# **Tuberculosis R&D Investments:**
# A Preliminary Assessment

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# Foreword

by Mark Harrington

This report presents preliminary results from TAG's effort to ascertain who were the major funders of tuberculosis (TB) research and development (R&D) in 2005–the last year for which relatively complete data are available–what kinds of research activity they funded, and how much research activity is already taking place. This assessment will help policymakers, funders, researchers and advocates to understand the current state of research on TB, and provides a baseline for understanding how much TB research will need to increase in order to bring TB under control over the next decade.

TAG's researcher/writer, Cindra Feuer, assisted by TB/HIV Project Director Javid Syed and me, contacted leading institutions worldwide to ascertain their TB R&D investments in 2005. Fifty-two institutions provided information in time for this preliminary assessment. We are grateful to all who provided useful data and responded to, in many cases, repeated queries. Here we are able to provide preliminary estimates of the total amount spent on TB R&D by the top 30 donors in 2005–$348 million–and estimates of the relative proportion spent on basic science, applied research on new TB tools including diagnostics, drugs, and vaccines, and operational research to optimize the use of existing interventions in routine program settings. Though it is an inexact art, a recent bibliometric paper which assessed outputs and expenditures on health research in eight disease areas, including TB from 1996-2001, estimated a similar level of investment, $350 million per year (Lewison 2004). It is likely that the bibliometric assessment picked up some operational research in high-burden countries which we did not quantify. Their assessment of industry investment, $28 million, was fairly close to our assessment of $23 million, which only counted the four companies who reported actual figures to TAG.

The data indicate that investment in TB R&D lags far behind necessary levels. If new tools funding continues at its 2005 level of $182 million just $1.82 billion will be available for new tools research over the next decade, whereas *The Global Plan to Stop TB: 2006-2015* estimates that $9 billion will be needed. Thus, TB R&D investment needs to rise approximately fivefold to meet *Global Plan* targets. Still more is needed to expand basic science and operational research. All this will only come with worldwide political advocacy for a TB research movement, with ambitious and comprehensive targets for investment in the basic, applied, and operational research which can make TB history.

A final version of TAG's report on TB R&D investments will be released at the 37th Union World Conference on Lung Health in Paris, France, on 31 October–4 November 2006. TAG is eager to collect the most complete and accurate dataset for this report. If you are aware of TB research funding programs which are not captured in this preliminary assessment, or believe that TAG has not completely or accurately characterized TB research programs, please write to TAG directly and let us know so that we can ensure that the fall 2006 version of TAG's report on TB R&D Investments is as complete and accurate as possible.

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# Executive Summary

Tuberculosis, an ancient scourge dating back to the time of the Pharaohs (Zink 2003; Donoghue 2004), has persisted as a global public health disaster with one in three of the world's population infected. WHO estimates that there were nine million new cases and almost two million deaths caused by TB in 2004, and that global incidence rose by 1% that year (WHO 2004).

After biomedical interventions and economic development had reduced TB incidence through much of the 20th century, degradation of health care systems and a dramatic spike in HIV infections in resource-poor countries in the 1990s allowed a resurgence of the epidemic. The devastation of tuberculosis in the context of the HIV pandemic and the spread of multidrug-resistant (MDR) TB in the 1990s stimulated a global effort to scale up control through WHO's Direct Observed Therapy–Short course (DOTS) strategy. Despite this, it has become clear that our current tools are inadequate to control TB, and there has been increasing acknowledgment that investment in the discovery and development of new diagnostics, drugs, and vaccines will be required to eliminate TB as a public health problem in the 21st century.

The first five years of the new century have seen encouraging developments, including the establishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria, and the expansion of WHO's DOTS strategy into a new, more comprehensive Stop TB Strategy, which specifically includes TB/HIV, MDR-TB, and research and development (Raviglione 2006). The Stop TB Partnership's *Global Plan to Stop TB: 2006-2015* estimates that $9 billion will be needed for research and development (R&D) on new TB tools over the coming decade, but there is a paucity of comprehensive information about current levels of global research investment in tuberculosis.

Treatment Action Group (TAG) set out to map TB R&D investments and disbursements for the year 2005 in order to provide a baseline to inform advocacy efforts to mobilize greater resources for TB research. TAG surveyed institutions believed to be the likeliest funders of TB research, gathered information from publicly available sources, followed up with those who did and did not respond, and conducted in-depth qualitative interviews with key informants. The information presented in this preliminary assessment is not complete and will be added to as new funders and responders provide additional information. TAG will present a more complete assessment based on the best available data at the 37th Union World Conference on Lung Health, 31 October–4 November 2006.

Some notable potential major funders of TB research have not responded, particularly from public sector programs in some developed and developing countries. In addition most pharmaceutical and biotechnology companies contacted declined to provide R&D figures. We have included those that responded and noted those that declined to respond.

TAG also proposes here a more comprehensive, ongoing, and sustained effort to be undertaken to comprehensively map and annually update investments in TB R&D. This effort should include public, private, philanthropic, and multilateral research programs from developed and developing countries, and should be accessible through a public database. It should apply consistently defined coding criteria to clarify what area—for example, basic, diagnostic, treatment, vaccine—and what phase—preclinical, clinical (phases I, II, III, IV), and operational—is supported.

This preliminary assessment presents the results reported by 30 donors who provided $348 million for tuberculosis research in 2005 (*see Appendix A*). Broadly characterized, these donors fall into four categories and their donations into three strata.

The four main donor categories are public sector research and international development agencies (most of them from North America and the European Union), philanthropic private foundations (most notably the Bill & Melinda Gates Foundation), pharmaceutical and biotechnology companies (industry), and multilateral agencies (most notably the Global Fund).

The public sector provided $244 million or 70% of the total. The U.S. government alone provided $185 million or 53% of the total, with the National Institutes of Health (NIH) providing $157 million or 45.3% of the total. Philanthropic foundations provided $78.4 million (22.5%), with the Gates Foundation providing $57.4 million (16.5%). The four responding industry companies reported investing $24 million (6.9%). Multilateral agencies reported $1.8 million (0.5%).

NIH investment in TB research is impressive only when measured against a miserable worldwide total. Infused with new money to fight bioweapons, NIH spends more on smallpox and anthrax than it does on TB and malaria, two of the world's most lethal infectious diseases (*see Table 4*). To effect the revolution in TB required to address its terrible global toll, a fivefold increase in funding for TB research will be needed. TB research should look to the lessons of HIV/AIDS activism, which mobilized political commitment that led to $30 billion invested in HIV/AIDS research by NIH alone over the past 25 years (Fauci 2006), with consequent, dramatic, and evident—though still insufficient—results (Walensky 2006).

Donors to TB research fell into three major strata:

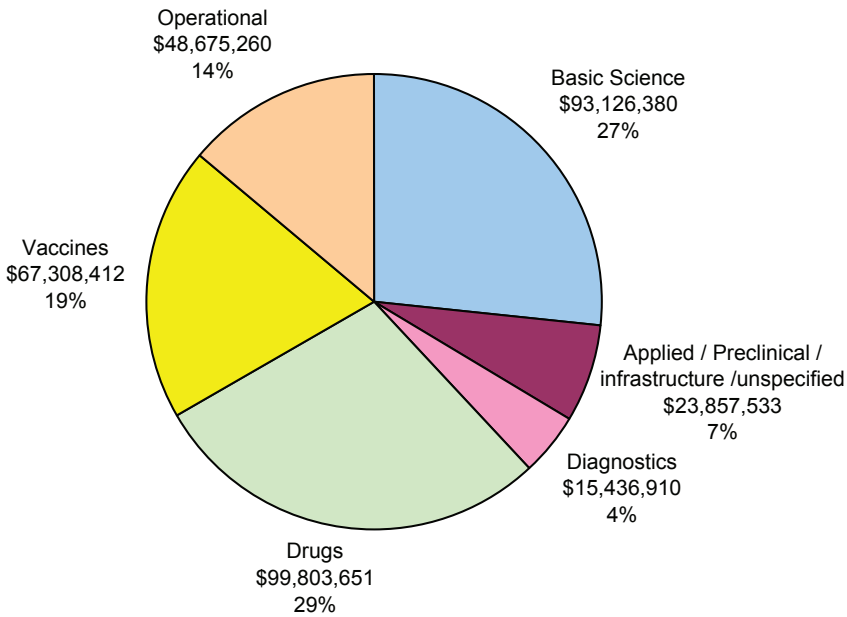
1. The top ten donors invested multimillion dollar amounts, ranging from $120 million (NIAID) to $8 million (AstraZeneca).

2. Twenty-two donors (the TB research 22) gave at least $1 million.

3. The cutoff for the top thirty donors in this preliminary assessment was quite low, at $140,350.

TAG asked donors to categorize their investments according to research area, including basic science, applied/preclinical and infrastructure development, diagnostics, drugs, vaccines, and operational research. Most donors were able to provide this information. Efforts to subcategorize within area—for example, by preclinical or clinical—were less consistent, as not all donors or recipients were able to specify the research phase. However, only six new drugs and five potential vaccines are in clinical trials, most of them early-stage (Syed 2006).

**Figure 1: 2005 TB Research: Investment by Category (Total = $348,208,146)**



Of the $348 million reported to TAG, $93 million (27%) went to basic research, $23.9 million (7%) to applied/preclinical/infrastructure or unspecified, $15.4 million (4%) to diagnostics research, $99.8 million (29%) to therapeutics research, $67.3 million (19%) to vaccine research, and $48.7 million (14%) to operational research.

The Stop TB Partnership's *Global Plan to Stop TB: 2006-2015* (henceforth *GP2*) aims to cut TB incidence and death rates in half from 1990 levels by 2015, and ultimately rid the globe of TB by 2050. The plan lays out cost projections for TB control and for research on new tools to control TB over the next ten years, including diagnostics, drugs, and vaccines. According to *GP2*, the world needs to invest $9 billion in R&D over the next decade to discover, develop, evaluate, and disseminate effective new TB diagnostics, drugs, and vaccines.

While *GP2* projects a $6.1 million funding gap for new tools over the next decade, the results of this preliminary assessment suggest that the baseline levels of funding for TB R&D are lower than estimated in *GP2*:

– Where *GP2* states that $59 million is needed for new diagnostics research (preclinical and clinical) in 2006, respondents reported only $15.4 million for this research in 2005.

– Where *GP2* states that $418 million is needed for new drugs research (preclinical and clinical) in 2006, respondents reported only $99.8 million for this research in 2005.

– Where *GP2* states that $285 million is needed for new vaccine research in 2006, respondents reported only $67.3 million for this research in 2005.

Thus, if the funding levels remain the same as in 2005, in year one of *GP2*, the world is already falling short by $43.6 million for diagnostics, $318.2 million for drugs, and $217.7 million for vaccines. (Some new money has become available—for instance, $15 million from the Gates Foundation to the TB Alliance in 2006 and a preclinical drug grant program Accelerator that is expected to provide $40 million over two years. On the other hand, CDC and NIH are slated for budget cuts this year and next.)

To avoid double-counting, TAG analyzed contributions to and disbursements by public-private product development partnerships (PDPs)—such as the Aeras Global TB Vaccine Foundation, the Foundation for Innovative New Diagnostics (FIND), the Global Alliance for TB Drug Development—and those to and by multicenter funding consortia—such as the mainly EU-funded EDCTP and TB-VAC consortia—separately from major funders. In 2005 the PDPs and research consortia reported a total of $49 million in disbursements. TB vaccines received the largest investment, $33.4 million

(68.2% of PDP/funding consortia investment), most of it by Aeras ($25.5 million). TB drugs received $6.2 million (13% of PDPs/funding consortia), and TB diagnostics $2.2 million (4.5% of PDPs).

It is obvious that investment in TB R&D by all sectors must increase substantially just to achieve baseline funding conditions specified in *GP2*. Results of this preliminary assessment suggest that in the first year of *GP2* we are not yet at the starting line in the race to achieve the 2015 targets. Of the $348 million reported by the 30 respondents whose R&D is summarized in this report, approximately $182.5 million is directly targeted at new diagnostics, drugs, and vaccines. This is 2% of the *GP2*'s estimated $9 billion needed for new tools R&D funding over the coming decade. *GP2* does not specifically call for greater investment in basic science, which underpins all discovery efforts, and does not fully account for the operational research needed to integrate new tools into health care systems.

The top challenges for this preliminary assessment were the lack of transparency from the commercial sector and the lack of standardized internal tracking systems for TB R&D in the public sector in G8 and high-TB-burdened countries. Future resource tracking efforts would benefit from greater openness and from commonly applied and reported definitions of research category, phase, and focus. Despite the data limitations, TAG's preliminary assessment reveals severe underfunding of TB R&D at all stages, including new tool discovery and development as well as basic science and operational research. The progress of science depends directly on funding. While *GP2* estimates that TB research needs to increase threefold over the coming decade, based on the shortfall identified herein, TAG estimates that an immediate fivefold increase is needed to win the battle against one of humanity's oldest and most lethal pathogens.

# 1. Introduction

## 1.1 The Importance of TB R&D

"There were approximately 9 million TB cases and approximately 2 million TB deaths in 2004." (WHO 2006). The tuberculosis organism, *Mycobacterium tuberculosis* (MTB) has been with humans since an early period of our evolution. It infects one-third of the world's population, at least two billion people. While 90% of those with latent TB infection (LTBI) never progress to active disease, 5–10% of them develop TB disease during their lifetime. In people coinfected with HIV this risk increases to 5–10% per year.

MTB was discovered in 1882, and its presence in sputum from infected individuals, detected as acid-fast bacilli (AFB) by sputum smear microscopy, was part of Robert Koch's contribution to the field. Koch also introduced tuberculin skin testing (TST), the first method for detecting TB infection by measuring the magnitude of an immune response on a skin test. The Bacillus Calmette-Guérin (BCG) attenuated *M. bovis* strain has been used to vaccinate three billion infants and children for TB since the 1920s. Each year, over 100 million children receive BCG; however, it fails to protect from pulmonary disease during adolescence and adulthood and may be dangerous in HIV infected infants. Effective drug treatment for TB has been available since the 1940s and is used either as single-drug preventive treatment for LTBI with isoniazid (INH), or as short-course combination therapy for TB disease, most commonly with two months of isoniazid, rifampin (rifampicin), pyrazinamide, and ethambutol (known together as HRZE) followed by four months of isoniazid and rifampin (HR) or six months of ethambutol and isoniazid (EH), though the latter is less effective.

Close contact with people with infectious TB creates ideal conditions for its epidemic spread. In Europe during the Industrial Revolution in the 1800s TB was the leading infectious killer, especially among people who lived in closely crowded quarters with poor access to light, fresh air, sufficient food, and clean water. Similar conditions now promote TB's spread in resource-poor settings around the world. TB rates dropped in Western Europe and the U.S. even before the discovery of BCG or treatments because rising economic development had improved sanitation and living standards, making TB easier to contain (Dubos 1952). Some people who became sick with TB were able to overcome or contain the disease within their bodies as well. The factors for this are not clearly defined but include T-cell immunity mediated through interferon gamma and interleukin 12 and were probably selected for over the millennia in which TB killed millions of humans.

Improved public health, economic development, widespread BCG vaccination, the introduction of antituberculosis treatment (ATT), and isoniazid preventive therapy

(IPT) for latent TB infection, resulted in dramatic global reductions in TB disease between 1940 and 1980. However, short-term TB control using BCG, TB drugs, isoniazid preventive therapy, and antibiotics led to complacency and a decreasing interest in infectious disease research and control. From 1980 on, the U.S. government, the International Monetary Fund (IMF), the World Bank, and others supported policies that weakened health systems in developing countries and undermined their ability to effectively address any emerging epidemic (Breman 2001; Gandy 2003).

As the HIV pandemic spread through the 1980s, TB came roaring back. In 1991 an outbreak of HIV-related multi-drug resistant (MDR) TB in New York City cost over $1 billion to contain. That year the World Health Assembly (WHA) set global TB control targets of detecting 70% of smear-positive TB patients and curing 85% of them by 2000 (Resolution WHA 44.8). In 1993 WHO declared TB a global emergency and the World Bank issued an influential report stating that TB control was one of the most cost-effective health interventions (World Bank 1993). In 1994 WHO launched the new TB control framework, branding it "DOTS" in 1995. Surveillance and monitoring systems were established in countries implementing the new approach. In the late 1990s the Stop TB Partnership was established, with its secretariat housed at WHO. Governments ascribed to the Amsterdam Declaration in 2000 and the Washington Commitment in 2001, which also saw the launch of the first *Global Plan to Stop TB* and of WHO's Stop TB Department. By the turn of the millennium several public-private product development partnerships (PDPs) were formed to accelerate product development for new TB vaccines, drugs, and diagnostics, with encouragement from the Rockefeller and Gates Foundations, among others.

Over the past decade DOTS coverage has grown worldwide and many countries are now scaling up their programs to reach 100% population coverage. However, despite these advances, TB incidence and mortality rates continue to grow worldwide, fueled by HIV in Africa and by collapsing health systems leading to multidrug-resistant MDR-TB in Eastern Europe. WHO has reported that global TB incidence rose 1% in 2004, while African TB incidence rose by 4% (WHO 2006).

Most of the existing tools to control TB—diagnosis through smear microscopy and TST, BCG vaccination, and combination chemotherapy—date from the years between 1880 and 1966, when the last new class of anti-TB drugs, the rifamycins, was discovered. In the 1940s and 1950s, which were considered a golden age of antibiotic drug discovery, TB was still a common killer disease in some industrialized nations, and therefore the pharmaceutical industry had incentives to invest in, test, and seek marketing approval for new drugs to fight TB.

But as TB incidence declined in the industrialized world, so did the profit motive for developing new tools. The recent resurgence in TB rates has sparked a renewed

commitment—though not by industry—to discover more efficient tools to combat the disease. To date, the leading investment in TB R&D has come from public sector R&D agencies in the U.S., the U.K., and to a lesser extent the E.U., and from the Bill & Melinda Gates Foundation, which itself is the second highest contributor to TB research. Private sector sources such as R&D-based pharmaceutical and biotechnology companies have either not stepped up to the challenge or are unwilling to share publicly the details of their investments in TB product development. However, as this report will demonstrate, overall TB research investments remain insufficient to the need.

In the 1990s, WHA declared TB a global emergency and world governments committed to detect 70% of all infectious (smear-positive pulmonary) cases and to cure 85% of these by 2000 (WHO 1991), later changing the goal to 2005, and still later to 2015 (Stop TB 2006). Today, more people die of TB than of any other curable infectious disease (WHO 2006).

In 2000 the UN's Millennium Development Goals established a target of halting and beginning to reverse by 2015 the ravages of multiple infectious diseases including HIV, malaria, and—by implication if not explicitly—tuberculosis. The Stop TB Partnership set for itself an even more ambitious goal of cutting TB incidence and death rates in 2015 by half from 1990 levels. Since 1990 was just before HIV began cutting its incendiary swath through Africa and just before MDR-TB began spreading in Eastern Europe, the Partnership estimates it will be unable to attain its own goals for Africa and Eastern Europe by 2015 (Stop TB Partnership 2006). The Partnership further calls for the elimination of TB as a public health threat (meaning less than one case per million people) worldwide by the year 2050.

With current tools alone, the world is unlikely to reach the 2015 goals. Reaching the 2050 TB targets seem utterly impossible, especially in Eastern Europe and in sub-Saharan Africa without a revolution in new TB diagnostics, drugs, and vaccines. Meeting such targets depends upon the successful discovery of novel and improved methods to diagnose, treat, and prevent the world's oldest scourge. As we hope to show, the world is already far from reaching its TB R&D investment targets in 2006, the base year from which *The Global Plan to Stop TB: 2006-2015* begins.

Today, investment lags behind the world's stated goals to curb and eventually eradicate TB. There are currently three vaccines, six drugs (four novel ones) in clinical trials, and a handful of new diagnostic technologies in pilot evaluation phases. These scientific advances show that progress is possible, albeit slow and unsteady, with current funding. However, according to *GP2*, over the next ten years the world needs to invest $9 billion in R&D to discover, develop, evaluate, and disseminate effective new TB diagnostics, drugs, and vaccines, and to provide additional resources for

operational research. According to Stop TB, approximately $2.9 billion in funding can be counted on, with a $6.1 billion gap in R&D funding for new TB tools over the next decade. *GP2* does not include a target for basic science and does not set a comprehensive goal for operational research.

In spring 2005, TAG began a preliminary resource mapping exercise to establish a baseline for TB R&D funding. This would enable us to assess current spending, identify donors, analyze research gaps, and provide recommendations for improving TB R&D in order to meet the 2015 and 2050 goals.

TAG surveyed organizations believed likely to be significant funders of TB-related R&D. In this preliminary resource mapping analysis we present results from the top 30 TB-related R&D funders who were willing to disclose details of their research investments. Ten pharmaceutical or biotechnology companies declined to provide details of their investments, and information requests to other potential sources remain outstanding (*see Appendix B*).

Total investments by the top 30 reporting funders of TB research in fiscal year (FY) 2005, our index year for comparison purposes, totaled $348 million. If projected at the same level over the next decade, $3.48 billion would be available for all categories of TB R&D.

Of the $348 million identified, $93.1 million (27%) was categorized as basic science and $48.7 (14%) as operational research. Research on new TB tools came to a mere $15.4 million (4%) for new TB diagnostics, $99.8 million (29%) for new TB drugs, and $67.3 million (19%) for new TB vaccines. Another 7% was categorized as spending on infrastructure or unspecified investments.

Total reported 2005 research funding for new TB diagnostics, drugs, and vaccines came to $182.5 million. If the 2005 level of resources are continued for ten years it will amount to $1.83 billion, far short of *GP2*'s projection of $2.9 billion in available funding. Thus we find a $7.17 billion gap in new tools R&D resources available for the next decade, exceeding Stop TB's estimate of a $6.1 billion shortfall. Obviously much more research funding will be needed to intensify basic research and carry out the full operational research program necessary to validate new tools and integrate them into TB control programs around the world.

## 1.2 Current TB Tools

The lack of a rapid and accurate point-of-care TB diagnostic is impeding progress toward improved TB case detection rates. Technology must move beyond the standard sputum microscopy discovered in the 1880s in order to improve diagnostic

rates. This 19th-century TB test fails to detect over half of all active cases, can take several clinic visits to yield results, is labor-intensive for both patient and provider, and is nonspecific for MTB. Furthermore, as nearly two-thirds of those who are TB/HIV coinfected are smear negative or have extrapulmonary TB, this test will not detect their infection. Its low sensitivity in HIV-positive and pediatric tuberculosis renders it even less effective precisely in people who are most likely to die from the disease. The Foundation for Innovative New Diagnostics (FIND) estimates that smear microscopy detects just 19% of TB cases worldwide (Nantulya 2006).

WHO's Stop TB's Working Group for New Diagnostics calls for the development of new diagnostic tests that can detect pulmonary TB disease with high or low bacterial loads, extrapulmonary TB, pediatric TB, drug-resistant TB, and latent TB infection (Perkins 2006).

Similar to the outdated diagnostic method, TB therapeutics—the last approved class was discovered 40 years ago—do not meet the demands of the current epidemic. Specifically, there's an urgent need for shorter regimens that cure more rapidly. Existing multidrug regimens, while technically effective in treating drug-sensitive pulmonary TB, require six months of treatment, which can lead to difficulties in completing therapy. A shorter regimen would benefit adherence, resulting in higher cure rates. There's also a pressing need for drugs that can be safely taken concurrently with antiretroviral therapy used to treat HIV. Rifampin, for example, has potentially dangerous interactions with commonly used antiretroviral (ARV) drugs, such as nevirapine and several protease inhibitors. Novel drugs are also needed for difficult-to-treat TB cases and for MDR-TB.

The live attenuated *M. bovis* Bacillus Calmette-Guérin (BCG), discovered in 1921, is the world's most widely used vaccine and can reduce post-natal and early childhood TB mortality rates by 90%, according to some studies (Anderson 2006). Despite its value in childhood, the vaccine has little to no efficacy in preventing pulmonary TB, the most common and most infectious form of the disease, among adolescents and adults. TB's resurgence in places where BCG vaccination is nearly universal indicates the vaccine's limits. Research using genetically modified BCG or MTB protein subunits is underway to develop a vaccine to prevent both new infections and reactivated TB disease (Lee 2006).

## 1.3 Objectives

TAG aims to highlight gaps in spending as well as in areas of scientific study by tracking major institutions that contributed to TB R&D. Findings from this unprecedented analysis will be used to advocate for strategic funding for new tools for TB diagnosis, treatment, and prevention, and for expanded basic and operational research efforts.

The focus year of TAG's analysis is 2005, the latest year for which complete data were available. This mapping of TB research provides an impression, not a comprehensive global tally, of the year's research investments. In order to capture the largest donors, the final report will be released at the 37th Union World Conference on Lung Health in fall 2006. It will primarily document contributions from G8 member nations' public research agencies, international development agencies, major nonprofit charitable foundations and trusts, pharmaceutical and biotechnology companies, and select high-burden countries (HBC), if we succeed in obtaining detailed information.

The figures presented in this report should not be interpreted as complete or absolute findings. Nevertheless, the ten top donors to TB R&D are likely included here.

## 1.4 Methodology

TAG used an e-mail survey to solicit: actual annual *disbursements* for TB research for 2004, 2005, and 2006 (not commitments or awards); the amount of funds an institution received or disbursed; a grant portfolio describing the research; and qualitative responses about priorities and obstacles in TB research. The one exception is the significant diagnostics BMGF Grant, acknowledged in the relevant section.

Funding data were collected largely from original-source donors; however, in some cases recipients of funding, such as research organizations, were tracked if the source was not available and/or the recipient organization plays an integral role in programming funding for TB research, e.g. WHO's Special Programme for Research and Training in Tropical Diseases (TDR). In addition to donors and researchers, TAG tracked public-private product development partnerships (PDPs)—funding managers that help expedite focused product-development research. Data were cross-referenced to avoid double-counting.

Data were collated from public and private sector sources and were supplemented by interviews with a range of experts in the TB research community, including Secretariat staff and/or chairs of Stop TB's Working Groups for new TB diagnostics, drugs, and vaccines. Most of the information is based on self-reporting by recipients and representatives of the funding sources, while some figures are garnered from donor web sites.

In addition to tracking *total* investments in 2005, TAG asked respondents to classify their TB R&D investments into five major research categories:

**• Basic • Diagnostics • Drugs • Vaccines • Operational**

TAG also requested respondents to classify their research by stage (preclinical or clinical), but this proved difficult for some respondents. Nevertheless, the number of new agents in clinical trials is still quite small at the present time (six new drugs, five vaccines).

To ensure exchange-rate consistency, on the recommendation of WHO's Global TB Surveillance, Planning and Financing Project (Floyd 2006), TAG used the Oanda Currency Site (www.oanda.com/convert/classic) and selected 1 July 2005 as the date to convert all foreign currency into U.S. dollars at interbank conversion rates. Different funders use different fiscal years, and domestic investments are not converted, so a purchasing power parity conversion may be more appropriate in some cases (e.g., India, Russia).

TAG's investigation of TB R&D contributions began in March 2006 and will continue through October 2006. TAG will continue to interview key stakeholders and activists to inform the report's recommendations for establishing better resource tracking mechanisms and developing a global TB research movement to mobilize significant and sustained increases in funding for TB research.

## 1.5 Limitations of the Data

A list of potential TB research funders was generated using information from the Stop TB Partnership web site, reports by Aeras, FIND, and the TB Alliance, and from desktop research. Key informants in the TB research community were consulted to assist in confirming a core list of significant donors. A preliminary survey was sent to sixty-six potential research donors or recipients. Thirty donors provided 2005 disbursement information. Ten respondents—mostly from industry—declined to provide data. The remaining responses are incomplete or unavailable at press time. Twelve agencies reported that they are not primary funders of TB research (*see Appendix B*).

Some of the surveyed sponsors did not have readily available data detailing research into new TB tools. Sometimes donor representatives cherry-picked information from disparate lines of funding, which resulted in incomplete data that can be difficult to categorize, resulting in their placement in the catchall "unspecified" category. In addition to poor internal tracking, there are no commonly agreed upon standards defining research categories across the field of TB research.

Some donors reported money awarded to research institutions that focus on infectious diseases but did not specify the amount apportioned to TB. In these cases, TAG relied on the recipient to report on spending activity; in a few cases there are discrepancies between stated donor funding and reports from the recipient agency. TAG deferred to donors when possible.

Funders and research organizations have various means of recording grants—for example, commitments or awards made one year may be disbursed the following year. TAG tried to adhere as strictly as possible to counting actual money disbursed in fiscal year 2005.

Only four out of fourteen surveyed pharmaceutical and biotechnology companies disclosed financial information. Ten declined, despite being given the option to have their totals be presented anonymously or only as an aggregate. Because the commercial sector is often unwilling to reveal investments or returns to the public, TAG, thus far, is not able to quantify industry support for TB research. The four responding companies are included in the total. They include AstraZeneca (the philanthropic arm of the company), Novartis, Otsuka, and Sequella, whose commitments to TB R&D and to R&D transparency are commended.

# 2. Results

**Table 1: Top 30 Funders of TB R&D Reported to TAG by August 2006**
(*see Appendix A for investments by research category*)

| Rank | Donor | Total |
|---|---|---|
| 1 | NIAID / NIH | 120,273,000 |
| 2 | Gates Foundation | 57,411,457 |
| 3 | Medical Research Council (UK) | 30,887,839 |
| 4 | Other Institutes & Centers / NIH | 20,334,300 |
| 5 | Centers for Disease Control | 19,903,000 |
| 6 | Wellcome Trust | 18,081,359 |
| 7 | NHLBI / NIH | 17,117,000 |
| 8 | European Commission 6th Framework | 13,322,711 |
| 9 | Otsuka | 12,300,000 |
| 10 | AstraZeneca | 8,000,000 |
| 11 | USAID | 6,694,000 |
| 12 | Netherlands Ministry of Foreign Affairs (DGIS) | 3,168,488 |
| 13 | Max Planck Institute | 2,500,000 |
| 14 | Canadian Inst. of Health Research | 2,376,098 |
| 15 | Novartis | 2,255,193 |
| 16 | Dept. for International Development (DFID) | 2,008,832 |
| 17 | Russian TB Institutes* | 1,930,343 |
| 18 | Rockefeller Foundation | 1,750,000 |
| 19 | Global Fund** | 1,648,083 |
| 20 | Research Institute for TB (RIT) / JATA, Japan | 1,487,961 |
| 21 | Sequella*** | 1,400,000 |
| 22 | Ellison Foundation | 1,000,000 |
| 23 | Food and Drug Administration | 651,231 |
| 24 | Swedish Int. Development Agency | 486,599 |
| 25 | Development Cooperation of Ireland | 360,000 |
| 26 | Netherlands Org. for Scientific Research (N.W.O.) | 199,716 |
| 27 | Swiss Agency for Development and Coop. | 195,099 |
| 28 | KNCV Tuberculosis Foundation | 170,666 |
| 29 | All India Institute of Medical Sciences | 154,821 |
| 30 | World Bank | 140,350 |
| | **TOTAL** | **$348,208,146** |

* Aggregate spending of four Russian Federation TB institutes.
** Global Fund figures estimated based on their reported activities.
*** Sequella spent $3.5 million; $2.1 million from NIH not counted twice.

## 2.1 Donor Categories

Investments by the top 30 reporting donors to TB R&D in 2005 came from the public sector (70%), private philanthropic foundations (22.5%), pharmaceutical and biotechnology industries (6.9%), and multilateral organizations (0.5%). In addition, product development partnerships (PDPs) and research consortia reported spending $49 million on TB R&D; this was not included in the global total to avoid double-counting.

## 2.2 Research Investment Categories

Scientific grants and research programs focusing on *Mycobacterium tuberculosis* (MTB) and tuberculosis (TB) disease are categorized according to the descriptions below that are adapted from *Shots in the Dark: The Wayward Search for an AIDS Vaccine* (Cohen 2001).

**Basic research** aims to uncover the knowledge that may have no immediate, specific, practical application but will eventually directly benefit TB by increasing the knowledge base, which will lead to new discoveries; it includes cell biology, genetics, immunology, mycobacteriology, and animal models of transmission and pathogenesis.

**Applied/preclinical research** involves studies which are directed toward a targeted aim in preparation for human study or use. For purposes of this preliminary assessment, it includes infrastructure or capacity building. This category also includes "unspecified" research, representing data that TAG was unable to code. It is placed here because some funders unable to subcategorize their research grants stated that their funding was going to TB research but that they were unable to specify in what category their investments fit.

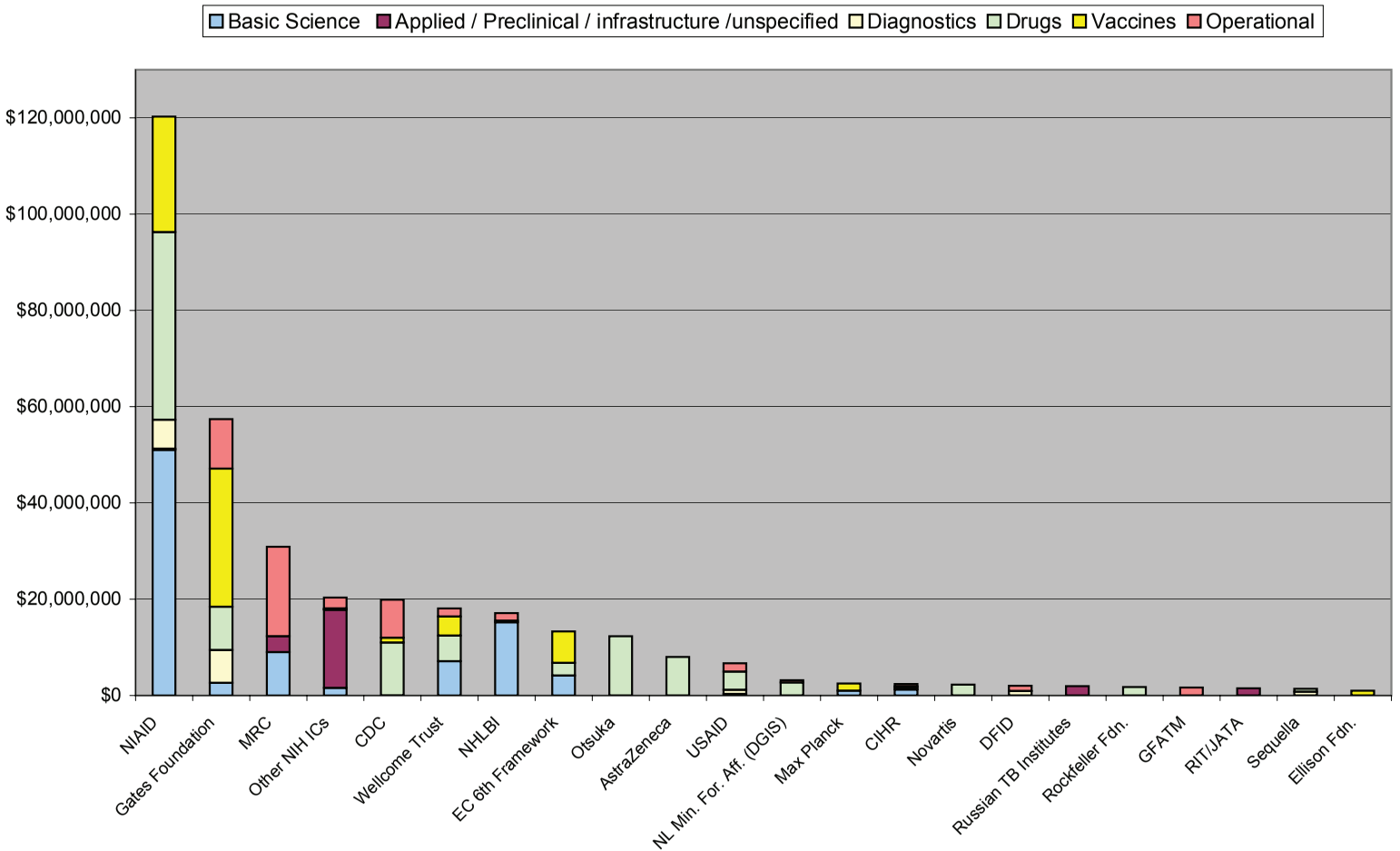
**Diagnostics research** is defined as R&D targeted at the discovery, development, and pilot-stage testing of new diagnostic tests to detect latent TB infection, active TB disease (pulmonary and extrapulmonary), drug susceptibility and resistance, or biomarkers, which predict prognosis or response to therapy. Some operational research on existing diagnostic tests which are being studied in new settings (for example, BACTEC-MGIT rapid liquid culture, ELISPOT, Quantiferon-Gold) may be included in this category.

**Drug research** is defined as early stage lead-compound optimization, and clinical trials in humans.

**Vaccine research** is defined includes preclinical development consisting of, for example, toxicology, and safety studies; capacity building of vaccine trial sites, and clinical trials in humans.

**Operational research** pursues the most effective methods of implementing new or existing products and helps answer broad questions that may impact on health care delivery or policy. This includes program-related epidemiology, natural history, and surveillance; targeted program monitoring and evaluation; and health policy. TB operational research includes both rigorously designed studies, such as those funded by the CREATE consortium, as well as less academic investigations of new or existing interventions in routine program conditions. As such it tends both to overlap with earlier phases of testing and with TB control programs, while at the same time remaining a bit of a research orphan. (PEPFAR, for example, refers to such research as "targeted evaluation.")

## Figure 2: Top 22 Donors of TB Research (over $1 million)



## 2.3 TB R&D: Ten Major Funders

### 1. National Institute of Allergies and Infectious Diseases (NIAID), National Institutes of Health (NIH)

The U.S. National Institutes of Health (NIH), the world leader in health research spending, is the world's biggest funder of TB research. In 2005 NIH awarded $157.7 million in grants and contracts to study tuberculosis, which is 45% of all TB research reported.

Eight institutes, offices, and centers awarded over $1 million dollars to TB in 2005. Given the paltry overall state of investment in TB R&D, any one of those eight institutes would have made it into the top twenty-two funders in our preliminary assessment.

We obtained detailed information on NIH TB spending from the Computer Retrieval of Information on Scientific Projects (CRISP, www.crisp.cit.nih.gov); from NIH's annual summary of spending on diseases and research areas (www.nih.gov/news/fundingresearchareas.htm); from key institute staff, such as Christine Sizemore at Division of Microbiology & Infectious Disease (DMID), NIAID, and Hannah Peavy at the National Heart, Lung & Blood Institute (NHLBI); from the NIH budget office; and from individual institute and centers' communications offices, which in some cases responded to Freedom of Information Act (FOIA) requests.

Compared with many agencies, NIH is a model of transparency, with full grant information readily available on every award. However, NIH's dispersed structure, currently involving 27 different institutes and centers, and even more offices, along with the antiquated nature of the CRISP database, calls for an updated approach to resource tracking. Some holes remain in our analysis; $12.8M—mainly from institutes with smaller TB portfolios from whom we await detailed responses—was coded as unspecified. In addition, the NIH Office of AIDS Research (OAR), which maintains the AIDS Research Information System (ARIS), a separate, more detailed database than CRISP, does not currently code for TB/HIV-related projects. Doing so will require queries to be sent to each NIH institute and center conducting HIV research to determine what proportion of it might be related to TB/HIV. TAG hopes to include the remaining NIH coding and OAR grants in the full review this fall.

In 2005, NIH's budget, appropriated by Congress, for all health research totaled $28.6 billion. Of this, $157.7 million, or 0.55%, went for TB research—approximately 52 cents per U.S. resident.

Within NIH, the National Institute of Allergy and Infectious Diseases (NIAID) alone awarded $120 million to TB R&D, 35% of all expenditures reported to TAG. NIAID was the biggest contributor to TB R&D in 2005, spending more than twice that of the

second major donor to TB research, the Bill & Melinda Gates Foundation (BMGF).

Of NIAID's $120 million in TB R&D disbursements, $51 million went to basic research and $39 million, $24 million, and $6 million was apportioned for TB drug development, vaccines, and diagnostics, respectively.

NIAID provided 76% of NIH's TB funding. Part of NIAID's mission is to "support a comprehensive extramural research program, encouraging and funding all aspects of basic, translational, and applied research, leading to a better understanding of TB, as well as to the development of novel vaccines, drugs, and diagnostics." (Sizemore 2006)

Neither the president nor Congress currently supports increasing the NIH budget in the near future. As long as the overall NIH budget is flat, it will be very difficult for advocates to succeed in attracting increased funding for any disease, no matter how deadly, until the entire NIH budget once again enjoys healthy multiyear growth as it did from 1994 to 2002. Current NIH-estimated levels of funding for TB R&D remain flat at $158 million for fiscal years 2006 and 2007.

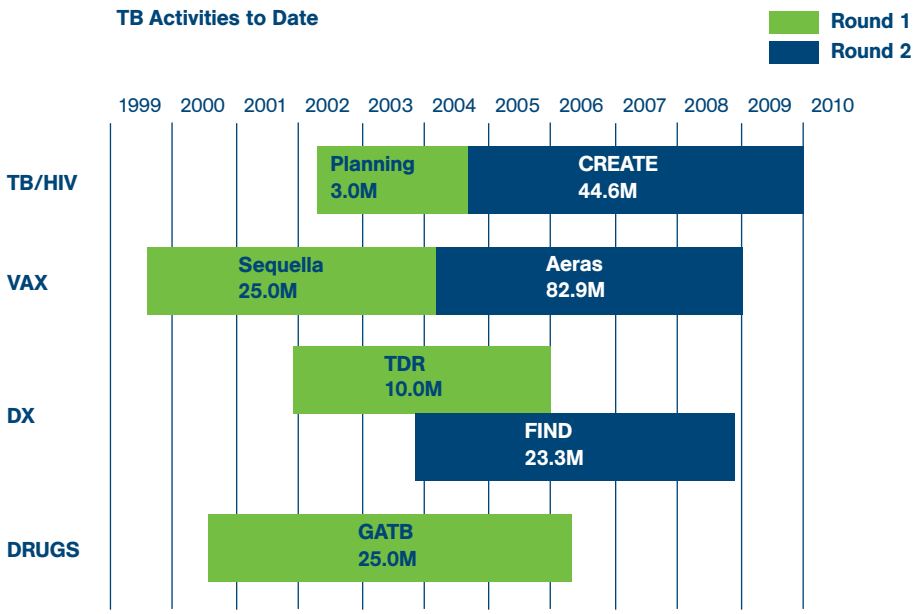
### 2. The Bill & Melinda Gates Foundation (BMGF)

The Bill & Melinda Gates Foundation (BMGF) is the world's largest private philanthropic organization with an endowment at the end of 2005 of $29.2 billion. That year the Gates Foundation distributed a total of $1.36 billion, of which $843,742,000, or 62%, went to the Global Health Program (Gates Foundation 2006); $57.4 million went to TB R&D. In coming years a historic gift from investor and philanthropist Warren Buffet will approximately double the Gates Foundation's annual spending.

At *GP2*'s launch in Davos last January, Bill Gates pledged up to $900 million in TB R&D funding over the coming decade, meaning an average annual commitment of $90 million. In 2005 about half of Gates Foundation TB spending—$28.7 million—was on new vaccine research, with $2.6 million going to basic research, $6.8 million to new diagnostics, $9 million to new TB drugs, and $10.3 million to operational research. New initiatives not yet funded in 2005 include the preclinical drug discovery Accelerator package ($40 million over two years, due to start later in 2006) and a $104 million five-year grant expansion for the Global Alliance for TB Drug Development (with $15 million in 2006).

The Gates Foundation's TB priorities are to prevent incidence and prevalence of disease by developing safe, effective, and affordable new tools, and by supporting the appropriate management of TB in regions with high HIV prevalence. To reach these goals, seven grant packages support the following work:

**Figure 3: Evolution of Gates Foundation TB Funding**




*Courtesy P. Small 2006*

**Aeras Global TB Vaccine Foundation** received $26,664,075 in 2004, $24,417,457 in 2005, and is projected to receive $31,800,000 in 2006. Its mission is to develop and license an improved TB vaccine for use in high-burden countries and to bring from one to three new vaccine candidates into early-phase testing.

**FIND**—the Foundation for Innovative New Diagnostics–received $4,269,000 in 2004 and $4,569,000 in 2006. It is projected to receive another $5,269,000 later this year. Its mission is to accelerate late-stage development of diagnostic tests for neglected infectious diseases including TB. Note: Because the first 2006 payment was committed as 2005 funding, we counted it in 2005, even though it was disbursed in 2006.

**TDR**—Tropical Diseases Research, housed at WHO—is a multipartner funding consortium focusing on neglected diseases of the developing world including TB. In 2005 the Gates Foundation awarded TDR $2.25 million to support development of new TB diagnostics.

**TB Alliance**—the Global Alliance for TB Drug Development—received $20,000 in 2004 and $5 million in 2005. Its mission is to develop new and effective anti-TB drugs that are affordable worldwide. This summer the Gates Foundation announced a new $104 million award to the TB Alliance, of which $15 million will be made available in 2006.

**CREATE**—the Consortium to Respond Effectively to the TB/HIV Epidemic—received $9.3 million in 2004, $10.2 million in 2005, and is slated to receive $8.3 million in 2006. Its mission is to develop and validate novel, community-level intervention strategies to reduce rates of TB in populations with epidemic rates of HIV infection and escalating TB incidence.

**Grand Challenges in Global Health** (GCGH) is a set of large grants to "transform health in the world's poorest countries, and bring state-of-the-art solutions to people who need them most. Some of the projects are focused on adapting existing health tools, such as sophisticated laboratory tests, to novel technology platforms to make them practical for developing countries. Other projects seek to fundamentally redefine our understanding of how to prevent and treat disease, potentially leading to entirely new vaccines and drugs for diseases of the developing world. Many of the projects are applying cutting-edge technology that has never before been used to advance global health. After the 14 challenges were published in the journal *Science* in October 2003, scientists submitted more than 1,500 project ideas. From these, 43 projects, involving collaborators in 33 countries, were selected for funding, some of which are described below. The Grand Challenges initiative is supported by $450 million from the Gates Foundation, $27.1 million from the Wellcome Trust, and $4.5 million from the Canadian Institutes of Health Research (CIHR). Four of the grants focus on TB:

– **GC5: Determine how to design antigens for effective protective immunity** (4 awards, one TB-related): Enhancing the immunogenicity and efficacy of vectored vaccines, Adrian Vivian Hill, Oxford, UK, $10 million over five years. Dr. Hill and colleagues will explore DNA and recombinant viral vector vaccinees for HIV, TB, and malaria; $2 million per year over five years.

– **GC6: Learn which immunological responses provide protective immunity** (6 awards, one TB-specific): Biomarkers of protective immunity against TB in the context of HIV/AIDS in Africa, Stefan H.E. Kaufmann, Max Planck Institute, Germany, $13.1 million over five years. Dr. Kaufmann will lead 15 institutions in Europe, Africa, and the U.S. to identify immune system differences between people exposed to TB who never become sick and those who develop serious disease, focusing particular attention on people with TB and HIV; $2.62 million per year.

– **GC11: Create therapies to cure latent infections** (one award): Drugs for treatment of latent TB infection, Douglas Young, Imperial College London, UK, $20 million over five years. Dr. Young will lead a collaboration among the U.K., the U.S., Singapore, Korea, and Mexico to investigate the fundamental biology of TB latency and use this to develop drugs effective against latent TB; $4 million per year.

– **GC12: Create immunological methods to cure latent infection** (4 awards, one TB-specific): Preclinical and clinical evaluation of a post-exposure TB vaccine, Peter Anderson, Statens Serum Institute, Denmark, $11.3 million over five years. Dr. Andersen will lead a team in Europe, the U.S., and South Africa to study the MTB organism to identify mechanisms that allow it to escape from normal immune responses, which help some people keep TB under control for a lifetime, while others (particularly those with HIV) succumb to serious illness. The goal is to pursue information leading to a therapeutic vaccine that will enable people with latent TB infection to eliminate the infection; $2.2 million per year (Gates Foundation 2005; see also www.gcgh.org).

**TB Accelerator** will provide up to $40 million over two years (2006–2008) to accelerate the discovery of new TB drugs. Proposals were due on 30 April 2006 and are likely to be announced later this year (www.gatesfoundation.org/GlobalHealth/Grantseekers/RFP/RFP_TB.htm).

### 3. Medical Research Council, UK

MRC is the U.K.'s publicly funded medical research agency. In 2005 its budget was approximately $943 million, 3% of which went for TB R&D. This $30.9 million made it the world's third largest TB research funding agency in 2005. MRC supports a broad biomedical research portfolio ranging from basic biology to medical practice. In 2005 the largest portion of MRC funding, $18.6 million, went to operational research, much of it at the long-established MRC research unit in the Gambia. MRC also spent $9 million on basic research and $3.3 million on applied preclinical research. In 2006 MRC funding for TB treatment research will increase, as it is supporting the University College of London (UCL) to conduct the ReMox study of two moxifloxacin-containing regimens in comparison to standard TB treatment in Africa.

### 4. National Institutes of Health (NIH): Other Institutes & Centers (ICs)

Of the NIH's 27 institutes and centers, 12 contributed $20.3 million to TB research in 2005, in addition to the much larger and more focused programs from NIAID and NHLBI spending, which are listed among the top ten donors (nos. 1 and 7, respectively); $1.6 million went to basic research, $16.2 million to preclinical applied or unspecified, $70,279 to new drugs, $205,000 to vaccines, and $2.3 million to operational research. Noteworthy among these other TB programs are the international training grants provided by the Fogarty International Center (FIC), almost $4 million in 2005, which are highly effective and should be expanded.

**Table 2: Other NIH Institutes & Centers TB Funding 2005**

| | |
|---|---|
| National Center for Research Resources (NCRR) | 4,534,000 |
| National Institute on Drug Abuse (NIDA) | 4,196,000 |
| Fogarty International Center (FIC) | 3,977,000 |
| National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) | 2,000,000 |
| Office of Director (OD) | 1,612,000 |
| NIH Roadmap initiatives | 1,279,000 |
| National Institute of Child Health and Human Development (NICHD) | 846,000 |
| National Institute of Alcohol Abuse & Alcoholism (NIAAA) | 742,000 |
| National Institute of Aging (NIA) | 518,000 |
| National Institute of Nursing Research (NINR) | 240,000 |
| National Center for Complementary and Alternative Medicine (NCCAM) | 140,000 |
| National Institute of Mental Health (NIMH) | 129,000 |
| National Institute of Dental & Craniofacial Research (NIDCR) | 121,000 |
| **Total** | **$20,334,300** |

### 5. U.S. Centers for Disease Control & Prevention (CDC)

The CDC's Division of Tuberculosis Elimination (DTBE) works to prevent and control TB in the U.S. and internationally. As part of its mission, DTBE conducts behavioral, health systems, and clinical research. The CDC disbursed $20.9 million for TB R&D in 2005. The largest investments went to the Tuberculosis Trials Consortium (TBTC) for clinical trials of TB treatments, totaling $11 million. The Tuberculosis Epidemiologic Studies Consortium (TBESC) spent $7.8 million on epidemiology and operational research. Another $1 million was given to Aeras Global TB Vaccine Foundation.

CDC funding for TB is falling, as is the CDC budget as a whole. Recently the TB Trials Consortium suffered a 10% budget cut. Along with USAID, CDC is programming some funds from the Office of the Global AIDS Coordinator (OGAC), the State Department unit which oversees the President's Emergency Plan for AIDS Relief (PEPFAR). While PEPFAR is an HIV initiative focused on prevention and treatment, not research, it is funding some important TB/HIV-related work, some of which might be relevant here (PEPFAR calls it "targeted evaluation" rather than "operational research"). We have not yet received TB research funding details from PEPFAR.

### 6. Wellcome Trust

The U.K.'s Wellcome Trust—a private philanthropy whose size and importance grew in the mid-1990s after the sale of pharmaceutical maker Burroughs-Wellcome to

Glaxo, now GlaxoSmithKline—runs a diverse range of grant programs supporting biomedical research, as well as activities in medical humanities, technology transfer, and public engagement with science.

The Wellcome Trust was the second largest philanthropic investor, and the sixth largest overall, in TB R&D in 2005, contributing $18 million. Basic research received the largest sum, $7.1 million; preclinical drug research received $5.3 million; vaccine studies received $4 million; and operational research was awarded $1.7 million.

### 7. National Heart, Lung and Blood Institute (NHLBI), NIH

NHLBI funds mostly basic research relative to cardiac, lung, and circulatory health. Many of its TB projects investigate host immune responses in the lung during TB infection. Information gained by this research may help in the discovery and development of new diagnostics, drugs, and vaccines, but is fundamentally basic biological science, much of which is investigator initiated. In 2005, NHLBI disbursed $17.1 million in TB research grants, $15.2 million of which went to basic science.

### 8. European Commission 6th Framework Programme (FP6)

The European Commission's financial contribution to TB R&D has almost doubled since 2002, in part due to the formation of a coherent framework to develop treatments and vaccines for TB. FP6 aimed to integrate European efforts toward small-scale, phase I clinical trials for vaccines and to establish production technologies for lead compounds for new anti-TB drugs. FP6 grants are funded through consortia of academic researchers across Europe, some working with mostly small biotechnology companies. The European Commission's 6th Framework Programme contributed a total of $13.3 million to TB R&D in 2005. Of this, $6.5 million went to preclinical vaccine studies, $4.2 million went to basic science, and $2.6 million went to preclinical drug studies (EC 2005).

### 9. Otsuka Pharmaceutical Co., Ltd.

Otsuka Pharmaceutical is a pharmaceutical company, based in Japan, investing in TB drugs with a focus on new drug classes. It has one drug in early phase II/early bactericidal activity (EBA) clinical trials. In 2005 Otsuka spent $12.3 million on drug development. As the drug company with the largest disclosed single investment in TB research in 2005, Otsuka deserves high regard.

### 10. AstraZeneca

AstraZeneca, based in London and Sweden with products available in 100 countries,

2005 sales of $24 billion, and profits of $6.5 billion, reported the second largest TB research investment from companies responding to TAG. AstraZeneca said it invested $8 million in TB drug R&D in 2005 through its philanthropic organization. In 2003 AZ announced it would invest over $10 million to establish a new TB drug discovery research unit in Bangalore, India, and in 2005 AZ collaborated with the TB Alliance to cosponsor the Open Forum on Key Issues in TB Drug Development. TAG salutes AZ for its forward-looking commitment to global TB R&D and for its relative transparency in disclosing its TB R&D figures for 2005. We hope that AZ and Otsuka will set a new tone for industry in the coming years.

## 2.4 Other TB R&D Funders

The second 12 of the 30 top reporting TB R&D funders represents funders at or above the million-dollar mark. Thus, the top 22 TB R&D funders can be called the "TB research 22," as WHO designates the 22 countries with the most TB cases the "TB 22." This middle tier of funders includes:

– two drug companies, #15, Novartis, at $2.26M; and #21, the small but intrepid Sequella, $1.4;

– three development agencies, #11, USAID; #12, the Netherlands Ministry of Foreign Affairs, $3.17M; and #16, the U.K. Department for International Development (DFID), $2M;

– three public research agencies, #13, Germany's Max Planck Institute, $2.5M, #14, the Canadian Institute of Health Research, $2.4M; and #17, the Russian TB institutes, $1.9 million;

– one multilateral funding mechanism, #18, the Global Fund to Fight AIDS, TB & Malaria (GFATM), $1.6M (mostly for operational research); and

– two foundations, $17, Rockefeller, $1.75M, and #20, Ellison, $1M.

All other funders who reported to TAG spent less than $1 million on TB research in 2005 (*see Appendix A*).

## 2.5 Challenges Estimating Industry R&D Investment

Four of fourteen companies surveyed agreed to provide at least overall TB investment figures for 2005; ten declined. All four who did respond made it into the top twenty, reporting a total of $23,955,193, mostly on drugs with smaller amounts allocated to diagnostics and vaccines.

It is difficult to estimate spending by the R&D pharmaceutical companies who declined to provide research investment figures. These include industrial behemoths such as Abbott, Bayer, BD Diagnostics, Eli Lilly, GlaxoSmithKline and GSK Bio, Johnson & Johnson/Tibotec, and Roche. Some of these companies still enjoy steady, if not stellar, revenue streams from TB products. Others have recently touted their increasing involvement in TB research.

Whether or not they are investing their own money or that of the Gates Foundation, via the product development partnerships (PDPs), such as Aeras, FIND, and the TB Alliance, is not at all clear. Reports from the PDPs made it clear that in some cases they were disbursing funds to industry, rather than the reverse—contrary to notions one might have about such partnerships. It may be that industry is providing matching funds, staff, facilities, or intellectual property. In any case, greater transparency by industry in regard to its R&D investments in neglected diseases of great global public health importance is clearly overdue. Enhanced industry investment would also be welcome.

## 2.6 Funding Recipients: Product Development Partnerships (PDPs) and Research Consortia

The resurgence of TB as one of the world's leading killers, plus a paucity of effective control methods, gave rise at the turn of the millennium to a new generation of nonprofit organizations known as public-private partnerships (PPPs) or product development partnerships (PDPs). These funding managers provide linkages and collaborative mechanisms enabling industry, governments, private philanthropic organizations, academic institutions, and public health programs to collaborate on specialized research agendas. Their formation may have spurred increased commercial sector involvement in neglected areas of new tool R&D development that has not traditionally yielded profits. They have also created opportunities for researchers who usually labor in isolated spheres to work across disciplines.

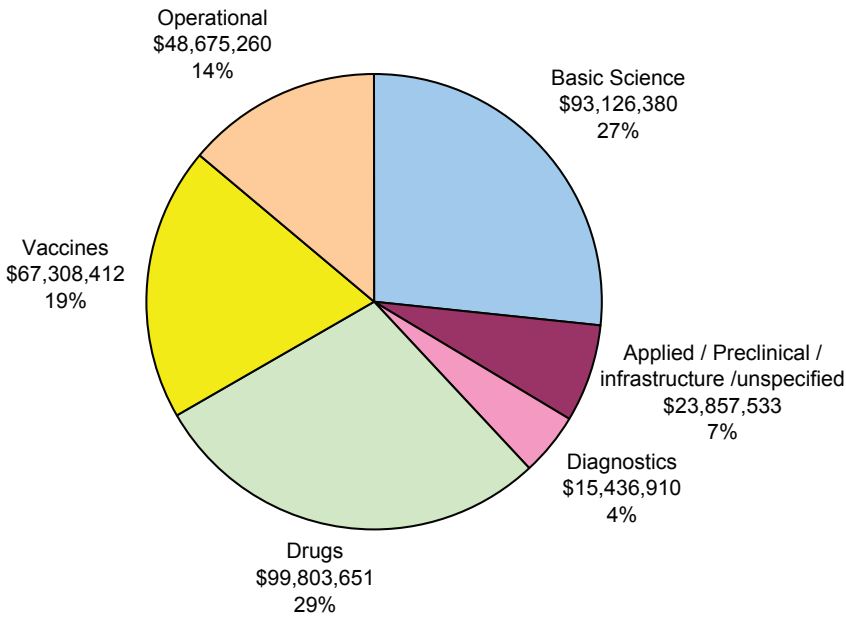
PDPs, along with other TB funding managers, such as research consortia and clinical trial networks, are not original funding sources. They both receive and disburse grants, and therefore do not appear in the preliminary assessment list of top TB R&D donors. The PDPs, along with other funding consortia were responsible for directing $49 million in R&D funds during 2005.

**Table 3: Significant TB R&D PDPs and Research Consortia**

| PDP/Funding consortium | 2005 TB spending (US dollars) |
|---|---|
| Aeras | 26,526,253 |
| TB-VAC | 6,778,239 |
| CREATE | 5,816,005 |
| Global Alliance for TB Drug Development | 5,556,397 |
| Foundation for Innovative New Diagnostics | 2,193,605 |
| TDR | 1,400,000 |
| EDCTP | 580,039 |
| WHO MDR-TB | 156,045 |
| **PDP/Funding consortia subtotal** | **$49,006,583** |

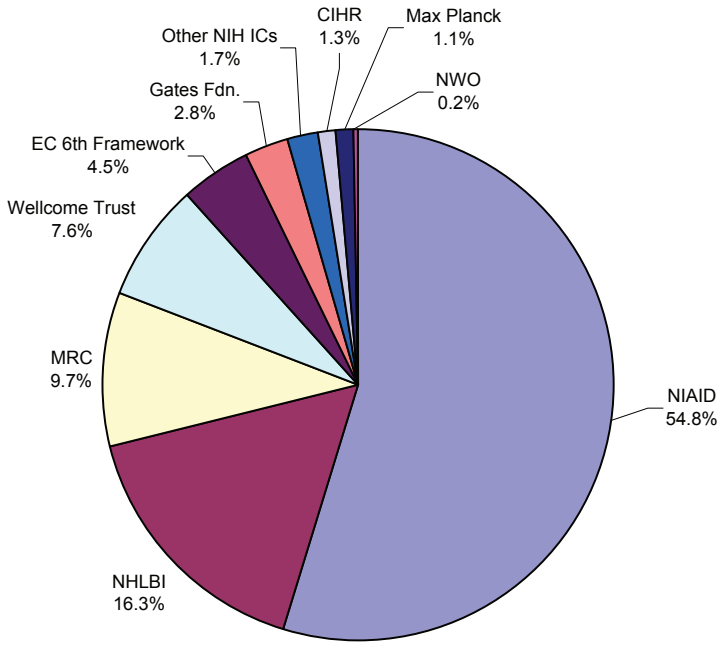
# 3. Tuberculosis R&D: A Close-up

**Figure 1: 2005 TB Research: Investment by Category (Total = $348,208,146)**



## 3.1 Basic Science

**Figure 4: Basic Science**
**(Total = $93,126,380)**

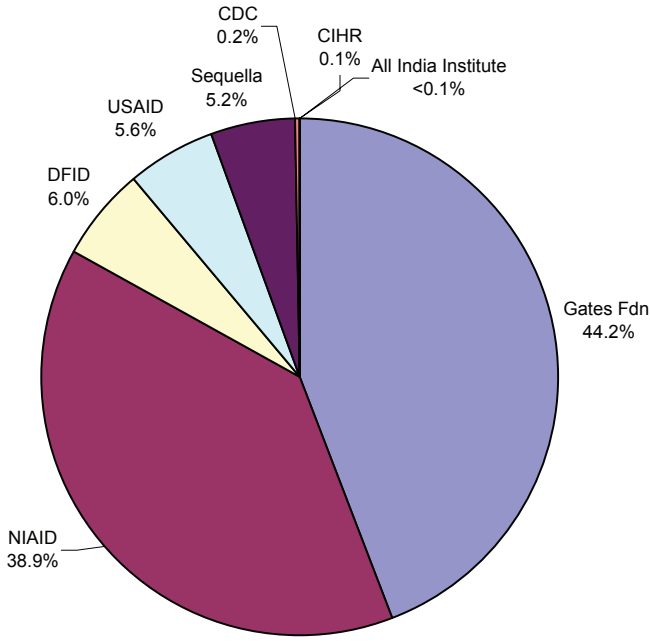



Total reported funding allocated to basic science on TB was $93 million in 2005. Of this, $51 million came from NIAID and $15 million from NHLBI; together they account for 71% of all basic R&D reported here. Besides NIH, the second and third largest donors were the U.K.'s Medical Research Council and the Wellcome Trust Foundation at $10.7 million and $7.1 million, respectively.

*GP2* did not make specific recommendation for increasing basic science funding, although this area of investment needs to be continually supported for the new tools pipelines to remain robust. The example of HIV/AIDS research, where basic science received a substantial boost in the early 1990s with continuing benefit to this day, demonstrates that basic science investment must be increased early and substantially to support a healthy research field.

## 3.2 TB Diagnostics

**Figure 5: Diagnostic Research (Total = $15,436,910)**

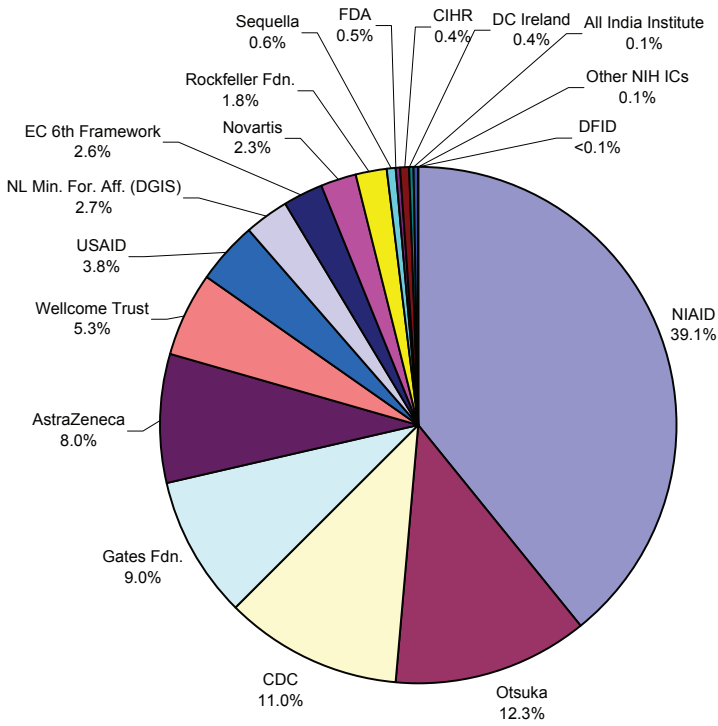



According to TAG's preliminary assessment, diagnostic research received $15.4 million in 2005, by far the least of all new tool areas. The largest single contributor was the Gates Foundation with a $2.3 million grant to WHO's Special Programme For Research and Training in Tropical Diseases (TDR) for the development of new diagnostics. BMGF also committed $4.6 million to FIND in 2005, but disbursed the money in 2006. This brings the Gates contribution to 44.2% of the total diagnostic Research committed in 2005. NIAID provided $6 million in applied/preclinical funding for diagnostics.Measured against WHO's *GP2*, which aims to develop a toolbox of widely accessible diagnostic tests over the next decade, investments in diagnostic development fall short of GP2's stated budget needs. In order to fulfill the *GP2* 2006 projected R&D costs, diagnostic spending would have to increase almost fourfold from $15.4 million in 2005 to reach its 2006 budget requirement of $59 million.

*GP2* estimates that $519 million over ten years is required to achieve its diagnostic R&D goals. According to the Working Group on New TB Diagnostics, the estimated available funding is $80 million, leaving a funding gap of $436 million. TAG's preliminary assessment uncovered a larger gap, given that reported donors gave only $15.4 million dedicated to diagnostic research.

## 3.3 TB Drugs

**Figure 6: Treatment Research**
**(Total = $99,803,651)**



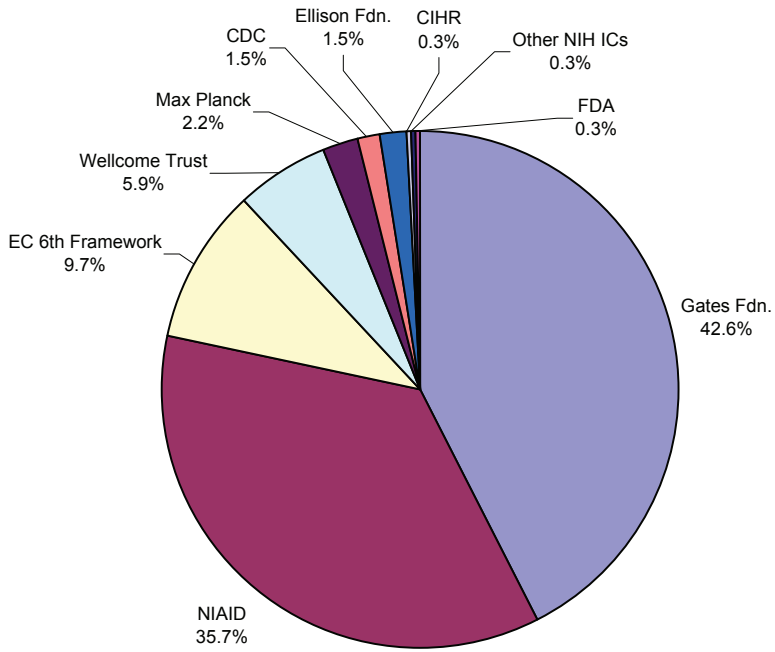

According to TAG's preliminary assessment, tuberculosis drug R&D totaled $99.8 million in 2005, making it the largest recipient of new tool investments.

NIH's NIAID was the single leading donor, investing $39 million in applied/pre-clinical research. The CDC spent $11 million on clinical trials of TB drugs. The Gates Foundation contributed $9 million to TB treatment research, $5 million of it to the Global Alliance for TB Drug Development to develop novel therapies. The Imperial College of London was awarded $4 million in Grand Challenge money to improve treatment for latent tuberculosis. *GP2*'s 2006 budget for drug R&D is $418 million, a fourfold increase from 2005 spending. The plan estimates that in order to achieve new, affordable TB drugs over the next ten years, $4.8 billion is needed, leaving a *GP2*-estimated funding gap of $4.2 billion. This preliminary assessment reveals that investment for new TB drugs in the first year of GP2 is short $319 million; if funding stays at constant levels for the next decade the funding gap for new TB drugs will be $3.8 billion.

This is another area where greater disclosure by industry would have been welcome. AstraZeneca and Otsuka are to be commended for reporting $8 and $12.3 million invested in new TB drugs, respectively, though they declined to subcategorize by preclinical or clinical. GlaxoSmithKline recently announced a new drug discovery research facility in Tres Cantos, Spain, focusing on HIV, TB, and malaria; and Johnson & Johnson/Tibotec is moving forward with at least one new TB compound, TMC207, now in early bactericidal activity (early phase II) clinical trials. If these companies' investments are on a par with those of AZ and Otsuka, it is likely that the TB drug total would increase by some $20 million. Still insufficient, but without direct reporting by the companies TAG is unable to estimate their contribution, since some reports received from public-private partnerships indicated that the PPP was giving money to industry, rather than the reverse.

## 3.4 TB Vaccines

**Figure 7: Vaccine Research**
**(Total = $67,308,412)**




TB vaccine R&D spending in 2005 was approximated at $67.3 million in TAG's preliminary assessment. The Gates Foundation was the leading benefactor supporting $28.7 million in vaccine R&D. Most of its funding was directed through the Aeras Global TB

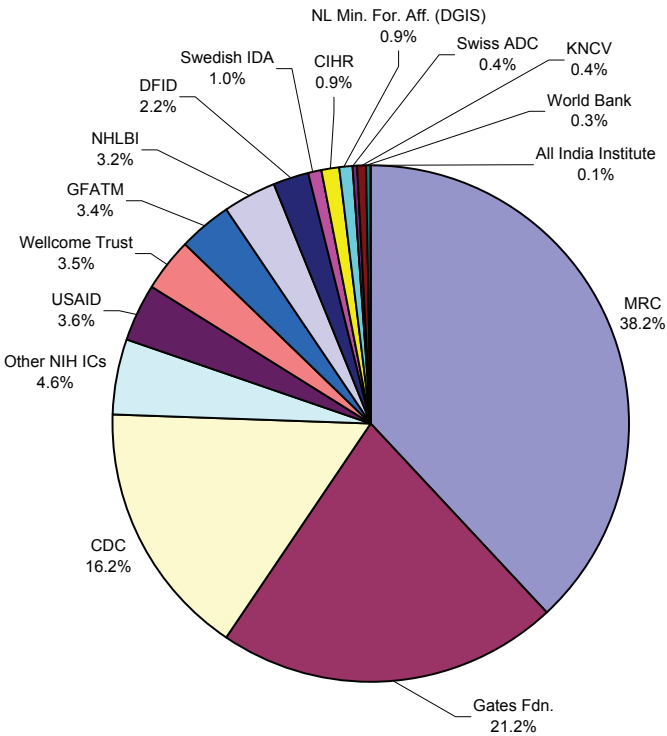
Vaccine Foundation where the majority of investments went to preclinical research. NIH's NIAID supported $24 million in vaccine research. Germany's Max Planck Institute and the Ellison Foundation spent $1.5 million and $1 million, respectively.

GP2 estimates that $291 million is needed to support TB vaccine R&D in 2006, requiring over a fourfold increase from TAG's 2005 preliminary assessment total.

Stop TB approximates that vaccine investments need to at least double over the next decade to achieve the $3.6 billion mark in order to reach Stop TB's goals of developing vaccination approaches that are effective in reducing prevalence and death by 2015. However, based on TAG's preliminary assessment, projected investment gaps are greater than GP2 suggests, necessitating a fivefold increase over the next decade.

## 3.5 Operational Research

**Figure 8: Operational Research**
**(Total = $48,675,206)**



In 2005, $48.7 million was spent on operational research related to TB. The U.K. Medical Research Council was the largest investor in this area at $18.6 million. Much of its research was carried out in a long-standing research program in the Gambia. The Gates Foundation invested $10.3 million in TB operational research, of which $10.2 million went to the Consortium to Respond Effectively to the TB/HIV Epidemic (CREATE), which is conducting three very large studies of interventions for TB and HIV in Brazil, South Africa, and Zambia. The Thibela-TB study is a randomized no treatment vs. treatment controlled study of isoniazid preventive therapy (IPT) among 70,000 South African gold miners, 35,000 of whom will be randomized (according to the mine shaft in which they work) to INH or no IPT. TB incidence in the South African mines is the world's highest at 4,000 per 100,000 per year. The ZAMSTAR study is a 24-community randomized study in South Africa and Zambia, investigating household TB/HIV integrated activities, intensified community-based TB case finding, strengthened DOTS, and clinic-based TB/HIV activities. The THRio study is a phased implementation program applying TB screening and isoniazid preventive therapy for 15,000 HIV-infected clinic patients in Rio de Janeiro, Brazil.

In addition to these very large and well-controlled operational research studies, which should yield clear data and impact on future program design for TB and HIV worldwide, many sponsors are supporting smaller operational research programs that in some cases are nested within TB control programs. CDC is supporting Botswana's HIV scale-up program and they are jointly implementing IPT in Botswana; CDC is also supporting a variety of intensified TB case finding activities in HIV programs in Africa, and HIV testing programs within TB programs. CDC spent $7.1 million on TB operational research in 2005. USAID spent $4.7 million on TB operational research in 2005 and estimates that it spent an additional 70% on country-level activities not reported.

# 4. Funding for TB R&D In Context

## 4.1 TB R&D Relative to TB Control

The WHO-recommended DOTS strategy contains the core elements of recent TB control efforts. The five elements which make up the DOTS strategy are:

- Sustained political commitment;
- Identification of infectious smear-positive cases of TB through sputum smear microscopy;
- Standardized short-course TB treatment regimens given in conditions of direct observation;
- Uninterrupted availability of treatments; and
- Monitoring and recording mechanisms that assure quality and outcomes

Based on decades-old principles and technology, DOTS was placed by WHO at the core of the global effort to scale up public TB control programs to reverse the epidemic's spread. Based on studies conducted by Karel Styblo in Tanzania, the DOTS strategy aimed to achieve 70% case detection of smear-positive pulmonary TB and 85% cure rates by 2000—and then, when that was not achieved—by 2005. In theory, detecting 70% of infectious cases and curing 85% of them would result in 6–7% decreases in TB incidence yearly, ultimately reducing disease prevalence. "The cost of TB control … including health system staff and infrastructure … [and National TB Program] budget requirements, is projected to be U.S. $ 1.6 billion in the 22 high-burden countries in 2006" (WHO 2006), with additional costs in the world's other 170 countries. This is over four times the amount spent on R&D in 2005.

Despite the past decade's progress in scaling up DOTS, its goals were not achieved. Case detection rates of smear-positive TB for 2004 were just 53% (WHO 2006). "DOTS can only be the foundation for global tuberculosis control," wrote S.K. Sharma of the All India Institute of Medical Science and J.J. Liu of the Chinese Centers for Disease Control. "To truly contain the disease, much more is needed in the control of multidrug-resistant tuberculosis (MDR-TB) and the development of drugs, diagnostics, and vaccines." (Sharma 2006).

## 4.2 TB R&D Funding Relative to Other Diseases

HIV, TB, and malaria are the world's three most common lethal infectious pathogens today. Both TB and malaria are curable, while HIV is treatable but incurable to date. Yet research funding for these three killer infections is far from proportionate to the damage they wreak. Although TB carries a high disease burden, NIH spends more on smallpox and anthrax than on TB and malaria research.

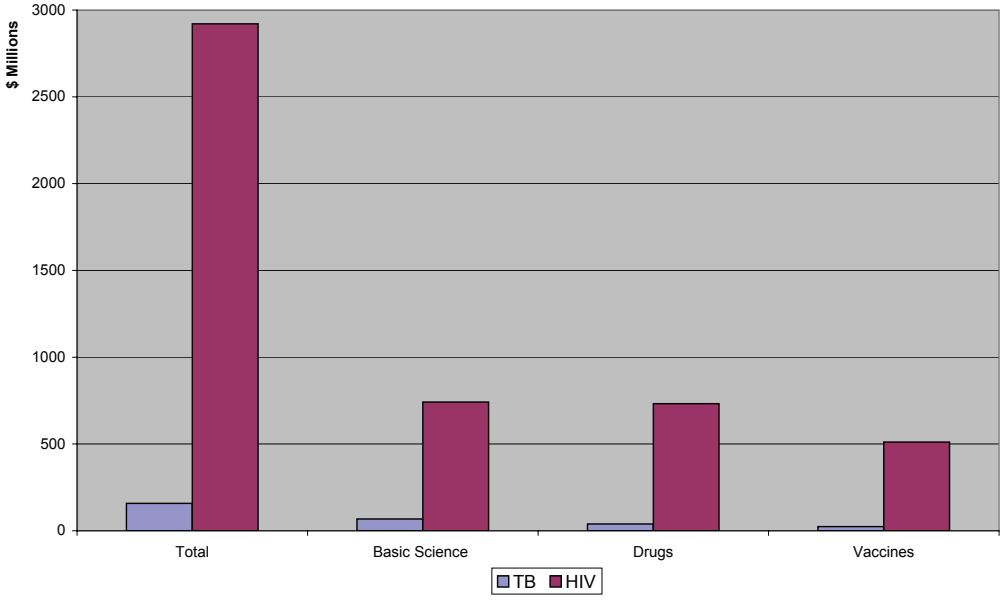
### Table 4: NIH Spending on Selected Infectious Diseases in 2005

| Infectious Disease | FY05 Actual (million $) |
|---|---|
| HIV/AIDS | 2921 |
| STDs/Herpes | 252 |
| Smallpox | 187 |
| Anthrax | 183 |
| Influenza | 164 |
| Tuberculosis | 158 |
| Pneumonia | 154 |
| Hepatitis C | 121 |
| Malaria | 104 |

HIV/AIDS received the most funding of any specific infectious disease in 2005 at $2.9 billion. This global pandemic, only 25 years old, became a priority research area in the 1990s due to its recent appearance, rapid pandemic spread, high mortality rates and the formidable AIDS activist movement, which placed unprecedented and historic pressure on the U.S. and other developed–and later developing–country governments to respond to this global emergency.

By contrast, and despite its worldwide toll and continuing advance, TB research receives far less than it is due.

### Figure 9: NIH Investment: TB vs. HIV (2005)



# 5. Recommendations: Resource Tracking

Because progress in biomedical research is directly linked to funding, it is imperative to advocate for well-directed, adequate investments. In order to do so, there needs to be a global assessment of baseline expenditures in specific research areas to identify and ultimately bridge existing gaps in funding and scientific pursuits. An accurate accounting of available and required resources to accomplish R&D targets will help to drive a credible advocacy agenda.

In a first-round compilation of investment information for TB R&D, TAG encountered two major obstacles: lack of transparency by industry and lack of internal tracking by both G8 and high-burdened countries. Specifically, in the commercial sector, transparency remains an obstacle to thorough investigation. Out of fourteen pharmaceutical and biotechnology companies surveyed, ten declined to disclose the requested information—even with an opportunity to present the figures in aggregate so that identification of the individual company would not be possible.

TAG recommends the private sector present its commitments publicly, or at the very least, allow its industry-funded TB research to be presented in aggregate form. This will help inform portions of the research agenda that need to be prioritized by other funders.

Coordination and communication also needs to be bolstered in the public sphere. While *GP2* lays out spending targets for research on new TB diagnostics, drugs, and vaccines, TAG's preliminary assessment uncovered a lack of coordinated research both within national institutes responsible for health research on TB and globally across major supporters of TB R&D.

While philanthropic organizations and public agencies were forthcoming with estimates for TB research, internal tracking systems were inconsistent and sometimes incomplete. Some funders did not code grants by specific disease, let alone TB-specific research category or phase.

TAG recommends the standardization of internal tracking systems according to disease, research category, and research phase to enable more comprehensive annual tracking of R&D investments in all diseases of global health importance, including TB.

TAG also recommends that agencies responsible for tracking global R&D investments in TB create uniform and consistent criteria for tracking programs and for reporting on them annually. This work could be carried out by the Stop TB Partnership, if it were fully funded and staffed at an adequate and sustained level,

but it would be important for the research tracking effort to be seen as independent of any particular institutional agenda, including that of the Stop TB Partnership. For this reason TAG suggests that the research tracking effort be carried out independently of the current new tools working groups whose work will be tracked. This will facilitate developing an accurate picture of R&D investments and needs forecasting specifically designed to measure progress toward achieving *GP2* funding targets.

## 6. Recommendations: Resource Mobilization

This Preliminary Assessment indicates that approximately $348 million was available for TB R&D in 2005 from the thirty top donors. Of this, $182 million was invested in research specifically directed towards discovery, development, and validation of new tools to better control TB, including new diagnostics, drugs, and vaccines. *The Global Plan to Stop TB: 2006-2015* indicates that $9 billion is needed over the coming decade for new tools research on TB and additional resources are necessary for operational research. While *GP2* does not specify target investment in basic science, clearly this area needs major increases in funding as well in order to provide the scientific foundation for discovery and development of innovative new interventions to control TB.

Based on the discrepancy between new tools investment identified for 2005 and the *GP2* targets, TAG estimates that investment in new tools must rise more than fivefold, from $182 million to approximately $1 billion per year in order to achieve the targets of *The Global Plan*. In order to ensure that basic science and operational research are adequately funded we estimate that these areas must rise fivefold as well. In other words, the world must invest at least $1.74 billion per year on TB R&D in order to lay the scientific foundation to eliminate TB as a public health threat by 2050.

If a fivefold increase in funding research on a specific disease seems unrealistic, let us recall that in 1988 the NIH received just $500 million for AIDS research. That fall AIDS activists led by ACT UP demonstrated at the U.S. Food & Drug Administration (FDA) to demand faster approval of new drugs for AIDS. In 1990 ACT UP demonstrated on the NIH campus in Bethesda, MD, to demand that NIH speed up research on new treatments for HIV and its associated opportunistic infections, and for NIH to incorporate activists and people living with HIV into programs planning and executing clinical trials. Public demonstrations and activist meetings with scientists, policymakers, and politicians led Congress to propose massive increases in funding for HIV/AIDS research at the NIH. In 1993, responding to an early report by TAG (Gonsalves 1992), Congress passed and President Clinton signed legislation strengthening the NIH Office of AIDS Research (OAR), giving it the ability to plan,

coordinate, and evaluate the entire NIH AIDS research budget across its multiple institutes. TAG's 1992 report also called for a doubling of the entire NIH budget in order to allow for healthy increases in AIDS research.

NIH convened an external group of scientists and activists to review its entire AIDS research program. The president and Congress increased the AIDS research budget to $1.3 billion in 1994. In the late 1990s both parties agreed that the entire NIH budget should be doubled by 2002. That year NIH received $23 billion and AIDS research received $2.5 billion. Much of the credit for this accomplishment goes to the AIDS activists who started demonstrating in the late 1980s to demand much greater federal investment in AIDS research. By contrast there has been little organized demand by advocates for other diseases of global public health import for scale-up of research on such a massive scale. To achieve the health related millennium development goals (MDGs), however, much greater investment in research on new tools as well as massive efforts to ramp up access to existing tools will be necessary.

More recently, the NIH budget has leveled off at $28.6 billion per year and the AIDS research budget is beginning to drop slightly from the $2.9 billion appropriated for 2005. Grants to new investigators have fallen, programs are being cut, and there is a very real danger that young people interested in scientific careers will be deterred by the increasing difficulty of obtaining NIH funding. This poses a present and real threat to researchers and advocates who are determined to find solutions to deadly diseases like TB and HIV/AIDS.

Since, according to TAG's data, the public sector funds 70% of TB R&D and the U.S. funds 53% of it, clearly solutions will have to be found for the present stagnation of U.S. public sector investment in research by the NIH and also by the CDC. Both agencies and the extramural research community need to be placed on a track of steadily increasing resources over the next decade so that planners, researchers, advocates, and policymakers can work to defeat lethal diseases such as AIDS, TB, and malaria.

Public sector research agencies in other countries need to increase their investment in biomedical research on global diseases, including TB and HIV, substantially as well. TAG was pleased that the U.K. Medical Research Council (MRC) with its historic record of funding breakthrough discoveries in TB research, including the first randomized streptomycin clinical trial in 1948, continues to be such an important presence. The MRC, the EU 7th Framework, and individual research agencies from G8 and other developed countries must substantially increase their investment in basic and applied research to control HIV, TB, and malaria, among other global pandemics.

The philanthropic sector, and particularly the Gates Foundation, has been providing leadership in filling important gaps in TB R&D in the past half decade, with particular focus on later-stage discovery and clinical evaluation of potential new tools, including TB diagnostics, drugs, and vaccines. TB diagnostics remains an orphan area, with just 4% of overall TB research funding, even though current diagnostic procedures in TB programs around the world rely on 19th century tests which cannot detect 40-60% of TB disease and which fail even more frequently among people living with HIV and among children.

A rapid point-of-care test for TB, which did not depend on electricity or a cold chain and could be read by clinical officers and nurses in field settings would be a major breakthrough which could open the door to earlier diagnosis and faster cure for millions each year. The Gates Foundation can further enhance its leadership position in this area by bringing together foundations to ensure that more of them invest in diseases of the poor—including TB—and that they work in concert to secure more investment from the public sector and from industry.

Investments in new TB drugs and vaccines are relatively healthier than in diagnostics. However, currently little clinical trials infrastructure exists for the large phase II-III studies which will be needed to validate these new interventions. The CDC-funded TB Trials Consortium (TBTC) is facing funding cuts; the European-Developing Countries Clinical Trials Program (EDCTP) is still quite small; and sponsors such as Aeras, the Global Alliance for TB Drug Development, and industry are not interested in building up clinical trials capacity aside from their individual product development efforts. Therefore the public sector from both donor and developing countries will need to invest in the infrastructure necessary to carry out the later-stage clinical trials of new TB drugs and vaccines. This will require many hundreds of millions of dollars.

The Global Forum for Health Research (GFHR, www.globalforumhealth.org) has published a useful set of reports on the need both for greater harmonization of resource tracking by funders of health research around the world and for greater investment by developing countries in this research. TAG heartily endorses the efforts of the Global Forum and we endorse their call for greater harmonization in research tracking and for greater investment by developing countries in health research.

We have discussed above the problems with tracking investments by pharmaceutical and biotechnology companies in TB research. We salute those who did declare their investments and hope that more companies will be willing to do so in the future. To assure ongoing involvement by industry, investment by the public sector in basic science, clinical trials infrastructure, and operational research is essential. Collaboration among industry and the product-development partnerships (PDPs) can also play a useful role. Industry has not yet fully realized the promise of greater

investment in diseases of the poor even in the HIV/AIDS field. Continuing conflicts between industry, developing country governments, and advocates demonstrate the difficulty of applying flexible regimens to achieve universal access, using a variety of mechanisms such as differential pricing, implementation of TRIPS flexibilities where needed, generic drug manufacturing, quality assurance, supply chain management, voluntary licenses, and free care to users at point of care. Industry involvement in HIV/AIDS research has been critical to progress in this area, and industry flight from other diseases of the poor including TB has had disastrous consequences. Thus industry involvement must increase, and advocates, donors, researchers, and industry must work together to overcome the barriers identified.

Multilateral agencies such as the Global Fund, WHO, and the World Bank will continue to be involved in various ways in supporting scale-up of effective programs, including operational research, in diseases such as TB. However their roles vary and it is not clear that the Global Fund or the Bank will ever be major funders of research per se, or whether they should be. WHO has a critical role to play as the world's normative health agency providing guidelines and technical assistance to countries. However, WHO does not conduct much research itself, and it is unclear despite a recent World Health Assembly resolution endorsing greater involvement in health research what the ultimate role of WHO will be. With respect to designing and implementing a global TB research agenda, WHO's role should be to assist in coordinating and establishing collaborations rather than planning to conduct most of the research itself. Its research unit at TDR is grossly underfunded and will be unable to significantly scale up its contribution to TB research anytime in the future. As for tracking of global TB R&D investments over the life of *The Global Plan 2*, perhaps WHO's best role would be to facilitate the work of Stop TB and the over 400 members of the Partnership in order to develop a universal TB R&D tracking mechanism, which reports annually and comprehensively on TB research programs underway and progress towards meeting the investment goals and R&D outputs demanded in *GP2*.

Most of all what is needed is an understanding by advocates and affected communities worldwide, and this means by the people of all countries, that TB, like HIV/AIDS and malaria and other global pandemics, will not ever come under control unless there is massive new investment to provide universal access to the best interventions currently available and in significantly increased research to discover, develop, validate, and disseminate new and better tools to eliminate these diseases in the 21st century.

# 7. Conclusions

**Figure 10: TB R&D Funding by Donor Category (2005)**

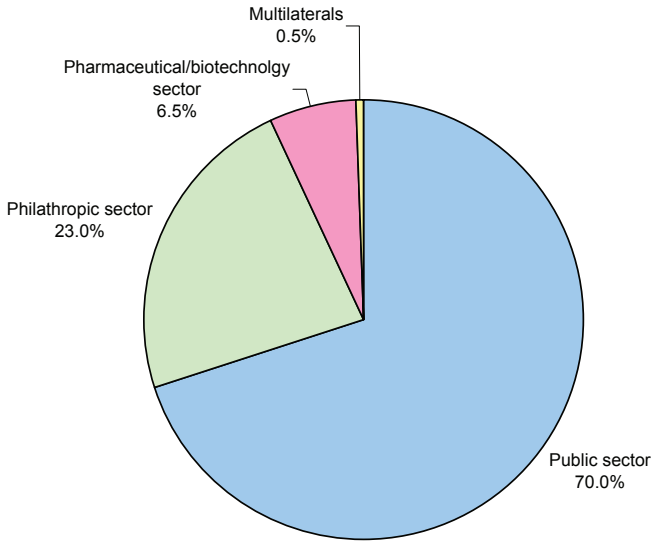



**Table 5: How Much Funding Is Needed?**
**(Dollars in Millions)**

| | FY05 actual | x3 | x5 | GP2 est. |
|---|---|---|---|---|
| **By sector** | | | | |
| Public | 244.1 | 732.3 | 1220.5 | |
| Philanthropic | 78.4 | 235.2 | 392 | |
| Industry | 24 | 72 | 120 | |
| Multilateral | 1.8 | 5.4 | 9 | |
| Total | 348.3 | 1044.9 | 1741.5 | |
| | | | | |
| **By category** | | | | |
| Basic | 93.1 | 279.3 | 465.6 | |
| Applied/unspec. | 23.9 | 71.7 | 119.5 | |
| Operational | 48.7 | 146.1 | 243.5 | |
| Basic, applied, operational subtotal | 165.7 | 497.1 | 828.6 | |
| | | | | |
| **By new tool category** | | | | |
| TB diagnostics | 15.4 | 46.2 | 77 | 50.9 |
| TB treatment | 99.8 | 299.4 | 499 | 479.2 |
| TB vaccines | 67.3 | 201.9 | 336.5 | 357.2 |
| New tools subtotal | 182.5 | 547.5 | 912.5 | 887.3 |
| | | | | |
| **Basic, Applied, New Tools, Operational** | **348.2** | **1044.6** | **1741.1** | **887.3** |

In 2005, 70% of reported TB R&D funding was from governments, 22.5% from foundations, 7% from industry, and 0.5% from multilateral agencies.

TB research funding has increased in recent years, most notably through the creation and expansion of public-private product development partnerships (PDPs) focusing on discovery and development of new TB vaccines, drugs, and diagnostics. Much of this new product development effort has been funded by the Gates Foundation. However, given the disease burden and the *GP2* estimate that $9 billion is needed for research on new TB tools over the next decade, TAG's preliminary assessment reveals that reported TB R&D spending in 2005 was a mere $348 million. Of that, only $182 million was spent on new TB diagnostics, drugs, and vaccines. Were 2005 funding levels to continue for the life of *GP2*, the funding gap would be $7.18 billion, or $717.5 million per year. In other words, new tools research needs to increase by fivefold over 2005 levels ($182 million x 5 = $910 million) each year to achieve the *GP2* target of $9 billion. Still more resources need to be put into basic science and operational research. Thus, while *GP2* estimates a threefold increase in TB research is needed to achieve its goals, TAG's preliminary assessment suggests that a fivefold increase in funding for new TB tools, as well as for basic and operational research, will be required.

Meeting global targets to halve TB prevalence and death rates by 2015, and ultimately ridding the world of TB by 2050, will only become reality if there is a momentous change in R&D funding.

TAG will publish a more complete analysis of TB R&D, including a more detailed examination of gaps in research funding at the Union meeting in Fall 2006. Nonetheless, the results of this preliminary assessment are sufficient to make clear the case for dramatic and rapid increases in TB research funding worldwide.

# 8. Appendix A: Top 30 Reporting TB R&D Funders in 2005

| Rank | Donor | Total |
|---|---|---|
| 1 | **NIAID / NIH** | **120,273,000** |
| 2 | **Gates Foundation** | **57,411,457** |
| 3 | **Medical Research Council (UK)** | **30,887,839** |
| 4 | **Other Institutes & Centers / NIH** | **20,334,300** |
| 5 | **Centers for Disease Control** | **19,903,000** |
| 6 | **Wellcome Trust** | **18,081,359** |
| 7 | **NHLBI / NIH** | **17,117,000** |
| 8 | **European Commission 6th Framework** | **13,322,711** |
| 9 | **Otsuka** | **12,300,000** |
| 10 | **AstraZeneca** | **8,000,000** |
| | | |
| 11 | **USAID** | **6,694,000** |
| 12 | **Netherlands Ministry of Foreign Affairs (DGIS)** | **3,168,488** |
| 13 | **Max Planck Institute** | **2,500,000** |
| 14 | **Canadian Inst. of Health Research** | **2,376,098** |
| 15 | **Novartis** | **2,255,193** |
| 16 | **Dept. for International Development (DFID)** | **2,008,832** |
| 17 | **Russian TB Institutes** | **1,930,343** |
| 18 | **Rockefeller** | **1,750,000** |
| 19 | **Global Fund** | **1,648,083** |
| 20 | **Research Institute for TB (RIT) / JATA, Japan** | **1,487,961** |
| | | |
| 21 | **Sequella** | **1,400,000** |
| 22 | **Ellison Foundation** | **1,000,000** |
| 23 | **Food and Drug Administration** | **651,231** |
| 24 | **Swedish Int. Development Agency** | **486,599** |
| 25 | **Development Cooperation of Ireland** | **360,000** |
| 26 | **Netherlands Org. for Scientific Research (N.W.O.)** | **199,716** |
| 27 | **Swiss Agency for Development and Coop.** | **195,099** |
| 28 | **KNCV Tuberculosis Foundation** | **170,666** |
| 29 | **All India Institute of Medical Sciences** | **154,821** |
| 30 | **World Bank** | **140,350** |
| | | |
| | **TOTAL** | **$348,208,146** |
| | **% of total** | **100.00%** |
| | | |
| | ***Funding consortia* (*Funding managers*)** | |
| a | **Aeras** | **26,526,253** |
| b | **TB-VAC** | **6,778,239** |
| c | **CREATE** | **5,816,005** |
| d | **Global Alliance for TB Drug Development** | **5,556,397** |
| e | **FIND** | **2,193,605** |
| f | **TDR** | **1,400,000** |
| g | **EDCTP** | **580,039** |
| h | **WHO MDR-TB** | **156,045** |
| | ***F.C. subtotals*** | **49,006,583** |
| | ***% of F.C. subtotal*** | **100.00%** |

| Basic Science | Applied / Preclinical / infrastructure /unspecified | Diagnostics | Drugs | Vaccines | Operational |
|---|---|---|---|---|---|
| 51,000,000 | 273,000 | 6,000,000 | 39,000,000 | 24,000,000 | |
| 2,620,000 | | 6,819,000 | 9,000,000 | 28,677,457 | 10,295,000 |
| 9,016,676 | 3,284,736 | | | | 18,586,427 |
| 1,575,540 | 16,230,562 | | 70,279 | 204,968 | 2,252,951 |
| | | 25,000 | 10,975,000 | 1,000,000 | 7,903,000 |
| 7,115,258 | | | 5,326,924 | 3,958,080 | 1,681,097 |
| 15,207,488 | 330,931 | | | | 1,578,581 |
| 4,150,905 | | | 2,631,410 | 6,540,396 | |
| | | | 12,300,000 | | |
| | | | 8,000,000 | | |
| | | | | | |
| | 320,000 | 860,000 | 3,780,000 | | 1,734,000 |
| | | | 2,714,927 | | 453,561 |
| 1,000,000 | | | | 1,500,000 | |
| 1,240,797 | | 10,816 | 440,091 | 229,511 | 454,883 |
| | | | 2,255,193 | | |
| | | 919,296 | 35,840 | | 1,053,696 |
| | 1,930,343 | | | | |
| | | | 1,750,000 | | |
| | | | | | 1,648,083 |
| | 1,487,961 | | | | |
| | | | | | |
| | | 800,000 | 600,000 | | |
| | | | | 1,000,000 | |
| | | | 453,231 | 198,000 | |
| | | | | | 486,599 |
| | | | 360,000 | | |
| 199,716 | | | | | |
| | | | | | 195,099 |
| | | | | | 170,666 |
| | | 2,798 | 110,756 | | 41,267 |
| | | | | | 140,350 |
| | | | | | |
| **$93,126,380** | **$23,857,533** | **$15,436,910** | **$99,803,651** | **$67,308,412** | **$48,675,260** |
| **26.74%** | **6.85%** | **4.43%** | **28.66%** | **19.33%** | **13.98%** |
| | | | | | |
| | | | | | |
| | | | | 26,526,253 | |
| | | | | 6,778,239 | |
| | | | | | 5,816,005 |
| | | | 5,556,397 | | |
| | | 2,193,605 | | | |
| | | | | | 1,400,000 |
| | | | 471,103 | 108,936 | |
| | | | 136,045 | | 20,000 |
| | | **2,193,605** | **6,163,545** | **33,413,428** | **7,236,005** |
| | | **4.48%** | **12.58%** | **68.18%** | **14.77%** |

# 9. Appendix B: Actual or Potential TB R&D Funders Not Reported On

**Respondents not disclosing**

Abbott
Aventis Pharmaceuticals
Bayer
BD Diagnostics
Eli Lilly
GlaxoSmithKline
Health Protection Agency, U.K.
Howard Hughes Medical Institute
Johnson & Johnson
Roche

**Did not yet respond**

Crucell
Danish Agency for Science Technology & Information
Danish International Development Agency (DANIDA)
Fiocruz/Foundation Oswaldo Cruz
Indian Council of Medical Research
INSERM
Institute Adolfo Lutz
International Union Against Tuberculosis and Lung Disease (IUATLD)
Japan International Cooperation Agency
Italian Ministry of Health
Lupin Laboratories
Rede TB
Thailand Ministry of Public Health
U.S. Biotechnology Engagement Program, DHHS

**Not yet contacted**

Brazil Ministry of Health
Brazil Ministry of Sciences and Technology
Aventis Pharma
Indian Ministry of Health and Family Welfare
Indian Ministry of Science and Technology
Japanese Ministry of Health and Welfare
Italian Ministry of University & Research
Program for Appropriate Technology in Health (PATH)

**Respondents stating they are not original sources of TB research funding**

BORSTEL
German Technical Cooperation (GTZ)
German Ministry of Health (BMG)
German Ministry of Health and Cooperation (BMZ)
Karolinska Institutet
Institut Pasteur
Médecins Sans Frontières
Partners In Health
Robert Koch Institute
South Africa Medical Research Council
Statens Serum Institute
U.S. Military Infectious Disease Program Walter Reed Army Institute of Research

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