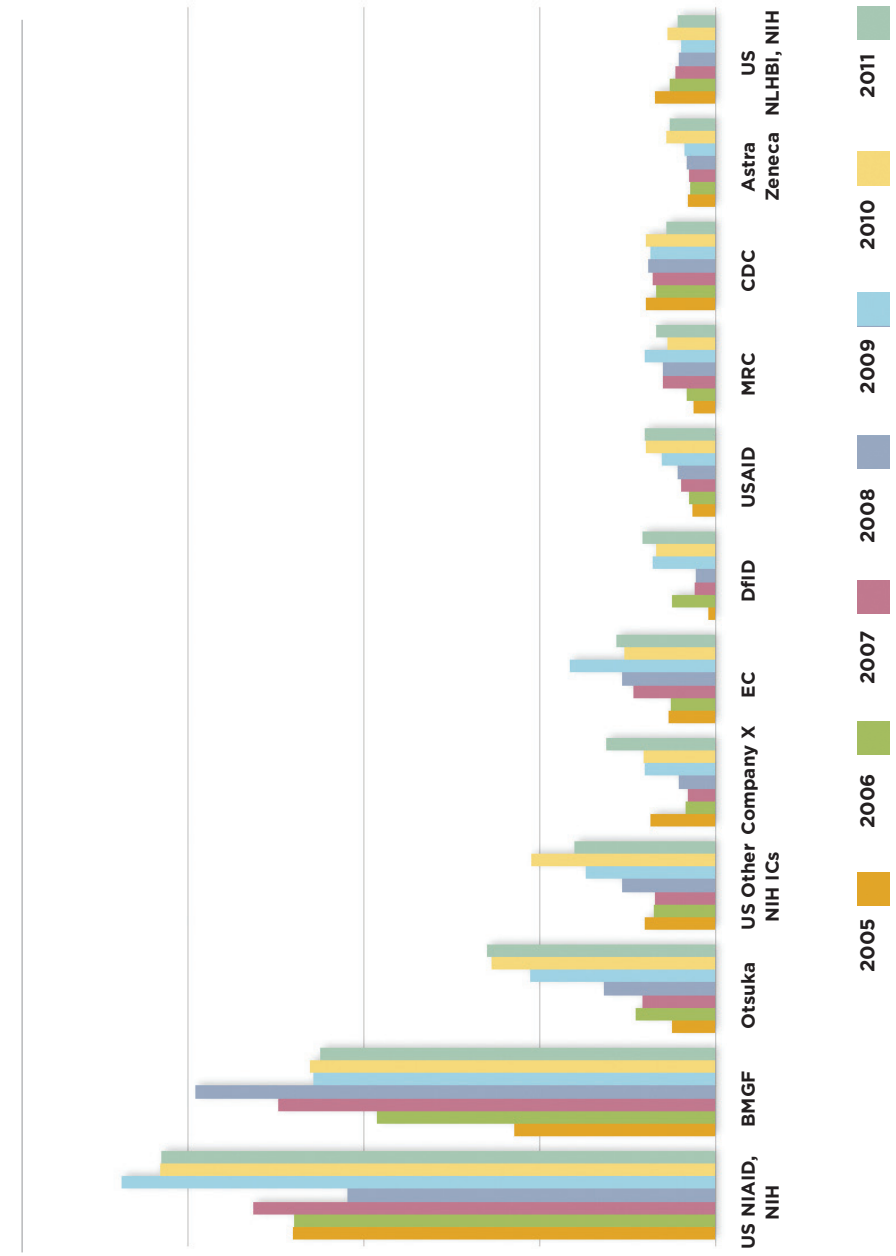


FIGURE 14

TB R&D Funders Ranked 13-24 That Invested Above $500,000 USD & Funders That TAG Has Tracked in Previous Years: 2005-2011

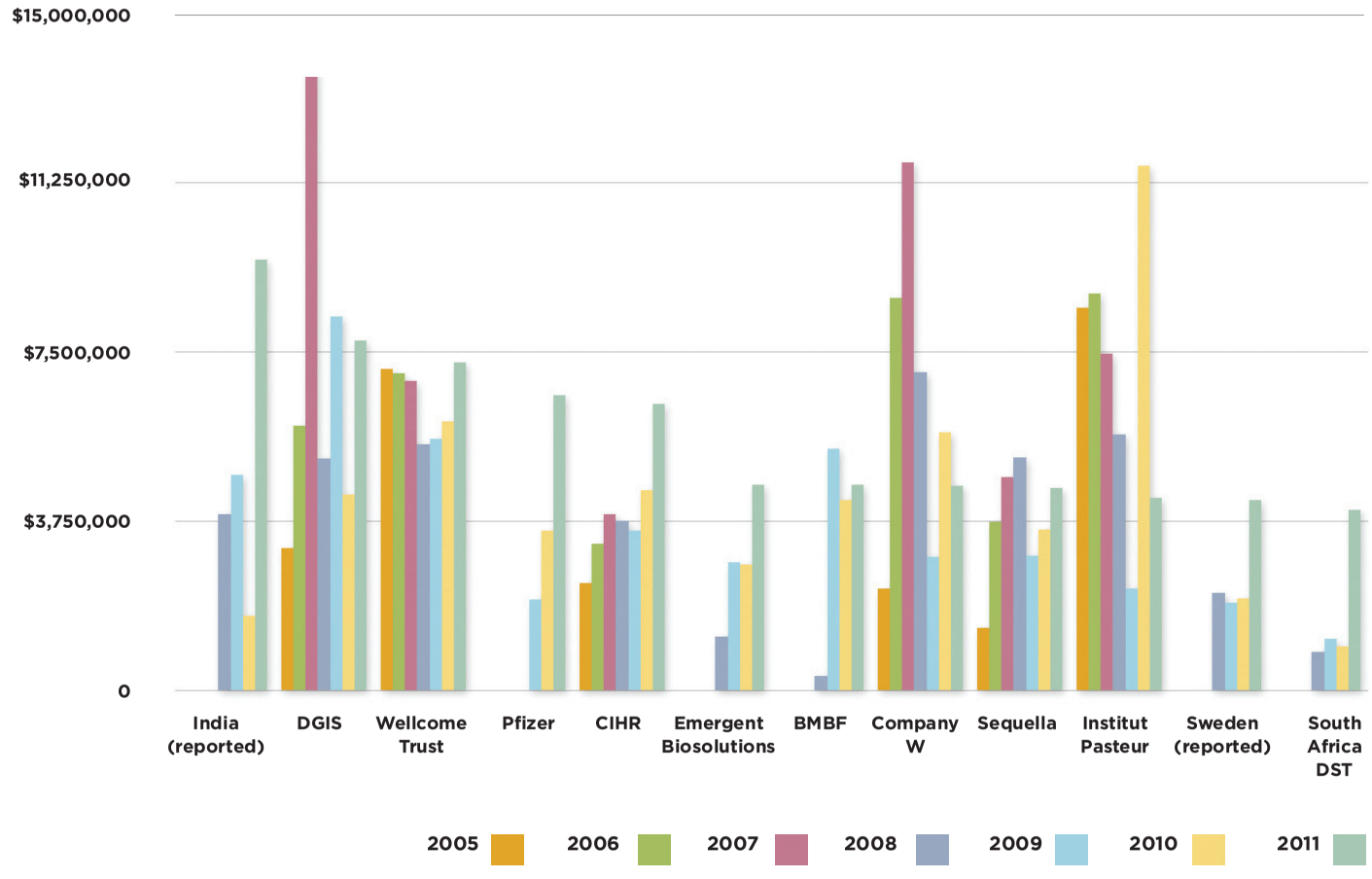


FIGURE 15

TB R&D Funders Ranked 25-35 That Invested Above $500,000 USD & Funders That TAG Has Tracked in Previous Years: 2005-2011

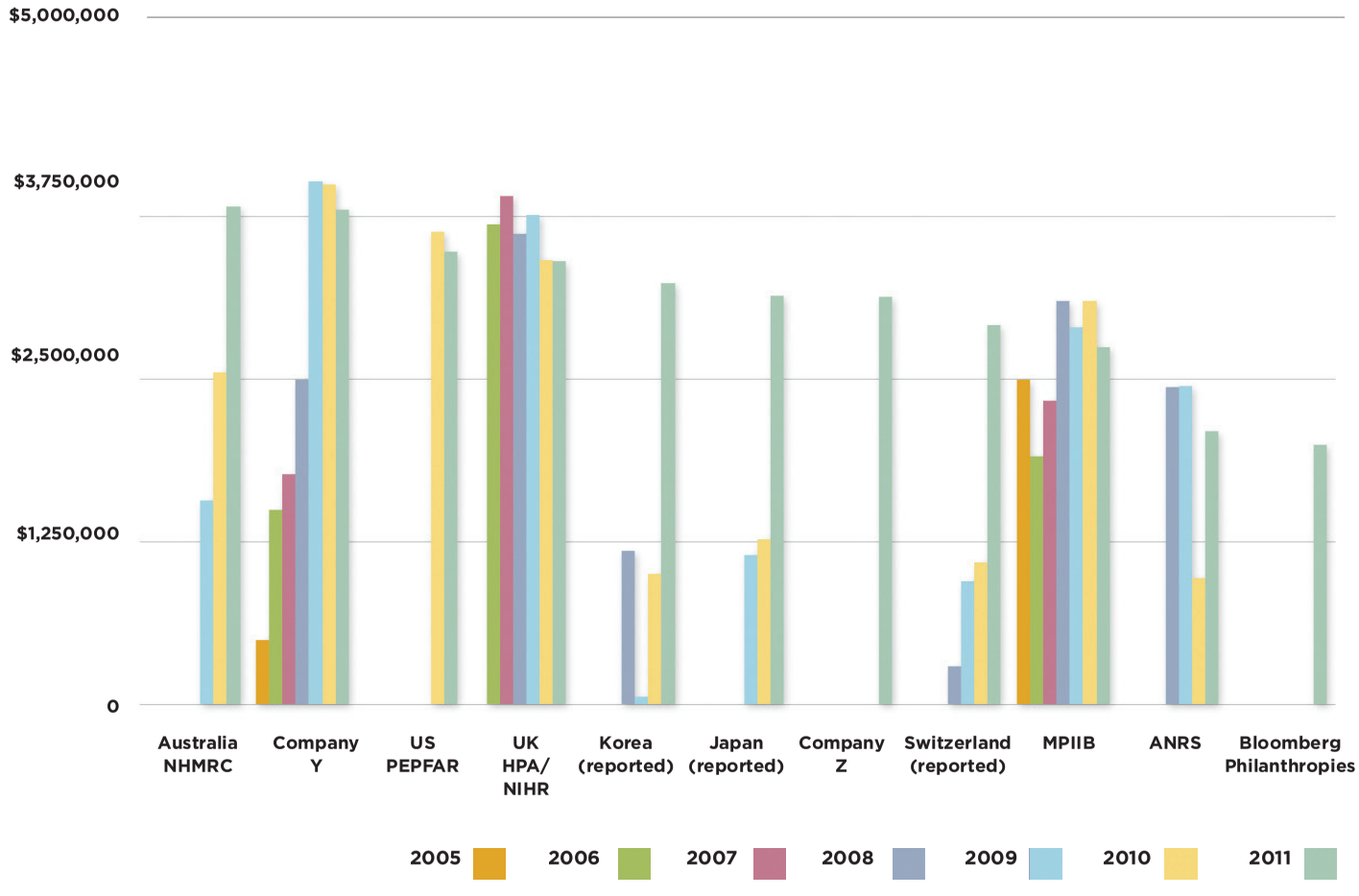


FIGURE 16

TB R&D Funders Ranked 36-49 That Invested Above $500,000 USD & Funders That TAG Has Tracked in Previous Years: 2005-2011

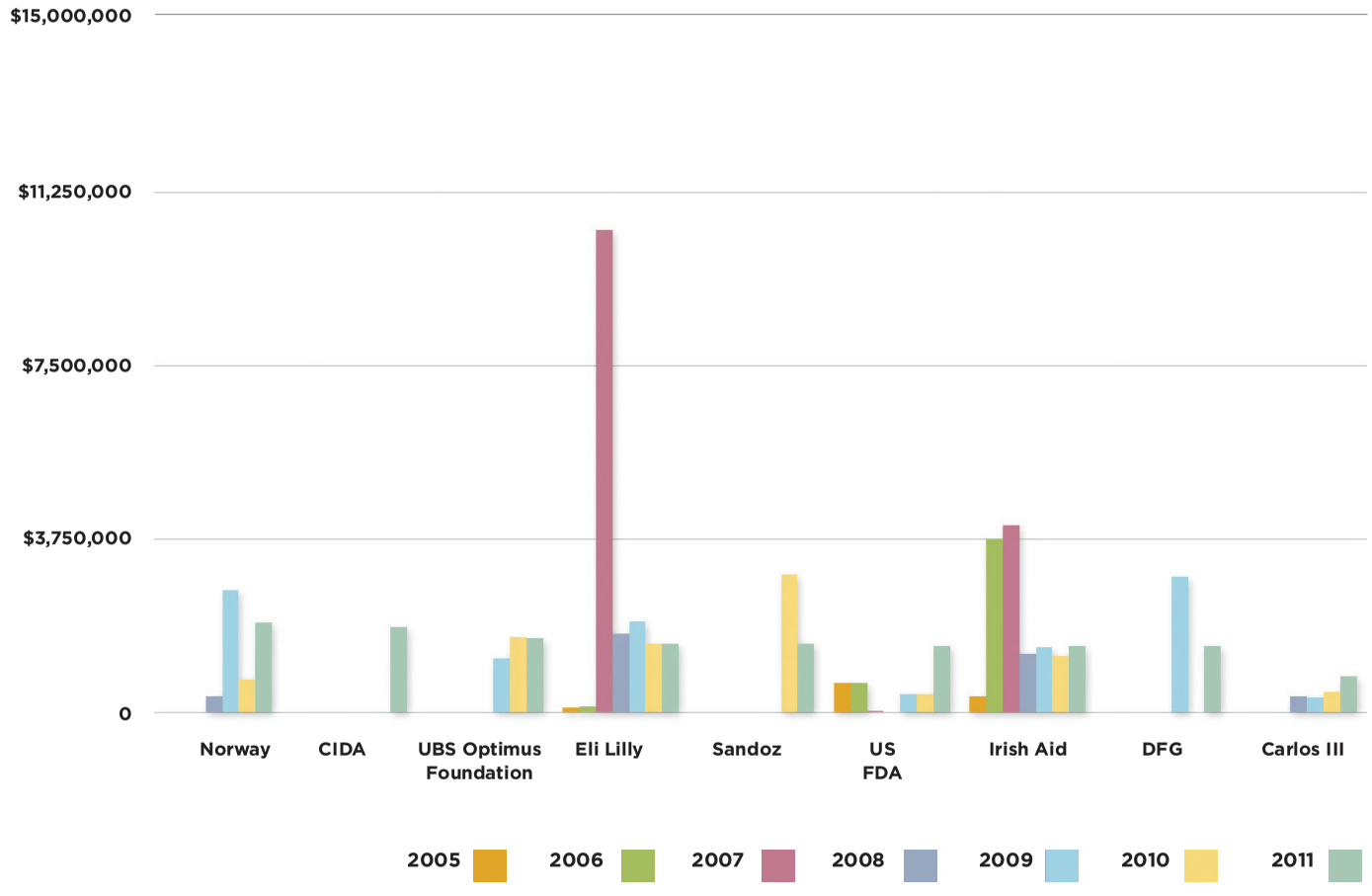


FIGURE 17

TB R&D Funders Ranked 50-62 That Invested Less Than $500,000 USD & Funders That TAG Has Tracked in Previous Years: 2005-2011

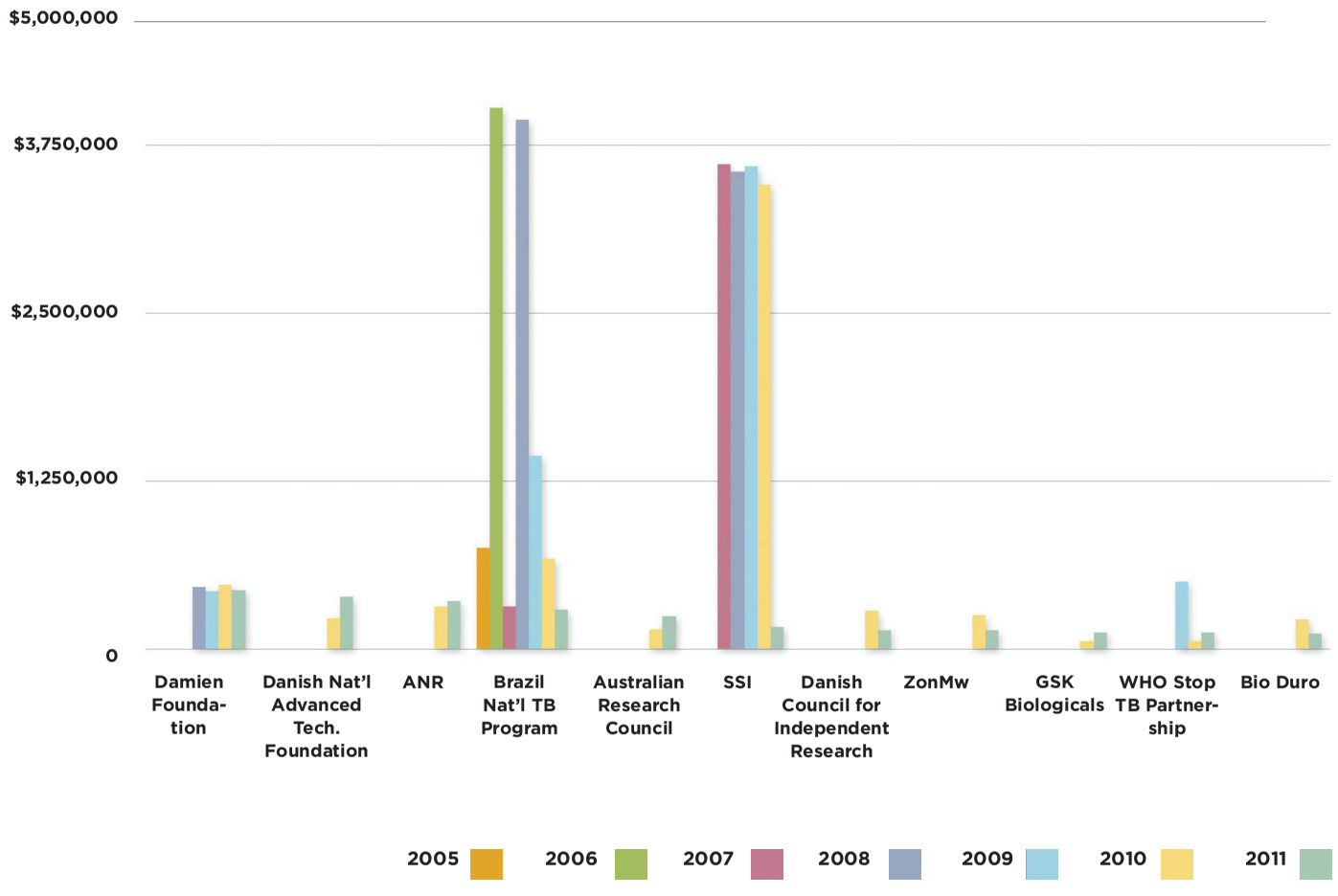


FIGURE 18

TB R&D Funders Ranked 63-79 That Invested Less Than $500,000 USD & Funders That TAG Has Tracked in Previous Years: 2005-2011

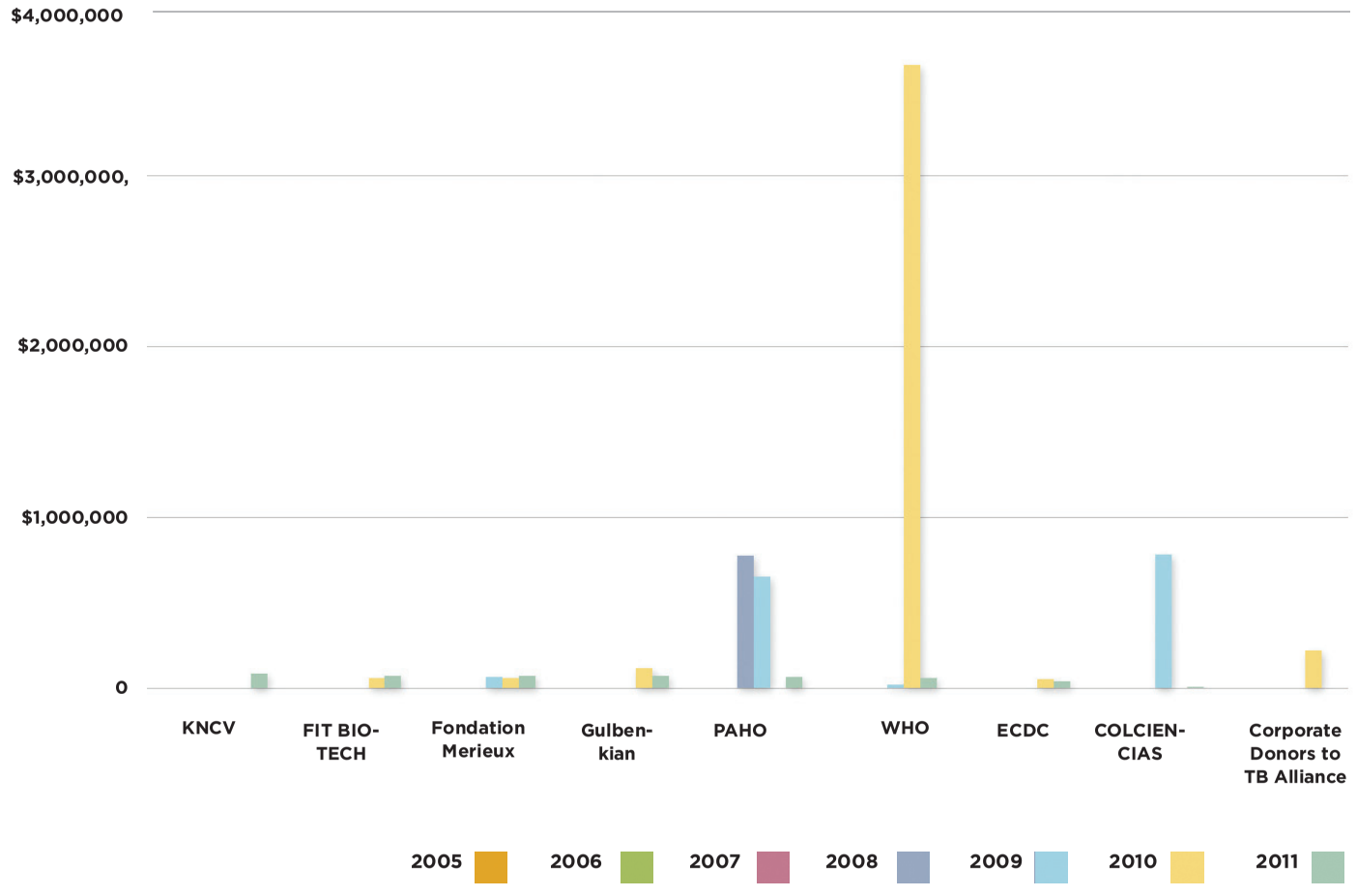


FIGURE 19

TB R&D Funders Inactive or Unresponsive in 2011, 1-12

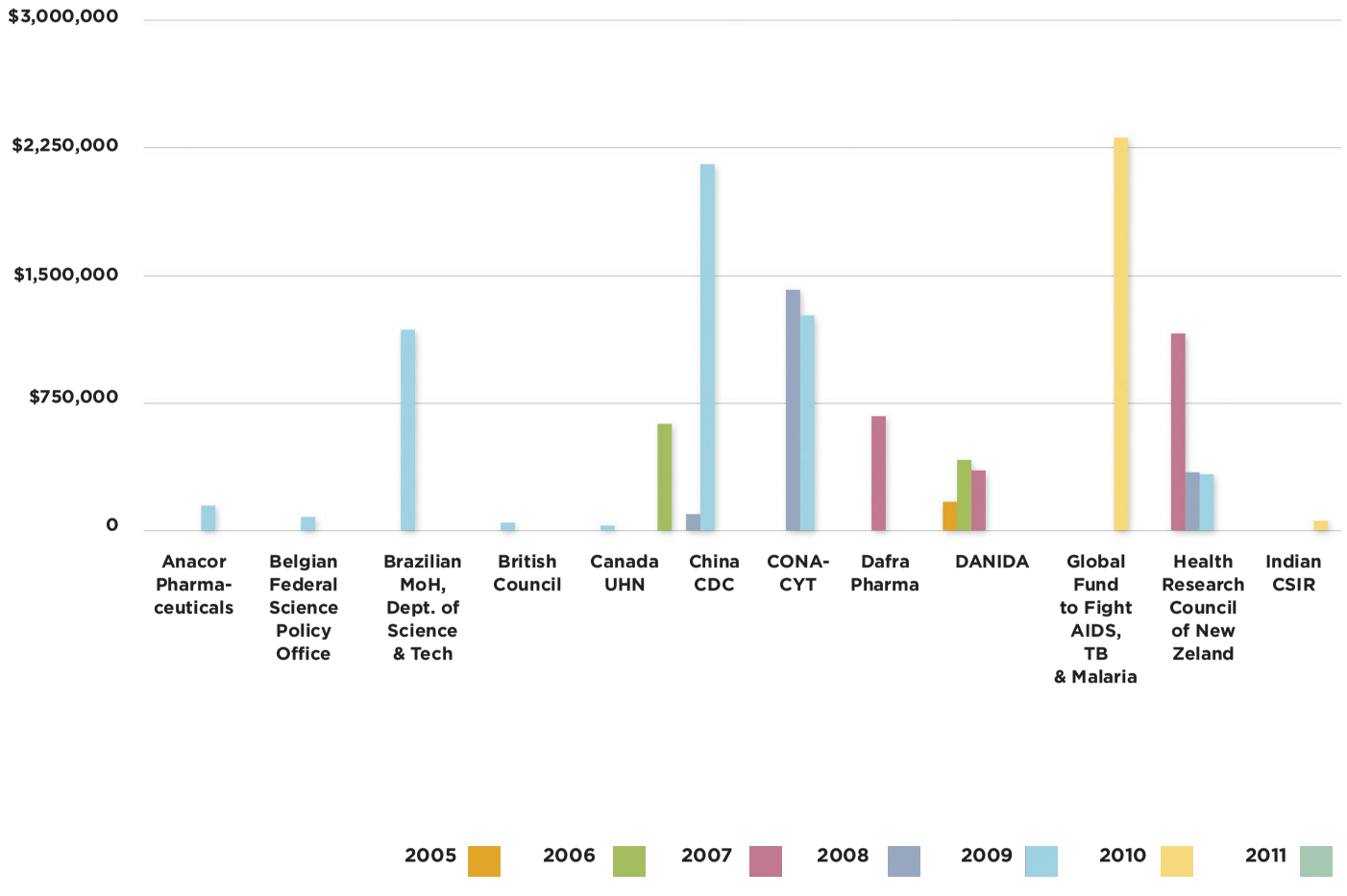
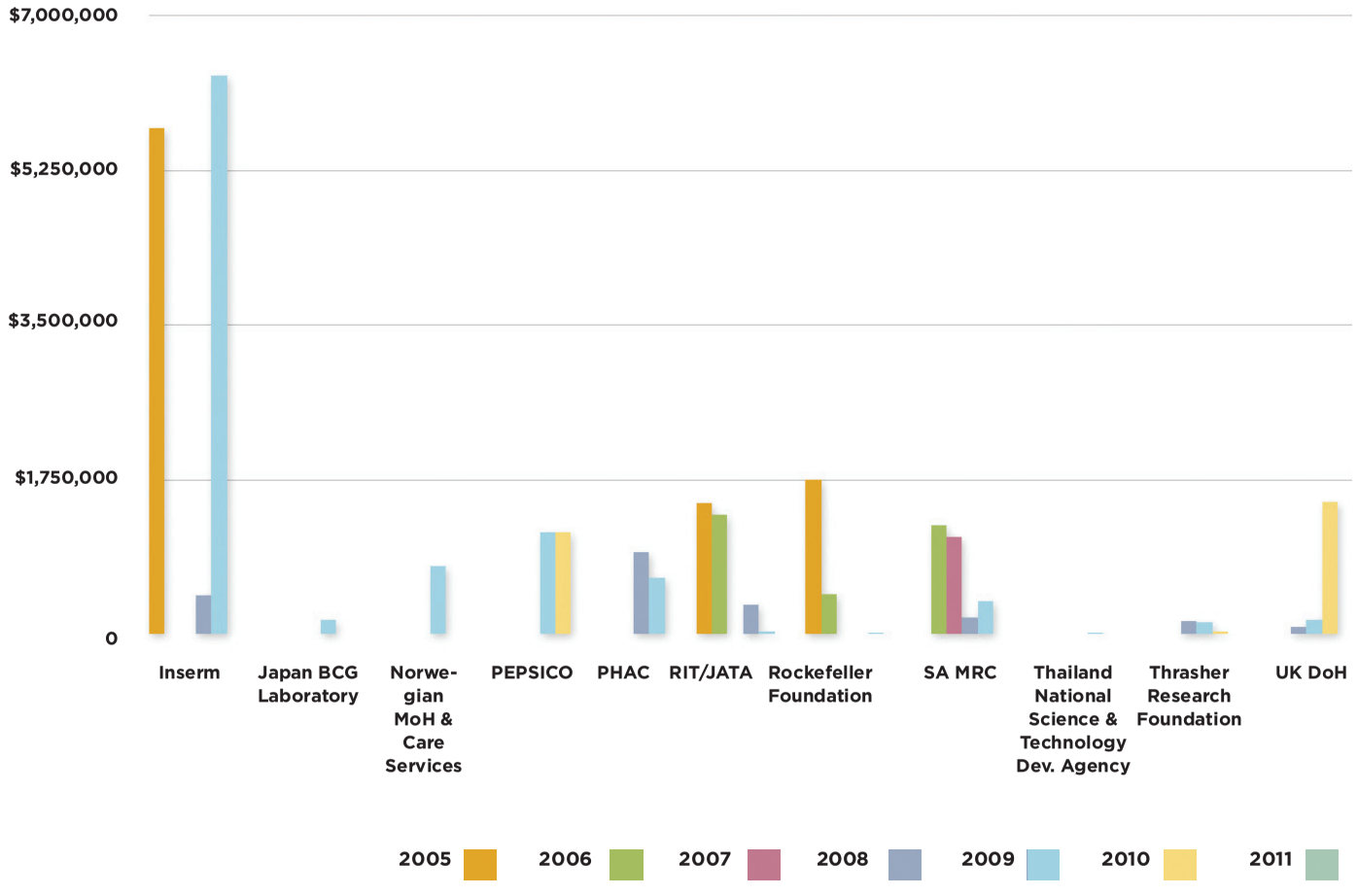


FIGURE 20

TB R&D Funders Inactive or Unresponsive in 2011, 13-24



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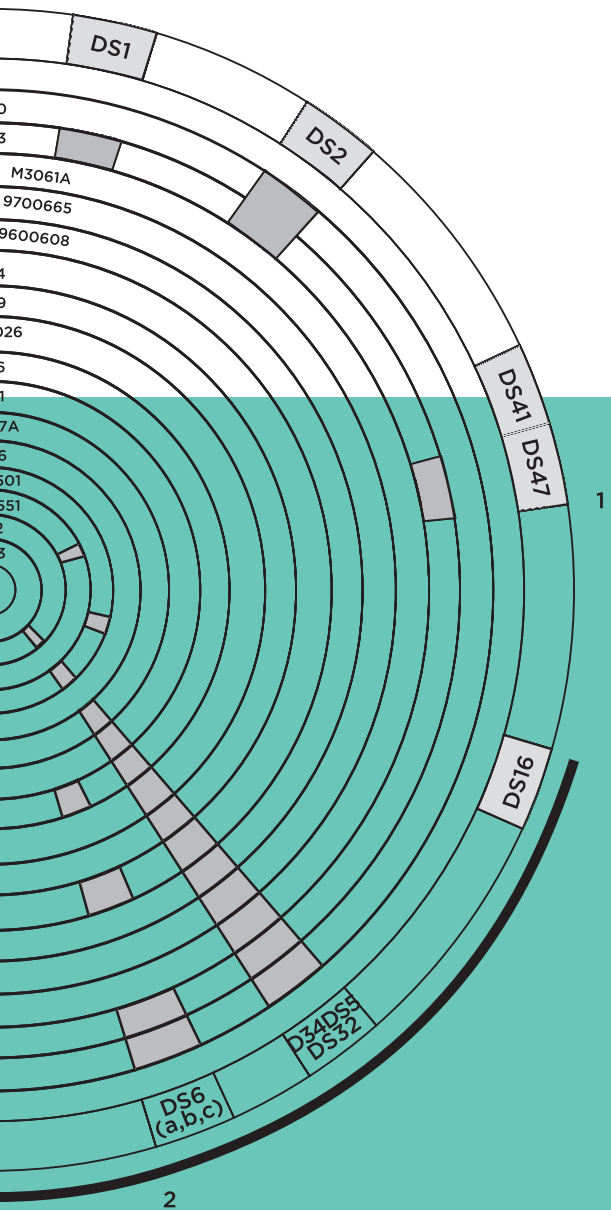

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