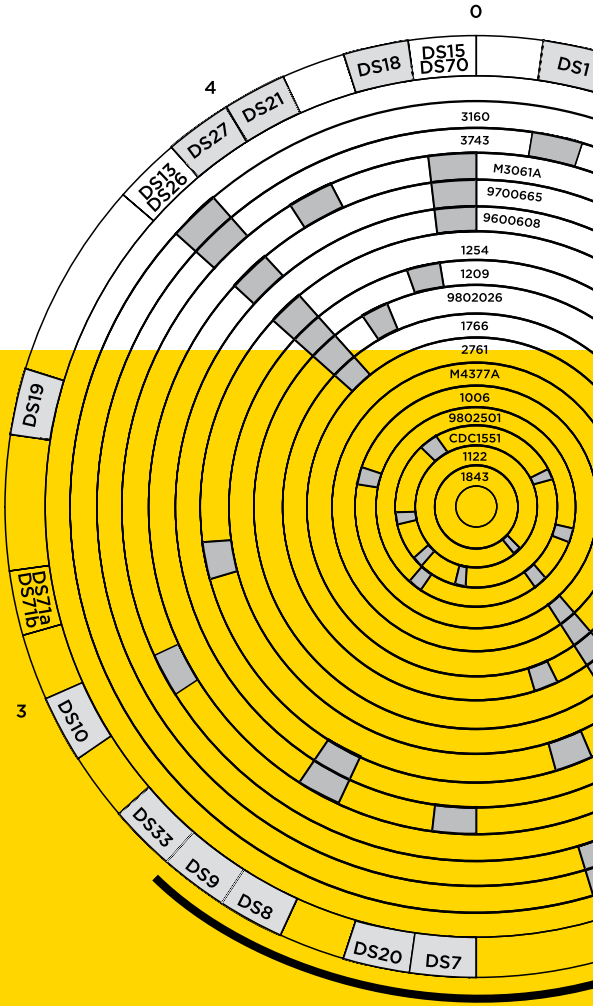
TAG
Treatment Action Group

Stop TB Partnership

TUBERCULOSIS RESEARCH
AND DEVELOPMENT:

2009 Report on Tuberculosis Research Funding Trends, 2005–2008

2ND EDITION



MARCH 2010

TREATMENT ACTION GROUP

Acknowledgements

Special thanks to the Stop TB Partnership for their collaboration and support of this project. Thanks to G-FINDER (Global Funding of Innovation for Neglected Diseases), a project of the George Institute and to all the TB R&D donors who provided information for this report; to the Bill & Melinda Gates Foundation for supporting Treatment Action Group's TB/HIV Advocacy Project; and finally, thanks to TAG's board of directors, staff, consultants and supporters who motivate and enable our work.

TAG's Mission

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

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

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Executive Summary

This is an update to Treatment Action Group's 2009 report on funding trends for tuberculosis (TB) research and development (R&D) from the baseline year 2005 through 2008, the last year for which full data are reported. This edition includes updated information about the R&D investments of the Bill & Melinda Gates Foundation, the Research Institute of Tuberculosis, Japan Anti-TB Association (JATA) and the Japanese government.

Our purpose remains to document the world's progress against the benchmark goals set forth by the Stop TB Partnership in the *Global Plan to Stop TB: 2006–2015* and in TAG's original report, which called for an increase in TB R&D spending to $2 billion per year, which will be required to eliminate TB by 2050.

For the 2009 report, TAG undertook this research tracking effort in conjunction with the Stop TB Partnership, and the George Institute's G-FINDER project to track Global Funding of Innovation for Neglected Diseases. In part, as a result of these partnerships, this years report tracks a larger number of donors than previously reported by TAG.

Here we report that in the year 2008, the top 71 reporting organizations invested a total of $491.5 million in TB R&D. This is a 4% increase over the 2007 total of $474 million—revised from the previously reported $483 million and a 38% increase in four years over the baseline year of 2005. While the absolute number continues to grow, the slow and steady pace of the increase is insufficient to achieve research investment levels needed to produce the new knowledge and tools that will be critical to eliminating TB.

Of the $491.5 million reported to TAG by the 71 investors in TB R&D in 2008, $265 million (54%) came from the public sector, $155 million (31%) from the philanthropic sector, and $72 million (15%) from the private sector.

Public-sector investment continued to decrease relative to total investment from nearly 65% in 2005 to 54% in 2008. Philanthropies—almost entirely represented by the Bill and Melinda Gates Foundation—made up the largest increase in proportion to total investment rising from 24% in 2005 to 30% in 2008. Private-sector investment rose slightly from 12% of total investment in 2005 to 15% in total investment in 2008.

In 2008, for the first time since TAG began reporting, the Gates Foundation outstripped the U.S. National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH) as the biggest funder of TB R&D at $148 million compared with NIAID's $105 million. The NIH as a whole spent $188 million on TB R&D in 2007 and just $142 million in 2008 according to recently revised estimates published by the NIH in "Estimates of Funding for Various Research, Condition, and Disease Categories" (http://report.nih.gov/rcdc/categories/; accessed on 26 October 2009). NIH investment in TB R&D may recover in 2009–2010 due to the American Relief and Recovery (economic stimulus package) Act of 2009, but will then fall back in 2011 unless the overall NIH budget increases substantially.

Investment in basic science decreased from 24% of TB R&D investment in 2007 to 20% at $99 million in 2008. Most publicly funded institutions that traditionally support basic research suffered from the economic crisis. The NIH supported 56% ($56 million) of global investment in basic science on TB in 2008, with 40% of it ($40 million) coming from NIAID alone.

Diagnostics research continues to be underfunded. The world only invested $50 million in this area of research in 2008, an embarrassingly slight increase from 2007's $42 million. In 2008 TB diagnostics R&D received just 10% of TB R&D funding.

For the fourth year, TB drug development received the greatest investment, 35% of the total, and had the most funders (over 28) of any research category. This area is showing great promise, with two drugs from entirely new classes advancing into phase 2 studies to treat drug-resistant TB, and phase 3 studies ongoing with fluoroquinolones for treatment shortening of first-line therapy. However, current infrastructure remains grossly insufficient to carry out further phase 3 and postmarketing studies of new TB drugs.

Inadequate funding for TB vaccine R&D has been a concern in past reports, but this area received a significant increase in funding last year, rising from 15% to 22% of the total TB R&D investment in just one year. Most of the increase was attributable to a large grant from the Gates Foundation to the Aeras Global TB Vaccine Foundation.

Investment in operational research remained flat in 2008 at $34 million, nearly the same as in 2007. This category is crucial to support studies that integrate new and

existing tools and knowledge into TB programs and to document their impact at the programmatic, national, and population levels. Insufficient funding for operational research will severely delay implementation of new and better tools.

In this report we are able to document significant or growing contributions to TB R&D from emerging economies with high TB-burden such as Brazil, China, India, South Africa, and South Korea. We are encouraged by their growing investment in TB, a disease that exacts such a high toll on their people and their economies.

Every year sponsors of TB research report a series of common concerns that the continued but anemic growth of R&D investment has failed to mitigate:

- There is need for increased basic science research as there are critical deficiencies in the understanding of pathogenesis of TB.
- Funding for TB R&D is grossly inadequate relative to its impact in terms of disease and death it causes.
- The lack of research capacity in areas of the world where the disease is common hinders rapid progress.
- Linked to the need for increased basic science research in particular is the lack of useful biomarkers that can be used to diagnose TB, provide a prognosis, and monitor the impact of vaccination or treatment.

In 2008, the TB research community was on the cusp of some major scientific breakthroughs. For the first time in nearly 40 years two new classes of TB drugs were close to entering phase 3 clinical trials. There was movement in the areas of genomics, biomarkers, and antigen research that, if coordinated, could yield a first generation point-of-care TB diagnostic test within a few years. However, current funding levels and research capacity and infrastructure are inadequate to conduct the studies needed. The trends that TAG documents in this report demonstrate the urgency of greater political leadership among policy makers, donors, researchers, and activists to increase the level of funding, address the bottlenecks in TB R&D, and fulfill the promise that the recent progress has made possible.

TABLE 1

2008 TB R&D Funders

2008 Rank	Institute	Total
1	Bill & Melinda Gates Foundation (BMGF)	147,827,264
2	US NIAID, NIH	104,645,069
3	Otsuka Pharmaceutical Company	31,769,216
4	European Commission Framework 6/7	26,744,573
5	US other institutes & centers, NIH	26,472,839
6	US Centers for Disease Control & Prevention (CDC)	19,097,813
7	UK Medical Research Council (MRC)	14,941,234
8	USAID	10,925,000
9	Company X	10,640,454
10	US NHLBI, NIH	10,439,385
11	AstraZeneca	8,300,000
12	Company Z	7,050,000
13	Institut Pasteur	5,665,271
14	UK Department for International Development (DFID)	5,583,287
15	Wellcome Trust	5,446,998
16	Sequella, Inc	5,157,298
17	Netherlands Ministry of Foreign Affairs (DGIS)	5,140,858
18	Brazil (aggregate)	3,940,014
19	India (aggregate)	3,907,318
20	Canadian Institute of Health Research	3,766,005
21	UK Health Protection Agency (HPA)+	3,614,697
22	Statens Serum Institute	3,550,643
23	Germany, Max Planck Institute for Infectious Biology	3,100,000
24	Company Y	2,500,000
25	Agence Nationale de Recherche sur le SIDA (ANRS)+	2,441,454
26	Italian Ministry of Health+	2,176,718
27	Sweden (aggregate)	2,167,769
28	Eli Lilly Foundation	1,700,000
29	Consejo Nacional de Ciencia y Tecnologia (CONACYT - Mexico)+	1,418,997
30	Irish Aid	1,262,674
31	Emergent Biosolutions (including Microsciences and Antex Biologicals Inc)+	1,196,000
32	South Korea (aggregate)	1,179,803
33	Japanese Government+	1,128,700
34	Public Health Agency of Canada+	927,328
35	South African Department of Sciences and Technology (DST)+	853,533
38	Inserm+	441,227
40	New Zealand, Health Research Council+	346,379
42	Research Institute of Tuberculosis, Japan Anti-TB Association (JATA)	340,660
45	Swiss Agency for Development and Cooperation	245,525
47	South Africa Medical Research Council (SA MRC)+	188,121
49	Anda Biologicals	127,818
50	China CDC National Tuberculosis Reference Laboratory+	100,000
54	KNCV Tuberculosis Foundation	39,450
	(New Funders under $500,000 (ranked 36-37,39,41,43-44,46,48,51-53,55-60)	2,969,526
		491,476,917

Note: + Funders reporting to G-FINDER whose investments TAG has not been able to corroborate.

FIGURE 1

Total TB R&D Funding: 2005–2008

1. Introduction

1.1 The Importance of TB R&D Resource Tracking

In its fourth year of publication, this report highlights the deficiencies in tuberculosis (TB) research and the critical need for increased funding. The year-on-year data collection continues to create an evidence base with which to analyze the resources available, as well as the gaps in funding needed to meet the Stop TB Partnership and Millennium Development Goals to reduce TB incidence and death by 50% by 2015 relative to 1990 levels and to eliminate TB as a global public health threat by 2050.

Whereas in past years TAG collected all data for these reports by itself, for this report, TAG undertook this research tracking effort in conjunction with the Stop TB Partnership, and the George Institute's G-FINDER project to track Global Funding of Innovation for Neglected Diseases. Both the Stop TB Partnership and G-FINDER provided TAG with useful data for 2008, and we thank them for their contribution.

1.2. Background

Starting in 2006, TAG documented global annual spending on TB R&D the year preceding the launch of *The Global Plan to Stop TB 2006–2015*. The 2006 TAG report established a baseline for TB R&D funding to enable analysis of future trends and raise awareness of funders responsible for distributing R&D resources and to inform activists whose lives were affected by these funding decisions. In each subsequent publication, TAG has endeavored to more accurately represent the data, include previously missing data, and correct data that was misreported in previous years.

The TAG report has become the reference standard for TB R&D investment tracking and is widely cited in peer reviewed literature and at international scientific conferences. Most recently, in July 2009, data from TAG's most recent report was cited by Dr. Anthony S. Fauci, Director of NIAID, at the meeting "HIV/TB Research: Innovation, Funding and Networking" held in conjunction with the Fifth International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment, and Prevention in Cape Town, South Africa.

1.3. Objectives

TB killed 1.7 million people in 2007, with 456,000 deaths—nearly a quarter—among people with HIV. Though when properly diagnosed TB is usually curable, the most commonly used diagnostic test, sputum-smear microscopy, fails about half the time it is used, and is even less accurate in people with HIV and in children. While TB treatment can cure 95% of drug-sensitive cases, treatment lasts for at least six months and is contraindicated with several commonly used HIV medications. TB diagnosis and treatment are particularly challenging in people living with HIV, people with drug-resistant TB, and pediatric cases—all situations that increase the risk of TB mortality. The programmatic need for research and development for new TB tools is well documented. The goal of this report is to provide an evidence base that can be used by all stakeholders in TB research and public health to advocate for increased R&D resources.

Data from this report have been used to track how the global investment in TB R&D measures up against the resource needs in the *Global Plan*. In part, due to TAG's highlighting of the urgent need for comprehensive research that includes basic science and operational research, the *Global Plan* research goals are currently being revised. The new research plans, with their accompanying evidence-based budget estimates and targets, are due to be published by the Stop TB Partnership in September 2010. Future publications of this report will continue to track annual investments against the revised research goals, which are likely to more closely resemble TAG's recommendation of $2 billion needed in TB R&D investment per year.

1.4. Methodology

This year, TAG collaborated with the Stop TB Partnership and G-FINDER to ensure a coordinated and comprehensive data tracking effort. To minimize reporting fatigue and yet maintain a high level of data accuracy, if a funder was already tracked by G-FINDER, TAG sent a survey to independently confirm the data as well as to request operational research information. Funders not reported by G-FINDER were contacted directly by TAG. Unlike in previous years, NIH data were not supplied by the individual institutes and centers (ICs), but were taken from the Research, Condition, and Disease Categories (RCDC) database previously mentioned. When we were not able to independently corroborate all data received by G-FINDER, we have so indicated.

TAG used an e-mail survey to solicit information from funders and recipients about actual annual disbursements (in contrast to commitments or awards) for TB research

during the calendar year 2008. The survey also collected information about future commitments, the amount of funding an institution disbursed or received, grant portfolios describing the research, and qualitative responses about priorities and obstacles in TB research.

All efforts were made to include institutions tracked since 2005 to allow for accurate trend analysis. Unfortunately, ten previously reporting institutions did not provide data for 2008. This year, in part due to collaboration with the Stop TB Partnership and G-FINDER, TAG is able to report on 28 funders previously not included in this report.

Of the 128 potential research donors or recipients queried, 78 reported on at least one year, but only 29 provided data for each of the four years, 2005–2008. The top 20 donors in 2008, which contributed more than 90% of the total funding, have been tracked for all four years.

G-FINDER, a project of the George Institute for National Health, tracks investment in basis science and new product development (but not operational research) on TB along with 29 other neglected diseases. This year TAG worked closely with G-FINDER to coordinate data collection efforts, and to share contacts and data. The data collected by G-FINDER differs in scope and classification structure from the methods used by TAG, and G-FINDER's methodology differs from TAG's in several ways: it does not include operational research, it does not report disaggregated contributions by individual private-sector companies, and it does not publish a complete dataset of TB R&D data organized by donor, by donor sector, by research category, or by charting investment trends year-to-year back to 2005. TAG's methodology reports institutional investments as reported by the original source funder, names the funding institutions (except for those companies wishing to remain anonymous), and covers the entire spectrum of research. TAG hopes that the comprehensive data included in this report will complement other resource tracking efforts as it provides critical information that can be used to inform research policy and advocacy.

1.5. Limitations of the Data

Over the past four years TAG has been able to continually improve the accuracy of the data tracked. However, several factors continue to impede a complete and fully accurate analysis of funding trends:

- Certain funders declined to provide data, preventing thorough tracking of funding levels and multiyear trends.

- Some funders have difficultly in separating commitments from disbursements or in apportioning multiyear grants into single years. In a few instances these funders asked that multiyear grants simply be divided by the number of years the grants covered; this does not always accurately align with actual disbursements. In other instances some funders that had given one grant to cover multiple diseases or research areas were unable to disaggregate their investment to the level of granularity that TAG requested. In these situations TAG asked these funders to estimate or contacted the grant recipient to collect the level of annual disbursement for TB and then confirmed this amount with the original funder.

- Sometimes the funder was aware that it was funding TB R&D but was not able to share its data with us. The Global Fund for AIDS, TB, and Malaria is one such instance. TAG regrets not being able to document the Global Fund's investment in operational research for the past two years.

- Most privately held companies that were surveyed declined to reveal their investments, despite the fact that they had the option to retain anonymity.

The data collected by G-FINDER followed a different classification structure than the one used by TAG. For the top 20 nonindustry funders, G-FINDER sought and gained approval to share the funders' complete grant portfolio allowing TAG to reclassify grants and identify operational research. However, for the funders not in the top 20, TAG received only the breakdown of funds according to G-FINDER's different classification scheme. Thus, we could confirm the data only for those institutions that completed the TAG survey. Where an institution did not complete the survey, operational research data may be missing.

An exception to the top 20 funders methodology is the analysis of the NIH. In 2008 the NIH announced a new policy stating that the only grant data it would release would be through the RCDC database. Whereas in previous years TAG was able to verify data directly with the different NIH institutes, this year TAG accessed grant information from the public database. As the RCDC website acknowledges, the revised method, which is computer generated rather than reported by the highly skilled NIH staff, produced an estimated investment by NIH of $188 million in 2007, compared with the historical method's $166 million—a highly disturbing $22 million discrepancy. The story only gets more confusing with the RCDC database's estimated 2008 investment of $142 million, which represents either a $24 million decrease (according to the historical method) or a whopping $46 million decrease (using the revised method) in 2008 when compared with 2007. We hope that recent trends in NIH funding such as the stimulus investments for 2010–2011 received as part of the American Recovery and

Reinvestment Act (ARRA) of 2009 will reverse this dismaying trend in US NIH funding overall, and for TB in particular. More systemically, we hope that public sector funding for TB R&D will grow rather than shrink, as it is particularly crucial, especially for basic science and operational research, and also provides infrastructure for development of new tools and new knowledge.

TAG hopes the specificity of data from the RCDC database will improve as coding of investments and the algorithms used for searching disease specific investments become more sophisticated. Current limitations include:

- The search function only allows one-word searches, and this prevents tracking multidisease grants (i.e., "Tuberculosis" not "Tuberculosis" and "HIV").

- The grants are double counted in their full amounts if they are multidisease grants (previously they were proportionately allocated by disease).

For all of the reasons mentioned above, the data reported are imperfect and incomplete, despite our best efforts. Some institutions, both public and private, did not provide complete data. In addition, how institutions tracked and reported their data has also changed in some instances. Nevertheless, most of the major sponsors of TB R&D are likely included in this report.

1.6. Corrections

Since 2005, the Wellcome Trust has reported commitments instead of disbursements. This has inflated its position in our ranking in previous years. However, figures in this report not only reflect accurate disbursements for 2008 but also correct the Wellcome Trust's figures for previous years. We are grateful to the trust for providing us with updated and accurate disbursement data for 2005–2008.

For 2007, we reclassified $11.7 million for Novartis. This amount that was classified as infrastructure/unspecified in the previous report has been correctly attributed to TB drug discovery in this report.

Since printing the first edition of this report in November of 2009, TAG has received updated information about the R&D investments of the Bill & Melinda Gates Foundation, the Japanese Government, and the Research Institute of Tuberculosis, Japan Anti-TB Association (JATA). All charts, graphs, and tables reflect these changes.

2. Results

2.1. Research Investment Categories

Scientific grants and research programs focusing on *Mycobacterium tuberculosis* (M. Tb.) and tuberculosis (TB) disease are categorized according to the descriptions below. We do not cover research on other mycobacteria such as *M. avium* or *M. leprae*; however, *M. africanum* and *M. bovis* are included, as genetically, they are part of the M. Tb. lineage.

- **Basic research**: undirected, investigator-initiated research that aims to uncover fundamental knowledge about M. Tb. and other closely related organisms.

- **Applied, preclinical, infrastructure, or otherwise unspecified**: research that the donor or funder was 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 tuberculosis disease (including prophylaxis, latent TB, and active TB).

- **Vaccines**: preclinical or clinical research on TB vaccines.

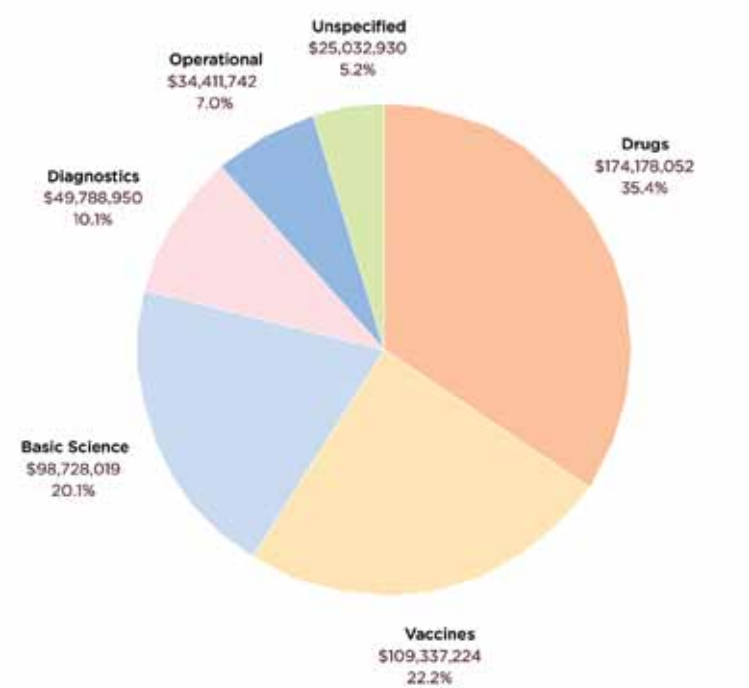
- **Operational research**: includes randomized controlled studies of existing interventions or targeted evaluation of new or existing interventions. Epidemiological studies are also included in this category.

TAG's data and analysis provide a more complete understanding of global investment trends on TB R&D from 2005 to 2008. The data represent individual organizations, donor categories, and research categories and tracks trends in each of these categories over the past four years.

FIGURE 2

TB R&D Investment by Research Category: 2008

$491,476,917



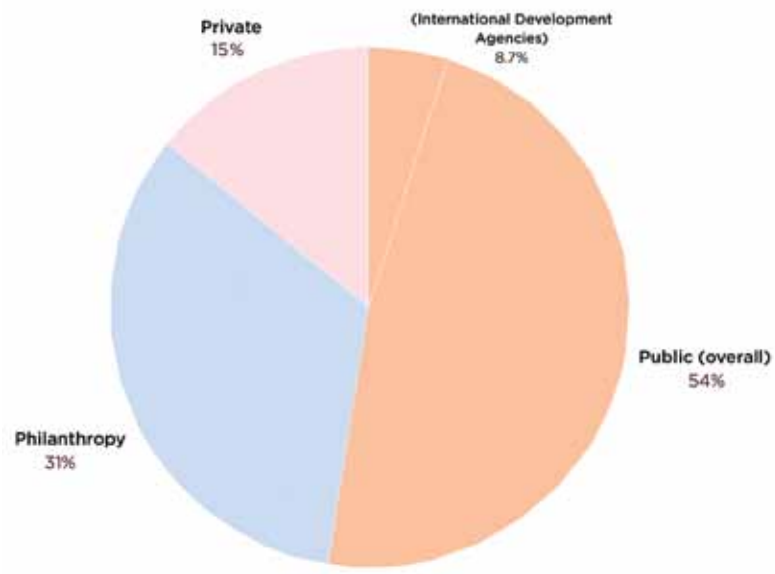
2.2. Donor Categories

Of the $491.5 million reported to TAG by the 71 investors in TB R&D in 2008, $265 million (54%) came from the public sector, $155 million (31%) from the philanthropic sector, and $72 million (15%) from industry.

To avoid double counting, TAG did not include disbursements by product development partnerships (PDPs) such as the Aeras Global TB Vaccine Foundation, Foundation for Innovative and New Diagnostics (FIND), and the TB Alliance, or by other research consortia such as Consortium to Respond Effectively to the AIDS/TB Epidemic (CREATE), TBVAC, or the WHO's Special Programme for Research and Training in Tropical Diseases, since their source funding is reported as a disbursement by the original source funder. These PDPs and consortia spent $171 million in 2008.

FIGURE 3

TB R&D Funding by Donor Sector: 2008

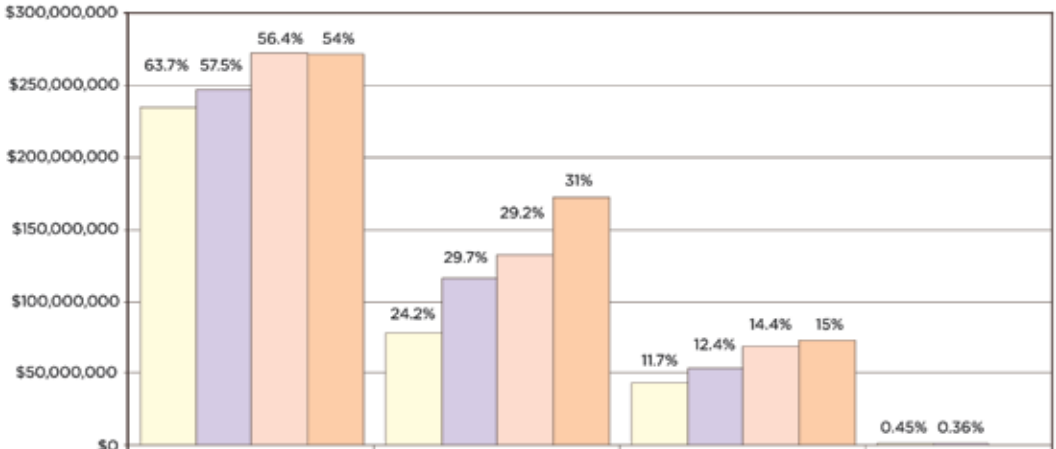


Despite the global economy, which suffered a near collapse in 2008, TB funding levels continued to grow, albeit sluggishly. Since most of the R&D funds were already committed before the economic crisis, its continuing impact may appear in the 2009 disbursements on which we will report in 2010. Conversely, 2009 will also see the impact of the American Relief and Recovery Act stimulus funds for the NIH and possibly other U.S. government agencies.

Nonetheless, it is disturbing that public-sector investments continued to decrease relative to total investment from nearly 65% in 2005 to 54% in 2008. Philanthropies made up the largest increase in proportion to total investment rising from 24% in 2005 to 31% in 2008. The private sector representing drug, vaccine, and diagnostic companies rose slightly from 12% of total investment in 2005 to 15% in 2008.

FIGURE 4

Amounts and Proportions of Total TB R&D Funding by Donor Sector: 2005–2008

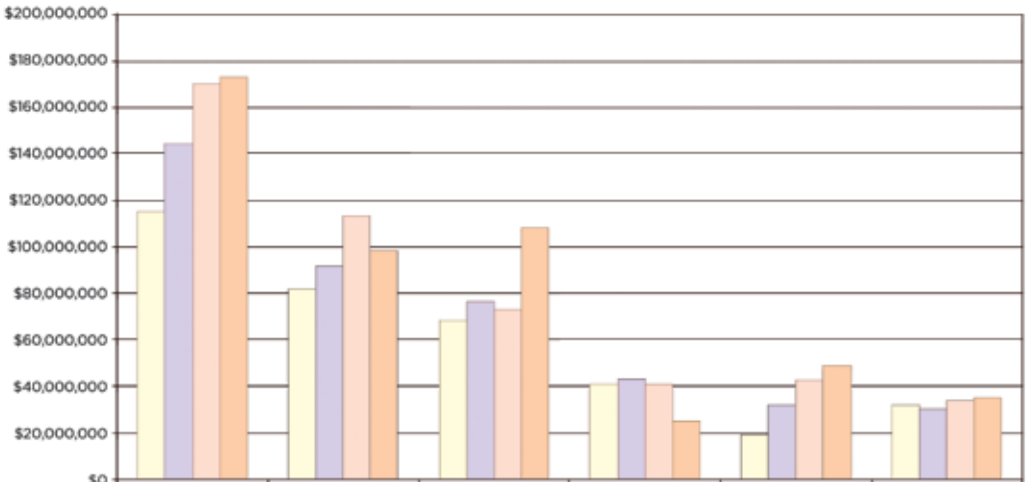


	Public	Philanthropy	Private	Multilateral
2005	$234,503,645	$78,178,708	$43,095,353	$1,648,083
2006	$246,862,858	$116,289,274	$53,138,347	$1,534,259
2007	$272,404,317	$132,326,981	$69,387,383	N/A
2008	$264,944,215	$154,513,987	$72,018,715	N/A

2.3. Trends in TB Research by Category

FIGURE 5

Investment in TB R&D by Research Category: 2005–2008



	Drugs	Basic Science	Vaccines	Unspecified	Diagnostics	Operational
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

1. Basic Science

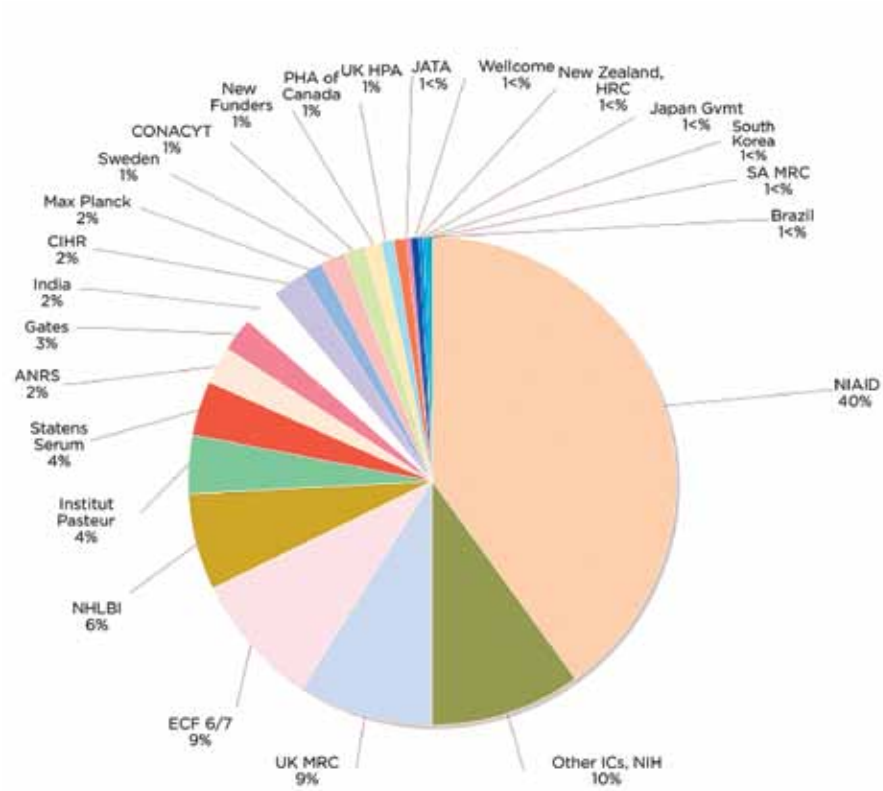
From 2007 to 2008, basic science slipped from 24% of the total TB R&D investment to 20%. Actual investment in TB basic science fell from $113 million to $99 million. Without a rededication to increased basic science on TB in the coming years, there will not be enough scientists working on the disease nor enough knowledge generated.

Providing incentives for a new generation of scientists is needed to take on the growing demand of TB research using new molecular tools, systems biology, genomics and proteomics, and other techniques well suited to study TB pathogenesis.

While the current Global Plan research goals do not make specific recommendations regarding basic science on TB, we believe that the research conducted in this area is essential for moving the field forward. The Stop TB Partnership, TAG, and NIAID are working together to cosponsor a workshop in March 2010 to move the field forward.

FIGURE 6

Basic Science $98,728,019



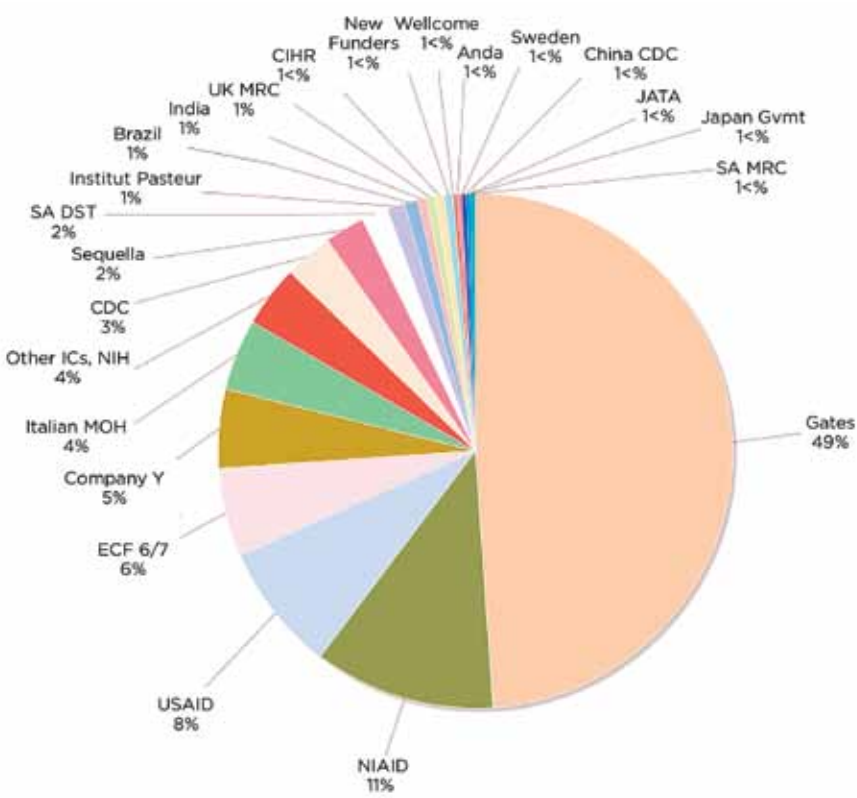
2. TB Diagnostics

The lack of an accurate TB diagnostic test that can be used at the point of care in field settings is the leading impediment for success of TB care and control efforts. There is a need for a well-coordinated effort that can translate the breakthroughs in basic science research into product development effort. Sample banks and laboratory infrastructure critical to expedite diagnostics research also need to be expanded. Global investment in TB diagnostics R&D was a meager $50 million in 2008, making up just 10% of total research.

In 2008, the Gates Foundation supported 49% of TB diagnostics R&D, while NIAID support fell from 20% in 2007 to 11% in 2008.

FIGURE 7

Diagnostics $49,788,950



3. TB Drugs

For the fourth year, drug development remains the most well-funded category in TB research. Funding for TB drug development made up 35% of total funding disbursed in 2008, almost the same proportion as in 2007. The Gates Foundation was the largest funder of TB drug development, giving 21% of the total.

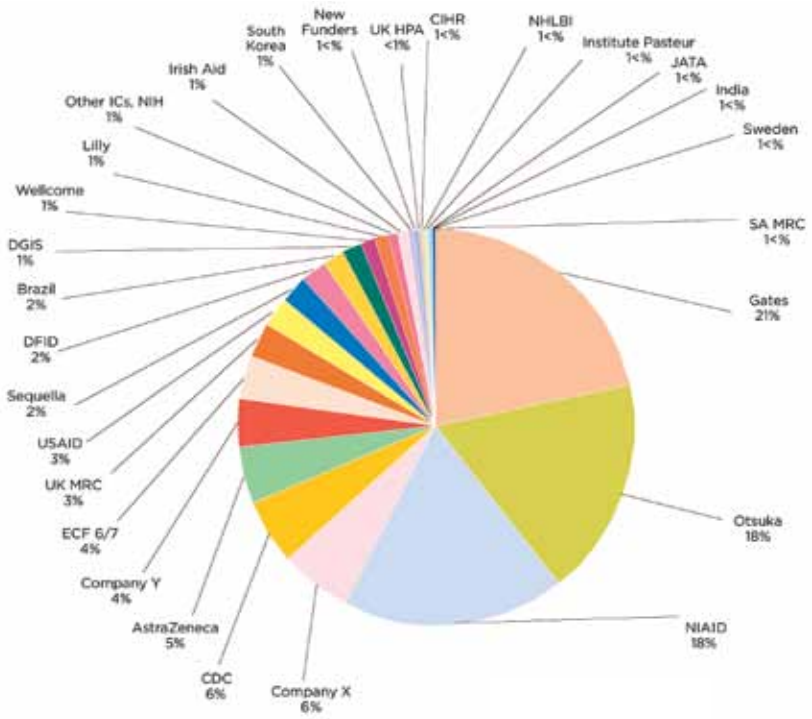
NIAID and Otsuka, at $31.7 million and $31.8 million, respectively, were ranked second and third in the list of funders who had contributed to TB drug development in 2008.

Of note, Otsuka gained third place in the overall global rankings of TB research investors in 2008 simply by moving its nitroimidooxazole compound OPC-67683 into phase 2 studies. Thus, one single company with a single drug in phase 2 spends more on TB research than the entire European Union Framework 6 and 7 programs.

An increase in regulatory openness and infrastructure for large-scale trials are essential to move TB drug development forward faster and in a more coordinated fashion.

FIGURE 8

Drugs $174,178,052



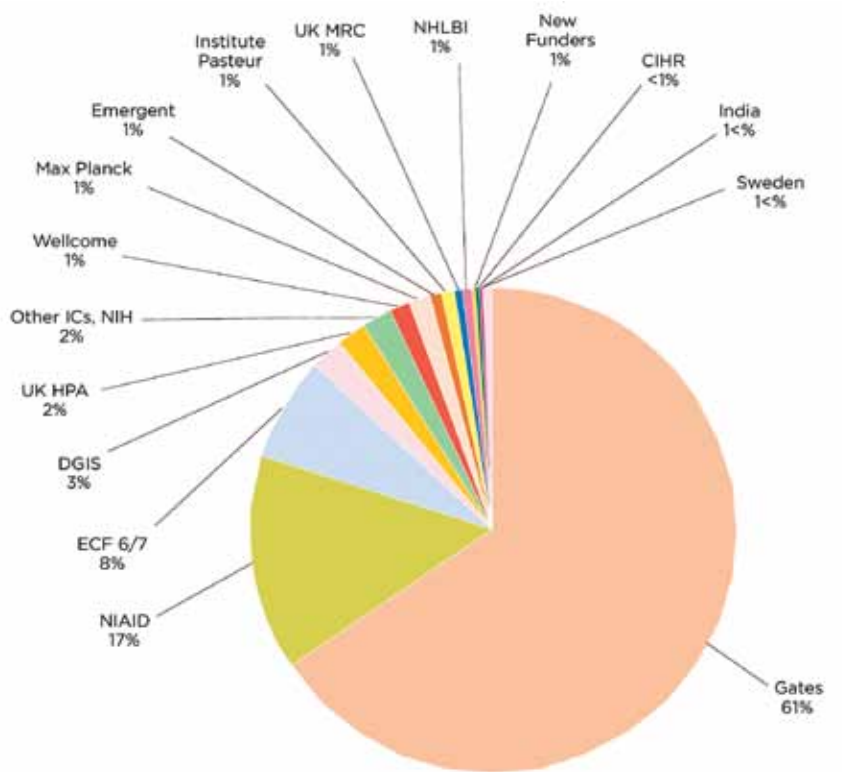
4. TB Vaccines

The lack of funding for TB vaccine development raised much concern in previous years; in 2007 just 15% of TB research funds went to vaccines. However, in 2008, investment in TB vaccines rose to 22% of TB funding, mainly based on the Gates Foundation's contribution of $67 million, of which $63 million went to the Aeras Global TB Vaccine Foundation.

In 2008 NIAID contributed $18.2 million to vaccine development and ranked second in that area of research representing 17% of the total investment in vaccines for 2008.

FIGURE 9

Vaccines $109,337,224



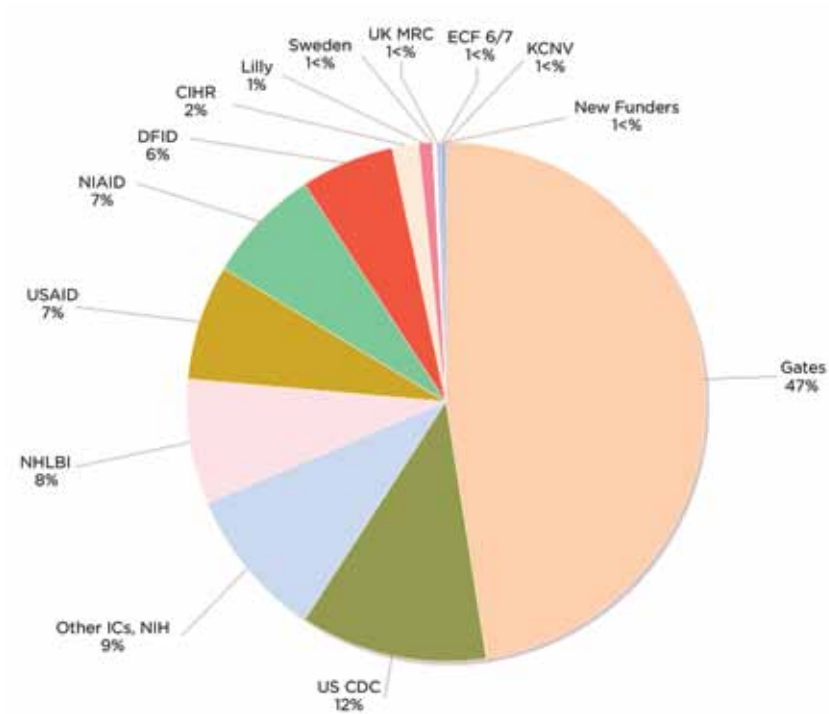
5. Operational Research

The investment in operational research remained flat between 2007 and 2008 at $34 million. Operational research represented 7% of total TB R&D in 2008.

Operational research is crucial to create the evidence base necessary for showing how to use new TB tools in programmatic settings in order to have the maximum impact on TB care and control efforts. Along with ascertaining the utility of new tools, operational research studies are critical to improve current strategies and provide evidence to optimize the utility and integration of existing tools in programmatic settings. Continued lack of funding for operational research will impede getting new treatments and tools into broad use, limiting their impact.

FIGURE 10

Operational Research $34,411,172



2.4. Top Ten Funders of TB R&D in 2008

Until now a clear coordinating mechanism for TB R&D has been lacking. The Stop TB Partnership has begun to address this gap through the establishment of the Research Movement to Stop TB. Its mission is to stimulate, support and expand research to ensure the elimination of TB as a global public health problem by 2050 by spurring commitments to TB R&D. The Partnership and its TB Research Movement will have a significant role in creating partnerships across funding sectors to collectively create a contiguous stream of resources that can overcome bottlenecks in TB research. This movement holds the promise to help move a basic science discovery from the laboratories into a new tools pipeline and ultimately into programmatic settings more efficiently. To succeed, the Partnership will need the full engagement of all current and future funders of TB research.

1. The Bill and Melinda Gates Foundation

The Bill and Melinda Gates Foundation is the world's largest private philanthropic organization, with a total endowment of $30.2 billion as of June 2009. The Gates Foundation disbursed $148 million for TB R&D in 2008, up 19% from the $124 million disbursed in 2007 and up 158% from the $57 million disbursed in 2005.

The Gates Foundation substantially increased its investments in vaccines from $30 million in 2007 to $67 million in 2008. The foundation's spending on basic science decreased from $5 million in 2007 to $3 million in 2008. Drug development decreased from $51 million in 2007 to $37 million in 2008. Operational research dropped slightly from $18 million in 2007 to $16 million in 2008.

For the first year since TAG has been tracking TB R&D resources, the Gates Foundation rose to the top of the TB R&D funding list, surpassing NIAID. Indeed, in 2008 Gates Foundation TB research investment was larger than that of the entire NIH ($148 vs. $142 million).

The Aeras Global TB Vaccine Foundation received the largest award from the Gates Foundation at $62.8 million for vaccine development. The second two largest grants went to the Global Alliance for TB Drug Development ($25.5 million) and to FIND ($23.6 million) for diagnostics.

2. The National Institute of Allergy and Infectious Diseases, (NIAID), National Institutes of Health (NIH)

For the first time that TAG has been tracking TB R&D resources in 2005, the leading public sector funder of TB R&D, the National Institute of Allergy and Infectious Diseases (NIAID) dropped to second place. In fact, the 2008 contribution of $105 million is 13% less than in 2005. Even combined with all NIH institutions, the total 2008 NIH investment in TB R&D comes in at $142 million, 4% less than that of the Gates Foundation. In 2008, NIAID contributed 74% of NIH's TB R&D support.

The focus at NIAID remains on basic science. Though the NIH funding has been essentially flat since 2004, the NIAID's funding for basic science dropped dramatically by 35% between 2007 and 2008. This dramatic drop cannot be wholly attributed to the "revised" RCDC funding formula. We hope that NIH spending on TB research will rebound immediately in FY 2011,the first year following the expiry of the American Recovery and Reinvestment Act (ARRA) stimulus funding. In particular we hope that basic science investment will rebound quickly, as otherwise this will limit the pipeline of future new drugs, diagnostics, and vaccines, not to mention the supply of well-trained TB researchers.

TABLE 2

2005–2008 NIH Funding for Select Infectious Diseases (in millions)

	2005	2006	2007	2008
HIV/AIDS	2,921	2,902	2,906	2,928
Smallpox	187	149	142	94
Anthrax	183	150	160	134
Tuberculosis	158	150	188	142
Malaria	104	98	112	132

NIH RCDC, 10 February 2010, http://report.nih.gov/rcdc/categories/

In 2009 and 2010, NIAID's contribution to TB R&D is expected to increase due to the infusion of monies the NIH received in 2009 under the ARRA. However, the short-term nature of these new monies will not enable the Institute to address the critical research gaps in TB R&D that require long-term and consistent funding.

One hopeful sign has been the statements by NIAID Director Anthony S. Fauci at the Pacific Health Summit, the Fifth IAS Conference, and elsewhere in 2009 that NIAID is considering broadening the use of its extensive international clinical trial resources, which are now focused on HIV, to include clinical trials to improve diagnosis, treatment, and prevention of related diseases, such as tuberculosis and hepatitis C virus infection. If this promise leads to action, NIAID will be well placed to play a critical role in hastening the development of better drugs, diagnostics, and vaccines for TB. If funding remains inadequate, Congress and the administration of President Barack Obama must step in to expand research support.

3. Otsuka Pharmaceutical Company

In 2008, Otsuka, a Japanese pharmaceutical company, was in phase 2 of clinical development of its TB drug OPC-67683. The company spent $32 million in 2008, up 53% from 2007. It is telling that just by moving its one compound into phase 2 trials in 2008, Otsuka has moved up to become the third largest funder of TB R&D. Otsuka's investments may increase further as it advances into phase 3.

As it moves closer to large-scale trials for its drug, Otsuka has raised concerns over the global regulatory agencies' lack of experience with trials of new, previously unlicensed TB compounds. Because Otsuka's drug is being studied to treat multidrug-resistant TB treatment, laboratory capacity needs to be strengthened as well.

To effectively and efficiently move into later stage clinical development, Otsuka has identified the need for prompt regulatory reviews, guidance, and increased TB clinical research capacity compliant with International Conference on Harmonization good clinical practice (GCP) standards to facilitate bringing a new TB treatment to market.

4. The European Commission's Sixth and Seventh Frameworks

The European Commission's Sixth and Seventh Framework Programmes (FP6 and FP7) are aimed at integrating European efforts toward small-scale, phase 1 clinical trials for new TB vaccines and to establish production technologies for lead compounds to treat TB. Disbursements for both frameworks continued to be made in 2008 even though the FP6 itself ended in 2006.

In 2008, the European Commission (EC) spent $27 million on all product areas, a 15% increase from 2007 and a 101% increase from 2005. Basic science funding fell from $10 million in 2007 to $9 million in 2008. Diagnostics R&D was flat ($2.6 million to $2.8 million from 2007 to 2008). Investment in drug development more than doubled from $3 million in 2007 to $6.5 million in 2008. Vaccine investments rose between 2007 and 2008 from $8 million to $8.8 million.

During 2009, the EC began funding studies to improve clinical management of multi-drug-resistant and extensively drug-resistant TB. The EC committed about $30 million for development of new TB drugs.

5. Other NIH Institutes and Centers

In addition to larger and more focused NIH efforts at NIAID and the National Heart, Lung, and Blood Institute, discussed separately, another 18 of the NIH's 27 institutes and centers spent $26 million on TB R&D in 2008, a 53% increase from $17 million in 2007.

6. U.S. Centers for Disease Control & Prevention

TB research funding at the U.S. Centers for Disease Control and Prevention (CDC) rose slightly from $18 to $19 million between 2007 and 2008. The 2008 expenditures still represent a 4% decrease from the funding levels of 2005. Diagnostics received $1.5 million in 2008, while drug development received $9.3 million and operational research received $4 million.

The CDC Division of TB Elimination (DTBE) made a long-term commitment to two research consortia, the TB Trials Consortium (TBTC) and the TB Epidemiologic Studies Consortium (TBESC). Both are funded in 10-year cycles. Most of CDC's external funding for TB research is placed through these two consortia. In 2009, the TBTC put out a call for proposal, sites applied to be part of the TBTC, and new 10-year contracts were awarded, including contracts to many new sites outside of North America. TBESC sites will also similarly reapply for funding within the next two years.

The DTBE is also interested in supporting translational research leading rapidly to the development and implementation of new diagnostic and therapeutic approaches to TB control. The division funded substantial studies of new technologies for diagnosis of latent TB infection, such as the interferon gamma release assays. The DTBE also provided modest support to applied studies of human and microbial genetics (e.g., studies of genetic factors that may increase susceptibility to TB infection and studies of genetic factors that may influence pharmacokinetics of TB drugs).

7. UK Medical Research Council

Since 2005, the UK Medical Research Council's commitment to TB increased 142%. The overall funding for TB dipped only slightly from 2007 to 2008. While the UK MRC's investment in diagnostics remained the same between 2007 and 2008, its funding for basic science increased by 66% from $5.3 million in 2007 to $8.8 million in 2008, and drug funding increased by 1% to $5 million. Research on TB vaccines dropped from $3.6 million in 2007 to $732,000 in 2008.

8. U.S. Agency for International Development

The U.S. Agency for International Development (USAID) has increased its funding of TB R&D by 63% since 2005, moving the agency into the list of top 10 funders for the first time since TAG started tracking TB resources. USAID's $11 million investment in TB R&D in 2008 was split among diagnostics ($4 million), drugs ($4.5 million), and operational research ($2.6 million).

Its largest grant—of $3.8 million—went to the International Union against TB and Lung Diseases (IUATLD) for its TB Research to Enhance the Prevention, Detection and Management of TB cases (TREAT TB) program. This grant focuses on modeling of the application of new diagnostic technologies within high-burden country settings. A small portion of the grant also goes toward a clinical trial to assess efficacy of fixed-dose combination treatment. USAID also gave $3 million to the TB Alliance in 2008 for clinical trials of PA-824 and moxifloxacin.

USAID also provided support to the CDC for the evaluation of the role of isoniazid preventive therapy in high-HIV-prevalence settings and for the evaluation of emergence of resistance in Green Light Committee (GLC)–approved settings compared to non-GLC-approved settings The WHO's Special Programme for Research and Training in Tropical Diseases (TDR) received funding for diagnostics and drug development. Support for diagnostics research rose significantly from $1.6 million in 2007 to $3.9 million in 2008.

In 2008, USAID committed $2.6 million or 24% of its total TB funding through its field missions for operational research.

9. Company X

Company X is a drug company with a TB drug in clinical development. In 2008, Company X spent $10.6 million. Like other drug companies, Company X identified the lack of clinical trial site capacity as a barrier to moving forward rapidly, and highlighted the need for TB research trial sites that can meet good clinical practice (GCP) standards.

10. The U.S. National Heart, Lung, and Blood Institute, (NHLBI), NIH

The U.S. National Heart, Lung, and Blood Institute (NHLBI), NIH funds basic research on cardiac, lung, and circulatory health and disease. In 2008 the NHLBI climbed into the top 10 list and disbursed $10.4 million on TB R&D. However, NHLBI funding for TB research dropped 10% from 2007 levels, and 39% since 2005. Basic science funding decreased by 25% from $8.4 million in 2007 to $6.3 million in 2008. Operational research funds increased by 80% from $1.5 million in 2007 to $2.7 million in 2008.

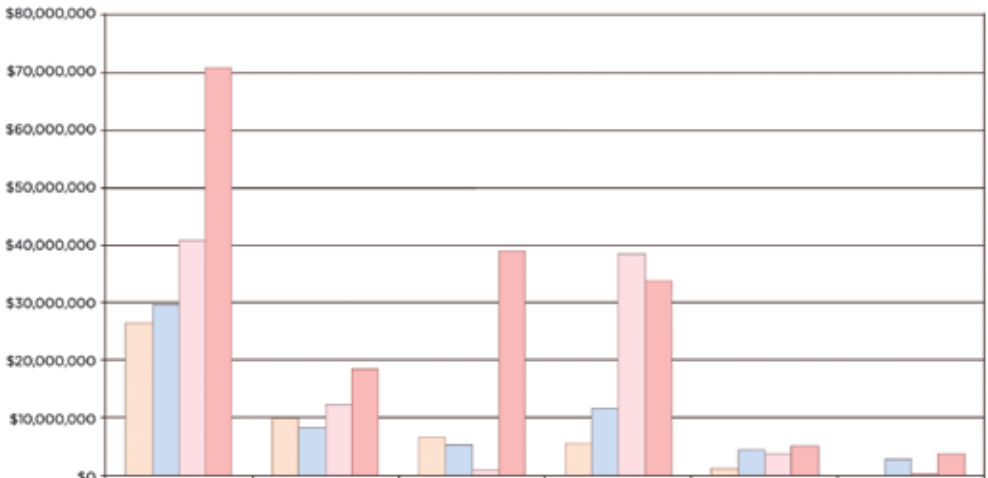
2.5. Product Development Public-Private Partnerships

Product development public-private partnerships (PDPs) are institutions that enable public, private, and philanthropic funders to pool resources to support research in neglected priority diseases. Along with research consortia and clinical trial networks such as the TBTC, PDPs are not original funding sources. PDP funding was not included in the global total in order to avoid double counting.

PDPs disbursed $171 million in 2008, a 76% increase from 2007 and more than a threefold increase from 2005.

FIGURE 11

TB R&D PDPs and Research Consortia: 2005–2008



	Aeras	CREATE	FIND	TB Alliance	TBVAC	TDR
2005	$26,526,253	$10,000,000	$6,778,239	$5,556,397	$1,400,000	N/A
2006	$29,740,656	$8,298,826	$5,492,942	$11,743,498	$4,597,321	$2,995,748
2007	$40,900,712	$12,357,000	$1,145,409	$38,543,147	$3,840,489	$453,382
2008	$70,878,639	$18,493,585	$39,055,500	$33,908,576	$5,096,940	$3,817,352

3. Conclusions & Recommendations

3.1. Conclusions

In 2008, the level of funding available for TB R&D increased by $18 million over 2007. At $491.5 million, this level of investment is less than one quarter of the $2 billion per year that TAG has estimated will be needed to meet research targets previously set out by the *Global Plan* after including the basic science and operational research components that were inadequately accounted for in previous versions of the plan. As Global Plan numbers are currently being revised, it remains to be seen how the 2008 level of investment measures up against the need, but it is clear that insufficient support is available.

The majority of the increase in 2008 funding can be attributed to the Gates Foundation, which emerged as the single largest funder in four of the six research areas that TAG has tracked—drugs, diagnostics, vaccines, and operational research. The foundation should be commended for its focus on innovation. In 2008, the Gates Foundation overtook NIAID as the leading funder of TB. Previously in each year since 2005 NIAID had been the leading funder.

As the lead funders of TB research, the Gates Foundation and NIAID have a key role to encourage other funders to follow suit and to continue fostering collaboration in the field.

This report also documents the contributions of emerging market economies—particularly China, India, Brazil, and South Africa. TAG commends the leadership of these high-TB-burden countries that have invested their own resources in a disease with disproportionate impact on their citizens. China, in particular, has made a significant, multiyear commitment to expand its TB R&D investments, and we look forward to documenting its progress in meeting this challenge. We hope that other developing countries will also rise in the rankings of the top TB research funders.

Every year TAG survey respondents have reported a number of common concerns, including:

- Critical deficiencies in the understanding of the pathogenesis of TB.
- Low-level funding support for TB relative to the importance of the disease and compared to funding directed toward other infectious diseases.
- Lack of research capacity in those areas of the world where the disease is prevalent.
- Lack of useful biomarkers to diagnose, stage, and monitor response to treatment or vaccination for TB.

TB research is at a critical juncture. For the first time in 40 years four new classes of drugs are in the pipeline nearing phase 3 clinical trials and possibly accelerated approval for treating drug-resistant TB. There is movement toward identifying biomarkers and antigens that might show the path to a point-of-care TB diagnostic test. All of these areas of research are impeded by lack of resources. Currently there is a dearth of available infrastructure to carry out the studies needed. In the present time of economic uncertainty where global markets are tenuously stabilizing, it is critical that the momentum for TB R&D be maintained and amplified to make the most of the scientific opportunities on the horizon.

3.2. Recommendations

TAG recommends the world invest $2 billion a year in research to eliminate TB as a public health threat by 2050. By not committing to these investments we are deferring an attainable goal and ignoring a public health crisis. All of the sectors need to partner with each other, as no one country, company, or organization can achieve eradication of TB alone. There must be an increase in communication and collaboration among sectors so that all stakeholders are aware of the pipeline, goals, and challenges. Better communication can lift the veil of the unknown, spur innovation, and increase excitement in discovery.

We call on all those who support TB research to come together and demand sufficient and sustained long-term support for TB R&D in order to discover, develop, distribute, and deploy new diagnostics, drugs, and vaccines that can make TB a disease of history, saving future generations from this oldest of human infectious diseases.

Appendix A: 2008 and 2007 Top Reporting TB R&D Funders

TABLE 3 2008 and 2007 Top Reporting TB R&D Funders Above $500,000 And Funders that TAG Has Tracked in Previous Years

2008 Rank	2007 Rank	Institute	Type of Funder
1	2	Bill & Melinda Gates Foundation (BMGF)	F
2	1	US NIAID, NIH	P
3	4	Otsuka Pharmaceutical Company	C
4	3	European Commission Framework 6/7	P
5	6	US other institutes & centers, NIH	P
6	5	US Centers for Disease Control & Prevention (CDC)	P
7	8	UK Medical Research Council (MRC)	P
8	13	USAID	P-D
9	14	Company X	C
10	11	US NHLBI, NIH	P
11	15	AstraZeneca	C
12	10	Company Z	C
13	16	Institut Pasteur	P
14	17	UK Department for International Development (DFID)	P-D
15	7	Wellcome Trust	F
16	18	Sequella, Inc	C
17	9	Netherlands Ministry of Foreign Affairs (DGIS)	P-D
18	32	Brazil (aggregate)	P
19		India (aggregate)	P
20	20	Canadian Institute of Health Research	P
21	21	UK Health Protection Agency (HPA)+	P
22	22	Statens Serum Institute	C
23	23	Germany, Max Planck Institute for Infectious Biology	P
24	24	Company Y	C
25		Agence Nationale de Recherche sur le SIDA (ANRS)+	P
26		Italian Ministry of Health+	P
27		Sweden (aggregate)	P
28	12	Eli Lilly Foundation	C
29		Consejo Nacional de Ciencia y Tecnologia (CONACYT - Mexico)+	P
30	19	Irish Aid	P-D
31		Emergent Biosolutions (including Microsciences and Antex Biologicals Inc)+	C
32		South Korea (aggregate)	P
33		Japanese Government+	P
34		Public Health Agency of Canada+	P
35		South African Department of Sciences and Technology (DST)+	P
38	***	Inserm+	P
40	25	New Zealand, Health Research Council+	P
42	N/A	Research Institute of Tuberculosis, Japan Anti-TB Association (JATA)	P
45	N/A	Swiss Agency for Development and Cooperation	P-D
47	26	South Africa Medical Research Council (SA MRC)+	P
49	33	Anda Biologicals	C
50	***	China CDC National Tuberculosis Reference Laboratory+	P
54	35	KNCV Tuberculosis Foundation	F
	27	Ellison Medical Foundation	F
	28	Mexico National Institute of Public Health+	P
	29	Dafra Pharma International Ltd.+	C
	31	Denmark Ministry of Foreign Affairs (Danida)	P-D
	34	Russian TB Institutes	P
	36	US FDA	P
	N/A	Ireland Health Research Board	P
	N/A	Rockefeller Foundation	F
	N/A	Thailand Ministry of Public Health	P
	***	Global Fund to fight AIDS, Tuberculosis and Malaria	
		New Funders under $500,000 (ranked 36-37,39,41,43-44,46,48,51-53,55-60)	
		TOTAL	

Notes: + Funders reporting to G-FINDER whose investments TAG has not been able to corroborate.
P = Public sector R&D agency, **P-D** = Public sector development agency,
F = Foundation/philanthropy, **C**= Corporate/private sector

Total	Basic Science	Infra/ Unspecified	Diagnostics	Drugs	Vaccines	Operational
147,827,264	2,973,209	0	24,614,680	37,031,565	66,909,941	16,297,869
104,645,069	39,466,455	7,192,902	5,607,846	31,692,505	18,176,979	2,508,382
31,769,216				31,769,216		
26,744,573	8,608,099		2,798,137	6,471,299	8,821,756	45,281
26,472,839	9,945,462	7,549,223	1,871,964	1,421,734	2,459,606	3,224,850
19,097,813	0	4,246,120	1,545,840	9,250,000	0	4,055,853
14,941,234	8,788,841	0	254,977	5,064,955	731,636	100,825
10,925,000	0		3,930,000	4,445,000		2,550,000
10,640,454				10,640,454		
10,439,385	6,283,661	545,262		370,635	589,585	2,650,242
8,300,000				8,300,000		
7,050,000				7,050,000		
5,665,271	3,849,555		602,955	364,774	847,987	
5,583,287	0	0	0	3,588,300	0	1,994,987
5,446,998	357,179	1,207,743	182,222	1,968,150	1,731,703	
5,157,298			1,197,851	3,959,447		
5,140,858	0	0	0	2,199,347	2,941,511	0
3,940,014	37,398	745,430	405,870	2,751,316	0	0
3,907,318	2,352,909	892,551	328,868	208,755	124,235	0
3,766,005	2,192,466	67,132	243,558	485,504	222,536	554,809
3,614,697	556,107			556,107	2,502,483	
3,550,643	3,550,643					
3,100,000	1,500,000		0		1,600,000	
2,500,000			2,500,000			
2,441,454	2,441,454					
2,176,718			2,176,718			
2,167,769	1,435,129	250,657	127,500	133,483	85,000	136,000
1,700,000				1,450,000		250,000
1,418,997	1,418,997					
1,262,674	0	0	0	1,262,674	0	0
1,196,000					1,196,000	
1,179,803	179,315	0	0	1,000,488	0	0
1,128,700	207,650	904,500	17,000	0		
927,328	927,328					
853,533			853,533			
441,227		441,227				
346,379	346,379					
340,660	28,820	224,320	27,520	60,000		
245,525		245,525				
188,121	94,417		31,212	62,492		
127,818			127,818			
100,000			100,000			
39,450						39,450
0	0	0	0	0	0	0
0						
0						
0	0	0	0	0	0	0
0						
0						
0						
0						
0						
2,969,526	1,186,547	520,788	242,880	619,852	396,265	3,194
491,476,917	**98,728,019**	**25,032,930**	**49,788,950**	**174,178,052**	**109,337,224**	**34,411,742**

Appendix B: Top TB R&D Funders: 2005-2008

FIGURE 12

TB R&D Funders Ranked 1-12 That Are Above $500,000 And Funders That TAG Has Tracked In Previous Years: 2005–2008

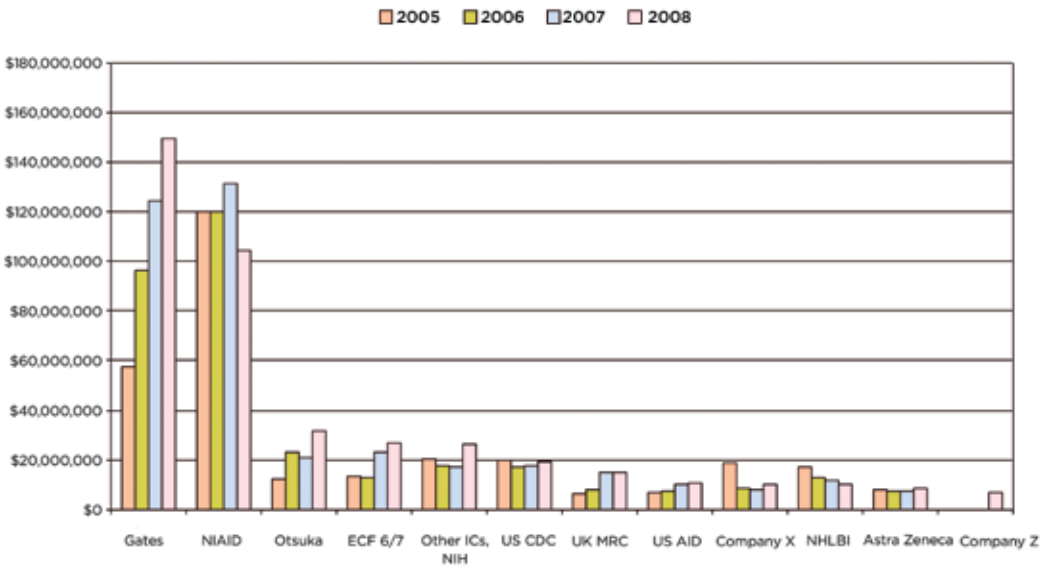


FIGURE 13

TB R&D Funders Ranked 13-22 That Are Above $500,000 And Funders That TAG Has Tracked In Previous Years: 2005–2008

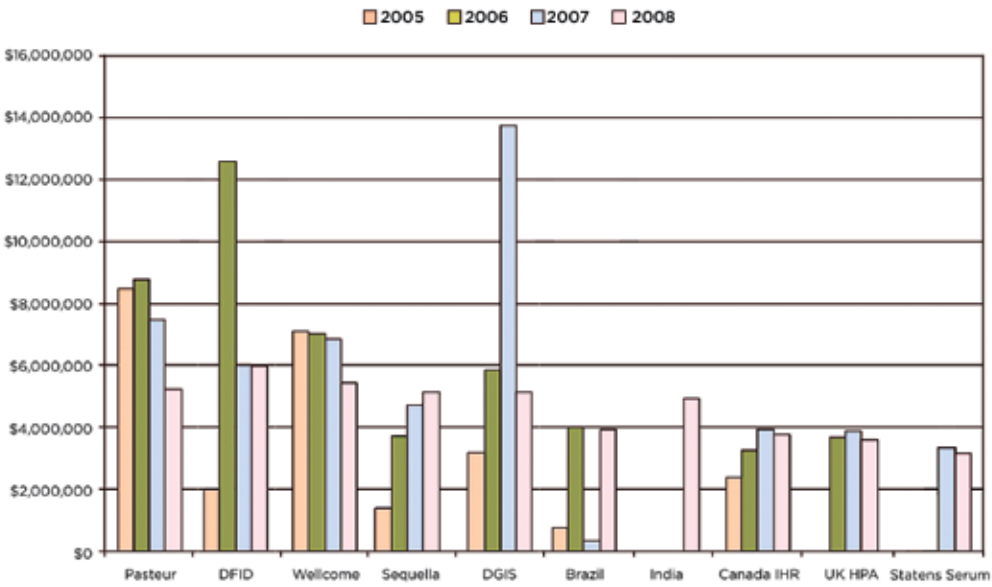


FIGURE 14

TB R&D Funders Ranked 23-31 That Are Above $500,000 And Funders That TAG Has Tracked In Previous Years: 2005–2008

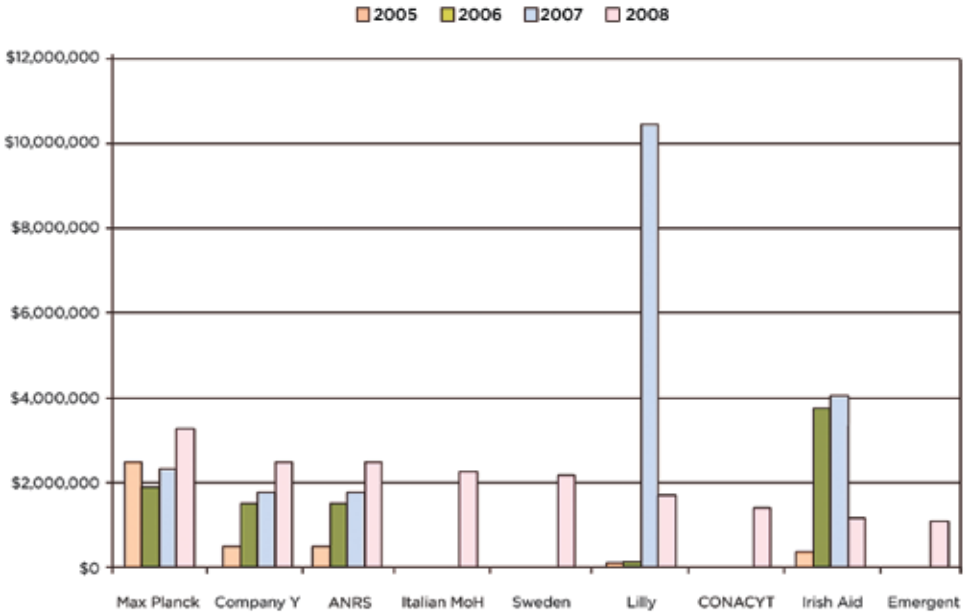


FIGURE 15

TB R&D Funders Ranked 32-54 That Are Above $500,000 And Funders That TAG Has Tracked In Previous Years: 2005–2008

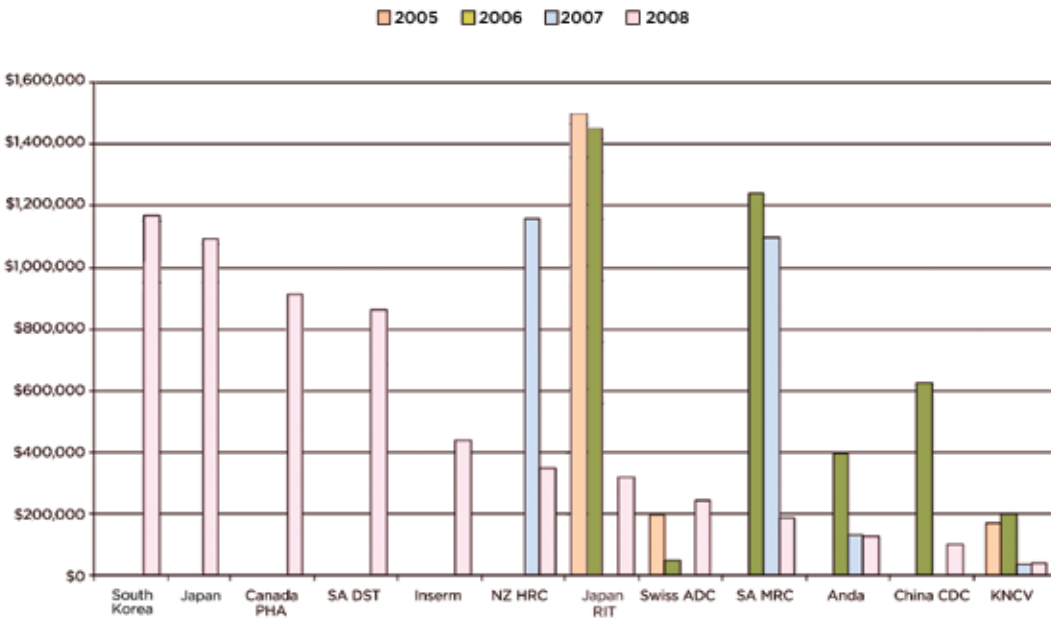
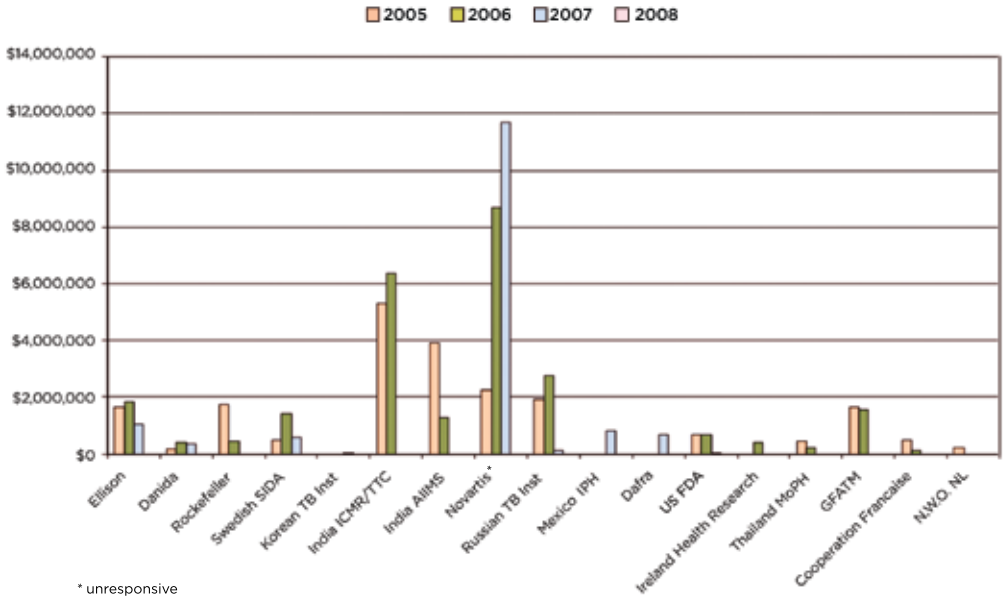


FIGURE 16

TB R&D Funders Inactive or Unresponsive in 2008



* unresponsive

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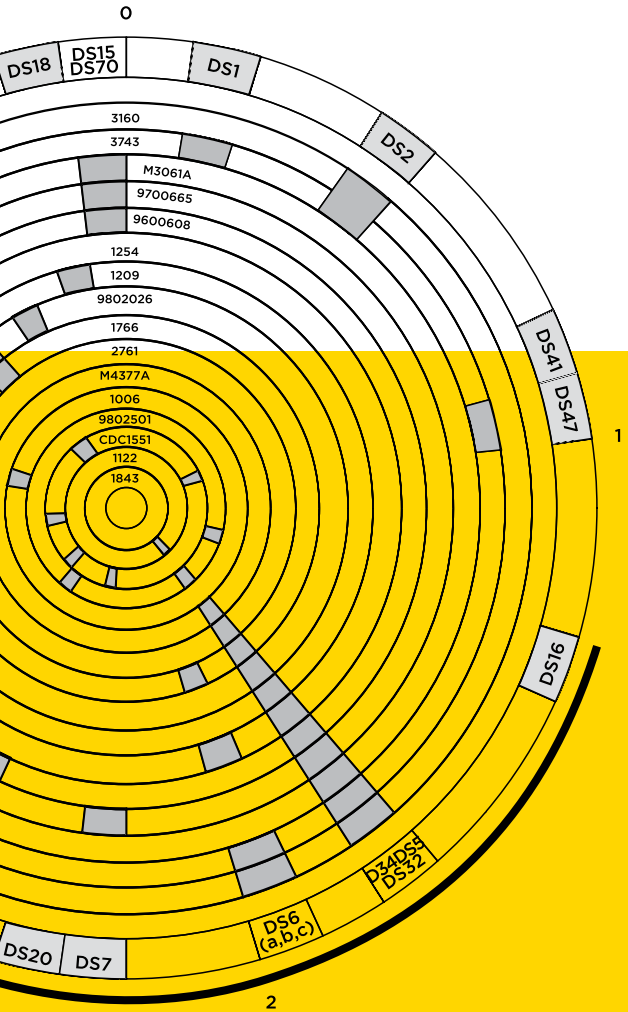

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