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Tuberculosis: International Efforts and Issues for Congress

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Tuberculosis: International Efforts and Issues for Congress

Summary

Infectious diseases are estimated to cause more than 25% of all deaths around the world. A number of infectious disease outbreaks over the past decade, such as H5N1 avian influenza and severe acute respiratory syndrome (SARS), have heightened concerns about how infectious diseases might threaten global security. International air travel and trade have complicated efforts to detect and contain infectious diseases. People could cross borders carrying a highly contagious disease before an infectious agent causes symptoms.

Debate ensued about countries' ability to contain diseases after a man known to be carrying a form of drug-resistant tuberculosis (TB) crossed a number of international borders unabated. The World Health Organization (WHO) estimates that someone contracts TB every second and that about one-third of all people in the world carry TB; most of these cases, however, are latent. In 2005, 8.8 million people contracted the disease globally, of whom 1.6 million died (an average of 4,400 daily deaths). About 84% of all cases in the world were found in 22 countries. Among the 15 countries with the highest estimated TB incidence rates, 12 are in Africa.

In 2005, TB prevalence rose only in sub-Saharan Africa and eastern Europe. WHO attributes a number of factors to this increase, including weak health systems, low-quality health care, minimal access to health facilities, insufficient staffing and little human resource development, ill-equipped and substandard laboratories, and limited coordination of TB and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) programs.

In FY2008, Congress voted to fund U.S. global TB operations at unprecedented levels. The House FY2008 Foreign Operations Appropriations (H.R. 2764) provided $313.5 million for international TB programs and $300 million for a U.S. contribution to the Global Fund to Fight HIV/AIDS, TB, and Malaria (Global Fund). The Senate version of H.R. 2764 included $200 million for U.S. global TB efforts and $340 million for a U.S. contribution to the Global Fund. Both houses included $300 million in FY2008 Labor, HHS, and Education Appropriations (H.R. 3043 and S. 1710) for a U.S. contribution to the Global Fund. S. Rept.110-107 of S. 1710 also suggested that $10 million more than CDC's FY2007 operating plan for TB be provided to improve CDC's efforts to prevent TB and its progression into XDR-TB. No appropriations bills that include funds for TB efforts have been enacted.

The House Foreign Affairs and Senate Foreign Relations Committees passed companion TB bills, Stop TB Now Act (S. 968 and H.R. 1567) to support global TB efforts and authorize $330 million in FY2008 and $450 million in FY2009. They also authorized $70 million and $100 million for anti-TB programs at the U.S. Centers for Disease Control and Prevention (CDC) in FY2008 and FY2009, respectively. Although Congress voted to increase support for global TB efforts, some Members expressed concern that the additional funds might be provided at the expense of other global health programs. This report discusses some key issues Congress might consider as debate ensues about the proper level and use of global TB funds.

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The Global Threat of Infectious Diseases

In January 2000, the National Intelligence Council (NIC) released a report, asserting that, "[n]ew and reemerging infectious diseases will pose a rising threat to U.S. and global security over the next 20 years. These diseases will endanger U.S. citizens at home and abroad, threaten U.S. armed forces deployed overseas, and exacerbate social and political instability in key countries and regions in which the United States has significant interests."[1] NIC cited a number of factors which heighten the infectious diseases threat, including increasing drug resistance, slow development of new antibiotics, urban sprawl, environmental degradation, and the growing ease and frequency of cross-border movements.

Over the past decade, there has been considerable debate about countries' abilities to contain and prevent infectious disease outbreaks. In 2002, the international community struggled to identify an unknown infectious disease that rapidly spread across 31 countries and ultimately killed 813 of the more than 8,400 people who contracted it. In 2003, when the disease was ultimately contained, scientists called the agent severe acute respiratory syndrome (SARS).[2] That same year, Influenza A/H5N1 (bird flu) reemerged and spread to more than 50 countries. As of November 7, 2007, more than 330 people have contracted H5N1.[3] About 61% of those who contracted the disease have died.

Tuberculosis

TB is one of the most widespread infectious diseases in the world. The World Health Organization (WHO) estimates that someone becomes infected with TB every second and that about one-third of all people in the world are currently infected with

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[1] National Intelligence Council, *The Global Infectious Disease Threat and Its Implications for the United States*, January 2000, [http://www.dni.gov/nic/PDF_GIF_otherprod/infectiousdisease/infectiousdiseases.pdf].

[2] For more information on SARS, see CRS Report RL32072, *Severe Acute Respiratory Syndrome (SARS): The International Response*.

[3] For most recent data on human H5N1 cases and deaths, see WHO website on avian flu at [http://www.who.int/csr/disease/avian_influenza/en/]. Also see, CRS Report RL33219, *U.S. and International Responses to the Global Spread of Avian Flu: Issues for Congress* and CRS Report RL33871, *Foreign Countries' Response to the Avian Influenza (H5N1) Virus: Current Status*.

TB; most of these cases, however, are latent.[4] TB is a highly contagious disease that spreads through the air when infectious people cough, sneeze, talk or spit. People with TB are only infectious when the bacteria is active. Those with active TB who do not receive treatment and are not properly quarantined infect, on average, between 10 and 15 people every year.[5] The bacteria can lie dormant in an infected person for years and may not cause any symptoms or illness. The TB bacteria most often becomes active and causes sickness when one's immune system is weakened, such as with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS).

Global TB Statistics. Although TB is curable, WHO estimates that in 2005 (the year for which the most current data are available), the disease killed 1.6 million people, including 195,000 who were also infected with HIV/AIDS (**see Table 1 in Appendix**). Some 8.8 million people were estimated to have contracted the disease in 2005, with about 84% of the cases having occurred in 22 countries.[6] All but three of those high-burden countries were found in Africa or Asia.[7] About half of all new TB cases were in six countries: Bangladesh, China, India, Indonesia, Pakistan, and the Philippines.

Although Southeast Asia had the highest number of new TB cases, incidence per capita was considerable higher in sub-Saharan Africa. Among the 15 countries with the highest estimated TB incidence rates, 12 were in Africa, due in part to relatively high rates of HIV co-infection.[8] Some 2.99 million people in Southeast Asia were newly infected with TB (1.8 per 1,000 people) and about 2.53 million in sub-Saharan Africa (3.4 per 1,000). Mortality rates reflected similar trends. About 512,320 people died in southeast Asia of TB (0.3 per 1,000 infected), while some 543,550 people died of TB in sub-Saharan Africa (0.7 per 1,000 infected). WHO asserts that a number of factors contribute to Africa's relatively high per capita rate. Key factors include weak health systems, low quality health care, poor access to

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[4] People who have latent TB infection do not feel sick, do not have any symptoms, and cannot spread TB to others. A person with latent TB can develop active TB, when one becomes infectious and begins to feel ill. Unless otherwise indicated, data in this section was taken from WHO, *2007 Global Tuberculosis Control Report*, [http://www.who.int/tb/publications/global_report/2007/pdf/full.pdf].

[5] Information in this paragraph was summarized from WHO's fact sheet on tuberculosis. [http://www.who.int/mediacentre/factsheets/fs104/en/]

[6] The 22 high-burden countries were: Afghanistan, Bangladesh, Brazil, Burma, Cambodia, China, Democratic Republic of Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Nigeria, Pakistan, Philippines, Russia, South Africa, Tanzania, Thailand, Uganda, Vietnam, and Zimbabwe.

[7] Of the high burden-countries, Afghanistan, Brazil, and Russia are not in Africa or Asia.

[8] The *incidence* of a disease is the number of new cases arising within a given time period, such as a year. The *prevalence* is the total number of cases that exist within a given time period. *Prevalence* is sometimes referred to as *burden*. Prevalence and burden are used interchangeably in this memorandum. The 15 countries with the highest TB incidence per capita rates (in order from highest to lowest rates) were: Swaziland, Djibouti, Namibia, Lesotho, Botswana, Kenya, Zimbabwe, Zambia, South Africa, East Timor, Cambodia, Sierra Leone, Mozambique, Malawi, and Cote d'Ivoire.

health facilities, insufficient staffing and other human resource constraints, ill-equipped and substandard laboratory services, and limited links between TB and HIV programs.

HIV/AIDS and TB. In areas with significant HIV/AIDS prevalence, the virus is contributing to rising TB prevalence, particularly in Africa.[9] People living with HIV/AIDS are at greater risk of becoming infected with TB because of their weakened immunity. Each disease speeds up the progress of the other, and TB considerably shortens the survival of people with HIV/AIDS. HIV/AIDS is the most potent risk factor for converting latent TB into active TB, while TB bacteria accelerate the progress of AIDS. Many people infected with HIV/AIDS in developing countries develop TB as the first manifestation of AIDS. The two diseases represent a deadly combination, since they are more destructive together than either disease alone. Other key facts about HIV/AIDS-TB co-infection include:

- In HIV-positive people, TB is harder to diagnose, progresses faster, is almost always fatal if undiagnosed or left untreated, and kills up to half of all AIDS patients worldwide;
- People with HIV/AIDS are up to 50 times more likely to develop TB in a given year than HIV/AIDS-negative people; and
- About 90% of people living with HIV/AIDS die within four to twelve months of contracting TB if they are not treated for TB.

In sub-Saharan Africa, HIV/AIDS and TB co-infection is becoming a growing problem. In 2005, about 80% of all HIV-positive people with TB were found in Africa. That year, nearly 630,000 people were co-infected with HIV/AIDS and TB, some 500,000 of whom were African. About 160,000 of the nearly 195,000 co-infected patients who died from TB were African, representing 82% of those deaths.

Drug Resistance to TB Treatments

Multi-Drug Resistant TB (MDR-TB)

MDR-TB is caused by TB organisms resistant to at least the two most potent first-line drugs (isoniazid and rifampicin).[10] Treating MDR-TB takes longer and requires drugs that are more toxic, more expensive, often of limited availability in resource-limited settings, and generally less effective, particularly in people living with HIV/AIDS. WHO advises that people with MDR-TB receive care outside of

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[9] Information in this paragraph was summarized from WHO, *Frequently asked questions about TB and HIV/AIDS.* [http://www.who.int/tb/HIV/AIDS/faq/en/index.htm]

[10] MDR-TB mostly arises from poor treatment adherence or incorrect drug usage. Adherence means taking accurately prescribed drugs in the right amounts at the correct time. If the wrong drugs or the wrong combinations of drugs are prescribed, providers fail to ensure that they are taken correctly on schedule, or if patients do not take their medicine for the full term, the bacteria causing TB may develop resistance to the drugs. When this happens, the patient who initially had treatment-responsive TB develops drug-resistant TB. MDR-TB cases must be aggressively monitored and treated, because those with MDR-TB spread MDR-TB to others rather than treatment-responsive TB.

normal HIV/AIDS care settings, because people whose immune systems are weakened and are susceptible to many illnesses can become severely ill or die if they contract MDR-TB. Separating MDR-TB patients from HIV/AIDS patients can be particularly challenging in resource-limited settings, where hospitals are frequently overcrowded and ill-equipped.[11]

WHO is uncertain about how many people have MDR-TB, though surveys conducted internationally in 2005, confirmed 18,422 cases worldwide; a number it concedes is considerably lower than the 500,000 estimate that it provided in its 2006 Global Plan to Stop TB report.[12] The highest proportion of laboratory-confirmed MDR-TB cases were in Europe (59%), particularly in Eastern Europe. For example, in 2004, 50% of MDR-TB cases detected in Europe were resistant to all four first-line drugs, compared to 12% in the rest of the world.[13]

Extensive Drug Resistant (XDR)-TB

XDR-TB is MDR-TB that is also resistant to three or more of the six classes of second-line drugs. WHO considers XDR-TB to be rare, although it acknowledges that the extent of XDR-TB remains unknown. The organization believes XDR-TB prevalence is relatively low, however, because it usually develops from MDR-TB.[14] A survey conducted by WHO and the Centers for Disease Control and Prevention (CDC) on data from 2000-2004 found that XDR-TB occurs in all regions of the world, but most frequently in the countries of the former Soviet Union and Asia.[15] In the United States, 4% of MDR-TB cases met the criteria for XDR-TB. In Latvia, a country with one of the highest rates of MDR-TB, 19% of MDR-TB cases met the XDR-TB criteria.

The press seemed to increase its coverage on XDR-TB after a May 2006 outbreak in Kwazulu-Natal, South Africa. Many health experts were alarmed by the high mortality rates. CDC and WHO studied 544 patients; 221 had MDR-TB, 53 of whom had XDR-TB. Forty-four of the 53 XDR-TB cases were tested for HIV/AIDS; all were HIV/AIDS-positive. Only one of the 53 patients with XDR-TB survived. On average, the 52 patients died within 25 days, including those who received anti-retroviral drugs. WHO believes that prevalence of drug resistant TB is relatively low in Africa, though it concedes that little research on drug resistance has been conducted on the continent. Available data, however, indicate that drug resistance is on the rise in Africa. Health analysts warn that drug-resistant TB could significantly

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[11] For more information on MDR-TB, see WHO, *Tuberculosis Infection Control in the Era of Expanding HIV/AIDS Care and Treatment*. 2007. [http://whqlibdoc.who.int/hq/1999/WHO_TB_99.269_ADD_eng.pdf

[12] WHO, *2007 Global Tuberculosis Control Report*.

[13] WHO, *2006 Global Tuberculosis Control: Surveillance, Planning, Financing*.

[14] WHO, *Frequently asked questions - XDR-TB.* Accessed on September 24, 2007. [http://www.who.int/tb/xdr/faqs/en/index.html]

[15] Information in this paragraph was summarized from WHO press release, "*WHO concern over extensive drug resistant TB strains that are virtually untreatable*." September 5, 2006. [http://www.who.int/mediacentre/news/notes/2006/np23/en/index.html]

increase mortality in countries with high HIV/AIDS rates, particularly in southern Africa.

U.S. Global TB Efforts

A number of U.S. agencies, centers, and departments implement a range of programs aimed at treating and containing the global spread of tuberculosis, though Congress only designates global TB funds to the U.S. Agency for International Development (USAID), while other agencies and departments use discretionary funds (**see Table 2 in Appendix**). Other agencies and departments, however, provide funds to fight the disease globally. Additional U.S. global TB initiatives might not be included here, such as research conducted by the National Institute of Health (NIH) to develop a new TB with a shorter regimen schedule.[16]

U.S. Agency for International Development

USAID is the leading U.S. agency involved in anti-TB efforts around the globe. In more than 35 countries, USAID-supported TB programs train health care workers on TB response and control, fund research and development of TB drugs and vaccines, facilitate the coordination and harmonization of TB and HIV/AIDS interventions, address MDR-TB issues, and improve the procurement and management of TB treatments. USAID is also a working member of several international TB partnerships and supports the WHO Global TB Monitoring and Surveillance project. USAID reports that in FY2006 it provided $91.0 million for global TB programs; it anticipates spending $91.0 million in FY2007; and requested $89.9 million for FY2008 activities.[17]

U.S. Centers for Disease Control and Prevention (CDC)

The Centers for Disease Control and Prevention supports global TB efforts by providing epidemiologic, laboratory, and programmatic support to USAID, WHO, and the International Union Against TB and Lung Diseases.[18] It also assigns expert staff to help implement global TB programs. CDC helps WHO develop and implement guidelines on TB prevention in resource-limited settings. Additional global TB technical assistance by CDC includes strengthening laboratory capacity and referral systems, developing protocols for epidemiologic studies, and refining information on TB prevalence and incidence. CDC reports that in each of FY2006 and FY2007, it spent approximately $2 million of its TB appropriation on global TB efforts and anticipates spending the same amount on global TB in FY2008. CDC also received transfers of $3.4 million in 2006 and 2007 to provide technical assistance to other countries. Through its Global AIDS Program (GAP), CDC supports the Global Fund (the Global Fund is discussed more comprehensively in the

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[16] The program descriptions below were compiled from interviews with Administration officials.

[17] Reported to CRS by USAID's Budget Office on March 15, 2007.

[18] This paragraph was compiled from interviews with CDC officials and the FY2008 HHS budget justification. [http://www.cdc.gov/fmo/PDFs/FY08_CDC_CJ_Final.pdf]

"International TB Efforts" section) and has technical staff working in the Office of the Global AIDS Coordinator (OGAC), USAID, the HHS Office of Global Health Affairs, WHO, and UNAIDS.

Department of State

On January 28, 2003, in his State of the Union address, President Bush proposed that the United States spend $15 billion over the next five fiscal years to combat HIV/AIDS, TB, and malaria through an initiative he called the President's Plan For AIDS Relief (PEPFAR). PEPFAR anticipated channeling $9 billion to HIV/AIDS prevention, treatment, and care services in 15 Focus Countries through the Global HIV/AIDS Initiative (GHAI);[19] $5 billion to bilateral HIV/AIDS, TB, and malaria programs and research efforts in more than 100 non-Focus Countries, and $1 billion to the Global Fund.[20] Congress appropriates the bulk of PEPFAR funds to the GHAI account through Foreign Operations Appropriations. GHAI was established to streamline funds for global HIV/AIDS, TB, and malaria programs to the 15 Focus Countries. The Office of the Global AIDS Coordinator (OGAC) at the U.S. State Department transfers funds from GHAI to implementing agencies and departments. OGAC also supports global partnerships that combat TB, such as the Global Fund. OGAC reports that, in FY2006, it transferred $48.6 million to implementing agencies for TB projects in the 15 Focus Countries, and anticipates spending $120.6 million in FY2007. The FY2008 budget justification did not specify an amount for global TB programs, though the House proposed allocating $150 for TB efforts through GHAI (H. Rpt.241-178 to H.R. 2764). The Senate did not include similar provisions.

International TB Efforts

A number of organizations collaborate to combat TB globally. Most of those adhere to guidelines and recommendations that WHO and its partners drafted. WHO is the directing and coordinating authority for health within the United Nations system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends.

World Health Organization and Implementing Partners

In 1991, the World Health Assembly (WHA) passed a resolution that recognized TB as a major global public health problem and established two goals for TB control: detection of 70% of new smear-positive cases, and cure of 85% of such

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[19] GHAI efforts include TB interventions for those co-infected with HIV/AIDS. The 15 Focus Countries are: Botswana, Cote d'Ivoire, Ethiopia, Guyana, Haiti, Kenya, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Tanzania, Uganda, Vietnam, and Zambia. For more on PEPFAR, see [http://www.pepfar.gov/]

[20] White House Fact Sheet, *"The President's Emergency Plan for AIDS Relief."* January 29, 2003. [http://www.state.gov/p/af/rls/fs/17033.htm]

cases, by the year 2000.[21] In 1994, WHO and global health experts developed and recommended that all health practitioners use the Directly Observed Treatment, Short-course (DOTS) strategy to combat TB.[22] DOTS has five key components:

- Political commitment with increased and sustained financing;
- TB detection through bacteriology, the recommended method of TB case detection;
- Standardized treatment with supervision and patient support;
- Effective drug supply and management systems; and
- Monitoring and evaluation systems, and impact measurement.

In 2000, WHO and its partners launched the first Global Plan to Stop TB, which outlined what actions needed to be taken from 2001–2005 to control TB. By 2004, more than 20 million patients had been treated in DOTS programs worldwide and more than 16 million of them had been cured. Mortality due to TB has been declining and incidence diminishing or stabilizing in all world regions except sub-Saharan Africa and eastern Europe. The global treatment success rate among new smear-positive TB cases had reached 83% by 2003 (just short of the WHA target of 85% by 2005), and in 2004 the case detection rate, which has accelerated globally since 2001, was 53% (against the target of 70% by 2005).

In 2005, WHO Member States passed a resolution to advocate that Member States provide sustainable financing for TB control and prevention and commit to achieve the TB-related targets included in the Millennium Development Goals (MDGs).[23] WHO and its partners have also developed additional policies, strategies, and working groups that facilitate the achievement of global TB control targets. Innovative mechanisms such as the Global Drug Facility and the Green Light Committee improve access to quality-assured and affordable drugs in resource-poor settings. These activities are described below.

WHO estimated that $56 billion would be needed from 2006 through 2015 to implement its Global Plan to Stop TB (**see Table 2 in Appendix**).[24] Of the estimated $56 billion needed to reverse the incidence of TB, WHO suggests that $28.9 billion be spent on expanding DOTS, $5.8 billion be spent on DOTS-Plus initiatives, $6.7 billion be spent on treating people co-infected with HIV/AIDS and TB, and $9.0 billion be spent on research and development. WHO estimates that

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[21] Resolution WHA44.8. Tuberculosis control program. In: *Handbook of resolutions and decisions of the World Health Assembly and the Executive Board*. Volume III, 3rd ed. (1985–1992). Geneva, World Health Organization, 1993 (WHA44/1991/REC/1):116.

[22] See WHO's website on DOTS at [http://www.who.int/tb/dots/en/index.html].

[23] In 2000, world leaders committed to support eight Millennium Development Goals, which range from halving extreme poverty to halting the spread of HIV/AIDS and providing universal primary education, all by the target date of 2015. See the list of MDGs at [http://www.un.org/millenniumgoals/].

[24] Figures in this section were compiled from *The Global Plan to Stop TB: 2006-2015*. [http://www.stoptb.org/globalplan/plan_main.asp]

governments and donors will provide about 45% of the funds needed, leaving a funding gap of an estimated $31 billion.

DOTS-Plus. In areas with moderate to high levels of MDR-TB, WHO and its partners implement DOTS-Plus, a strategy that provides guidance on issues, such as the appropriate use of second-line anti-TB drugs. DOTS-Plus is currently operational in Bolivia, Costa Rica, Estonia, Haiti, Latvia, Malawi, Mexico, Peru, Philippines, Russia, and Uzbekistan. Additional DOTS-Plus projects have been approved in Georgia, Honduras, Jordan, Kenya, Kyrgyzstan, Lebanon, Nepal, Nicaragua, Romania and Syria.[25]

Green Light Committee. The Working Group on DOTS-Plus for MDR-TB identified access to second-line anti-TB drugs as one of the major obstacles to the implementation of DOTS-Plus pilot projects. The Working Group made arrangements with the pharmaceutical industry to provide concessionally priced second-line anti-TB drugs to DOTS-Plus pilot projects. In some cases, treatment prices were 99% lower in DOTS-Plus countries compared with retail prices. Before second-line TB treatments are provided, the Green Light Committee[26] reviews requests for treatments through DOTS-Plus projects and determines whether it can provide the medication in compliance with international standards of care.[27]

Stop TB Partnership. Established in 2000, the Stop TB Partnership seeks to achieve universal access to high-quality diagnosis and treatment; reduce the human suffering and socioeconomic burden associated with TB; protect poor and vulnerable populations from TB, MDR-TB, and TB and HIV/AIDS co-infection; and develop new TB treatment and diagnostic tools and enable their effective use. The Stop TB Partnership is comprised of a network of international organizations, countries, donors, governmental and non-governmental organizations and individuals that have expressed an interest in eradicating TB.[28] Seven Working Groups within the partnership focus on TB-related issues and facilitate coordinated action. The seven groups are: Advocacy, Communication, and Social Mobilization; DOTS Expansion; MDR-TB; New TB Diagnostics; New TB Drugs; New TB Vaccines; and TB/HIV/AIDS. Each Working Group within the partnership is independently governed and collectively supports efforts to:

- increase access to accurate diagnoses and effective treatments;
- expand the availability, affordability and quality of TB drugs;

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[25] For more on DOTS-Plus, see [http://www.who.int/tb/dots/dotsplus/management/en/]

[26] The Green Light Committee is comprised of CDC, International Union Against Tuberculosis and Lung Diseases, Medical Research Council of South Africa, National Tuberculosis Programs of Estonia and Latvia, Partners in Health, and WHO.

[27] For more on how the Green Light Committee determines which applications to approve, see WHO, *Instructions for Applying to the Green Light Committee for Access to Second-Line Anti-Tuberculosis Drugs*. 2006.
[http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.369_eng.pdf]

[28] [http://www.stoptb.org/stop_tb_initiative/]

- promote research and development for new TB drugs, diagnostics and vaccines; and
- ensure appropriate use of and access to affordable new and improved TB prevention and control tools.

Global Drug Facility (GDF). GDF, housed in WHO and managed by a small team in the Stop TB Partnership Secretariat, is a financing mechanism that provides technical assistance in the management and surveillance of TB drug use, as well as procurement of high-quality TB drugs at a relatively low price.[29] Countries can purchase TB treatments directly from GDF at prices below market value or apply for grants to purchase first-line TB treatments. GDF regularly assesses and monitors the use of its funds to ensure that grant recipients adequately detect and monitor TB cases, properly prescribe and oversee the use of medicines, transparently use finances, and consistently administer drugs without interruption. GDF also works with grantees to estimate drug needs for the next year of GDF support.

The Global Fund to Fight AIDS, Tuberculosis, and Malaria

The Global Fund, headquartered in Geneva, Switzerland, is an independent foundation intended to attract and rapidly disburse new resources for fighting the three diseases.[30] The Fund is a financing vehicle, not a development agency, and its grants are intended to complement existing efforts rather than replace them. Since it was created in 2002, the Fund has approved about $8.6 billion to fund more than 450 grants in 136 countries, making it the single largest donor for TB and malaria control and among the three largest donors for HIV/AIDS programs. About 17% of Global Fund grants are targeted at TB control and treatment. According to the Fund's website, it has supported treatment for 3 million TB cases under the DOTS program.[31]

Bill and Melinda Gates Foundation

From 1999 to 2007, the Gates Foundation provided $424.7 million to combat TB globally.[32] The foundation also pledged $650 million to the Global Fund to Fight

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[29] [http://www.stoptb.org/gdf/]

[30] Information in this paragraph was summarized from Global Fund, *Monthly Progress Update*, January 31, 2007. [http://www.theglobalfund.org/en/files/publications/basics/progress_update/progressupdate.pdf] For more information on the Global Fund, see CRS Report RL33485, *U.S. International HIV/AIDS/AIDS, Tuberculosis, and Malaria Spending: FY2004-FY2008*, and CRS Report RL33396, *The Global Fund to Fight AIDS, Tuberculosis and Malaria: Progress Report and Issues for Congress*.

[31] Global Fund website, accessed on November 9, 2007 at [http://www.theglobalfund.org/en/about/tuberculosis/default.asp].

[32] Compiled by CRS from Gates Foundation website's list of grants and announcements.

AIDS, Tuberculosis, and Malaria, of which $350 million has been paid to date.[33] Gates Foundation grants support projects that focus on four key areas:

- TB research that focuses on developing more accurate and rapid diagnostics for resource-poor settings, more effective TB vaccines, and more effective drugs and shorter regimens to treat active disease;
- innovative strategies that fight TB, including identifying effective ways to manage TB in areas heavily affected by HIV/AIDS;
- new TB control and prevention tools; and
- advocacy and coordination with an emphasis on joint TB and HIV/AIDS programs.[34]

Issues for Congress

Since PEPFAR was launched in FY2004, overall U.S. spending on international TB initiatives has hovered around $90 million (**see Table 3 in Appendix**). In FY2004, Congress provided USAID $100 million for global TB efforts, $87.8 million in FY2005, $91.5 million in FY2006, and an estimated $91.0 million in FY2007. In FY2008, Members are considering a boost in support of global TB efforts. The House version of FY2008 Foreign Operations Appropriations included H.Amdt. 359, which proposed an additional $50 million for global TB efforts; bringing total U.S. support to $313.5 million. The Senate version of H.R. 2764, FY2008 Foreign Operations, included a floor amendment that provided an additional $89.8 million for global TB efforts, bringing the total to $200 million.

The House Foreign Affairs and Senate Foreign Relations Committees also unanimously passed companion TB bills, S. 968 and H.R. 1567, Stop TB Now Act. The bills are aimed at fighting tuberculosis overseas and authorize $330 million in FY2008 and $450 million in FY2009 for related foreign assistance programs. They also authorize $70 million in FY2008 and $100 million in FY2009 for anti-TB programs at CDC. Although Congress voted to increase support for global TB efforts, some Members expressed concern that the additional funds might be provided at the expense of other global health programs. The section below presents some issues Congress might consider as it debates the appropriate level of funding for global TB initiatives.

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[33] Global Fund, *Pledges and Contributions*, accessed on October 9, 2007, [http://www.theglobalfund.org/en/files/pledges&contributions.xls]; and Global Fund, *Progress Report*, August 2007, [http://www.theglobalfund.org/en/files/publications/basics/progress_update/progressupdate.pdf].

[34] Gates Foundation website, *Grantmaking priorities for Tuberculosis.* Accessed on March 15, 2007. [http://www.gatesfoundation.org/GlobalHealth/Pri_Diseases/Tuberculosis/TB_Grantmaking.htm]

Strengthen Health Systems

WHO asserts that weak health systems play a key role in the continued spread of TB across Africa. Many health practitioners argue that inadequate access to rapid and accurate diagnostic tests significantly contribute to the rise in new TB cases on the continent. Some health advocates, estimate that diagnostic tests fail to identify at least 50% of TB cases.[35] Others assert that the absence of tests to detect smear-negative TB cases contributes to the disproportionately high TB mortality rate in Africa, particularly among HIV-positive patients.[36] Culturing, a process requiring laboratory diagnosis, is the most definitive method of detecting TB, particularly among smear-negative cases. Six of the 22 high-burden countries have the minimum proportion of laboratories capable of culturing samples; South Africa is the only country in Africa that meets this criteria.[37]

Laboratories must also be capable of conducting drug susceptibility tests (DST) to determine which medications will kill the type of TB bacteria that the patient carries and to determine which medicines will kill the bacteria. Of the high-burden countries, Bangladesh, Pakistan, and Afghanistan have no DST labs; 7 have one for the entire country; and six meet the minimum of one per 10 million people (**see Table 4 in Appendix**). Some observers suggest that scientists identified the May 2006 XDR-TB outbreaks in South Africa primarily because it is the only country in the region with the laboratory capacity and health care infrastructure to conduct drug susceptibility tests.

Other symptoms of poor health systems also minimize the effectiveness of TB efforts. Many countries struggle with stock-outs of TB treatments, caused by poor

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[35] Gates Foundation, "*Tuberculosis Backgrounder*." Accessed on September 24, 2007. [http://www.gatesfoundation.org/GlobalHealth/Pri_Diseases/Tuberculosis/TB_Backgrounder.htm]

[36] A smear-positive test detects the presence of TB bacilli in a sputum (material that is coughed up from the lungs) sample. A smear-negative test detects no TB bacilli in a sputum sample, though the person carries TB. People who are co-infected with HIV and TB frequently have smear-negative results and subsequent chest x-rays, if available, may also look normal. TB diagnoses are often belatedly made in co-infected people, since many with HIV develop forms of TB outside of the lungs. Culturing the organism can usually provide a definitive diagnosis, but culturing takes weeks, and requires laboratory capacities that are usually unavailable in many resource-limited settings. See WHO, *2007 Global Tuberculosis Control Report*; WHO, *Improving the Diagnosis of Smear-Negative Pulmonary and Extrapulmonary Tuberculosis Among Adults and Adolescents*, 2006, [http://www.who.int/tb/publications/2006/tbhiv_recommendations.pdf]; and Schluger, Neil, "Changing Approaches to the Diagnosis of Tuberculosis," *American Journal of Respiratory and Critical Care Medicine*, Volume 164, Number 11, December 2001. [http://ajrccm.atsjournals.org/cgi/content/full/164/11/2020]

[37] WHO recommends that countries have at least one laboratory per 5 million people that is capable of culturing samples. Brazil (5.0), Cambodia (1.1), China (1.2), South Africa (1.9), Thailand (3.1), and Vietnam (1.8) meet this criteria. Shah, N. Sarita et al., "Worldwide Emergence of Extensively Drug-resistant Tuberculosis," *Emerging Infectious Diseases*, Volume 13, Number 3, March 2007, [http://www.cdc.gov/eid/content/13/3/380.htm]

data collection, deficient road and transport conditions, and sporadic distribution systems. Inconsistent use of medication can reduce the potency of TB treatments, extend the term of use, and result in drug resistence. Health advocates argue that in order to boost the impact of TB programs, congressional support for TB efforts must be accompanied by funding of health systems, including laboratory systems.

Address Health Worker Shortage

The shortage of health care workers and health centers in the high burden countries, particularly in Africa, complicate efforts to adhere to WHO's recommendation that TB patients be housed separately from those being treated for AIDS. WHO maintains that in order for countries to effectively control TB and prevent increases in MDR-TB and XDR-TB cases, it is essential to establish teams of health workers specifically trained to manage drug resistance and work in hospitals or isolation units dedicated to TB patients. Most of the 22 high-burden countries, however, do not have enough health workers to meet the most basic health care needs, including monitoring TB treatment (**see Table 5 in the Appendix**).[38]

High HIV prevalence in Africa further complicates shortage issues, because HIV and TB patients are usually housed within close proximity in the scarce facilities. In addition, many of the health centers are unable to contain airborne infections and have a significant amount of HIV-infected health workers who pose a risk to themselves and their patients.[39] WHO contends that all of these issues converged to cause the extremely high mortality in the KwaZulu-Natal cases.[40]

It is widely understood that MDR-TB is caused in large part by poor treatment adherence. Health worker shortages lessen the likelihood that medication provision will be properly supervised. WHO fears that the inability to manage sufficiently first- and second-line treatments will lead to a rise in XDR-TB cases.[41] Global health advocates urge Congress to increase support for health worker training; fund initiatives that supplement the salaries and provide incentives for indigenous health workers; and stop recruiting health practitioners from countries with shortages to fill U.S. health positions.

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[38] WHO, *2006 World Health Report: Working Together for Health*, [http://www.who.int/whr/2006/en/]. The Joint Learning Initiative (JLI), a network of global health leaders, defines a shortage as less than 2.5 health care professionals per 1,000 people; the minimum proportion it deemed necessary to provide 80% of a country's population with basic health care.

[39] WHO, *2007 World Health Report, A Safer Future: Global Public Health Security in the 21st Century*. [http://www.who.int/whr/2007/whr07_en.pdf]

[40] *Ibid*.

[41] WHO, *2007 World Health Report, A Safer Future: Global Public Health Security in the 21st Century*. [http://www.who.int/whr/2007/whr07_en.pdf]

Integrate HIV/AIDS and TB Programs

Global health experts are concerned about how HIV/AIDS and TB are converging to worsen mortality rates, particularly in Africa. Early diagnosis and treatment of both diseases can extend life expectancy and, in the case of TB, decrease transmission rates. Greater awareness about the intersection of these diseases has led many health practitioners to routinely test TB patients for HIV. While WHO applauds those efforts, it expressed concern that HIV patients are not yet routinely tested for TB. WHO asserts that countries could significantly improve TB case identification if health professionals would routinely test all those newly diagnosed with HIV for the disease. Proponents of this idea contend that the practice could ameliorate outcomes of HIV and TB programs; reduce overall program costs; and make TB and HIV/AIDS efforts more efficient. In FY2006, OGAC reportedly allocated nearly $50 million to TB efforts in the 15 Focus Countries, and estimates that it will have spent about $120 million in FY2007. Health advocates urge Congress to increase funding for programs that integrate HIV/AIDS and TB responses.

Provide Additional Funds for Research

Many health experts assert that congressional support for TB research could lead to the development of treatments with shorter regimens, which might improve adherence. On average, patients must take their medicines daily for six-to-eight months to be fully cured. Supporters contend that improved adherence might reduce the incidence of emergent drug-resistant TB strains. Advocates maintain that congressional support for TB research should include TB vaccine research. Health experts assert that Bacille Calmette-Guerin (BCG), a vaccine currently administered to millions of newborns around the world, effectively prevents TB in childhood, but not in adulthood. Proponents urge Congress to fund research for a vaccine that protects the innoculated throughout their lives. International organizations also stress the need for the development of diagnostic tests that could be more easily used in low-resource settings. At present, culturing is required to provide a definitive diagnosis. Culturing, however, takes weeks and requires laboratory capacities that are usually unavailable in many resource-limited settings. Advocates urge Congress to support efforts, such as WHO's Tuberculosis Diagnostics Initiative (TBDI), which forms partnerships with the private sector, academic researchers, and national and local health officials to facilitate and accelerate the development of diagnostic tools.[42]

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[42] For more information on TBDI, see [http://www.who.int/tdr/diseases/tb/tbdi.htm]. Other TB research initiatives include Global Tuberculosis Research Initiative (GTRI) at WHO, [http://www.who.int/tdr/diseases/tb/gtri.htm]; Center for Tuberculosis Research at Johns Hopkins University, [http://www.jhsph.edu/dept/IH/Centers/TB_Research.html]; Consortium to Respond Effectively to the AIDS TB Epidemic (CREATE), [http://www.tbhiv-create.org/]; The Action TB Program at University of Cape Town, [http://web.uct.ac.za/depts/mmi/lsteyn/glaxo.html]; and Aeras TB Vaccine Development Program, [http://www.aeras.org/vaccines/index.html].

Appendix: Tables

Table 1. Global Tuberculosis Cases (2005)

	New TB Cases		TB-HIV/AIDS Co-infected		TB-related Deaths			
	Number	**Number per 1,000**	**Number**	**Number per 1,000**	**Number**	**Number per 1,000**	**Number TB-HIV/AIDS Co-infected**	**Number TB-HIV/AIDS Co-Infected per 1,000**
Africa	2,572,988	3.56	600,394	0.83	586,911	0.81	205,602	0.28
The Americas	363,246	0.41	22,481	0.03	52,240	0.06	5,852	<0.01
Eastern Mediterranean	644,531	1.22	9,814	0.02	142,193	0.27	4,588	<0.01
Europe	444,777	0.50	13,898	0.02	69,018	0.08	3,714	<0.01
Southeast Asia	2,967,328	1.82	77,992	0.05	535,278	0.33	23,560	0.01
Western Pacific	1,925,332	1.11	16,548	<0.01	307,411	0.18	5,064	<0.01
Total	**8,918,202**		**741,127**		**1,693,051**		**248,380**	

Source: WHO, *2007 Global Tuberculosis Control Report*

Table 2. U.S. International Tuberculosis Spending

($ millions)

Agency or Department	FY2004 Actual	FY2005 Actual	FY2006 Actual	FY2007 Estimate	FY2008 Request	FY2008 House	FY2008 Senate
USAID	$100.4	$87.8	$91.5	$79.0	$89.9	$163.5	$200.0
Department of State	n/a	$26.2	$48.4	$120.0	$0.0	$150.0	
CDC	$2.0	$2.3					

Source: USAID figures derived from appropriations legislation; Department of State and CDC figures compiled from interviews with Administration officials.

[Note: The Department of State did not collect program data on TB/HIV funding in FY2004.]

Table 3. Global TB Financing Needs and Outcomes

Sub-Saharan Africa		
Program	**Needs**	**Estimated Results**
DOTS expansion	$13,278	16.9 million treated for TB
DOTS-Plus	$71	29.0 thousand treated for TB, including MDR-TB
TB/HIV/AIDS	$4,940	2.7 million treated for HIV/AIDS/AIDS
Other Programs	$1,111	
Africa Total	**$19,400**	**Avert 4.4 million deaths**
Eastern Europe		
Program	**Needs**	**Estimated Results**
DOTS expansion	$4,809	2.2 million treated for TB
DOTS-Plus	$3,928	410.0 thousand treated for TB, including MDR-TB
TB/HIV/AIDS	$186	31.0 thousand treated for HIV/AIDS/AIDS
Other Programs	$177	
Eastern Europe Total	**$9,100**	**Avert 218 thousand deaths**
Southeast Asia		
Program	**Needs**	**Estimated Results**
DOTS expansion	$3,778	16.0 million treated for TB
DOTS-Plus	$678	145.0 thousand treated for TB, including MDR-TB
TB/HIV/AIDS	$1,112	31.0 thousand treated for HIV/AIDS/AIDS
Other Programs	$631	
Southeast Asia Total	**$6,199**	**Avert 5.1 million deaths**

Source: WHO, *The Global Plan to Stop TB 2006 - 2015*.

Table 4. Laboratory Capacity in High Burden Countries (2005)

Country	Population Thousands	Access to Diagnostic Services					
		Sputum Smear		Culture		DST	
		Number of Labs	Per 100,000 Pop.	Number of Labs	Per 5 Million Pop.	Number of Labs	Per 10 Million Pop.
Afghanistan	29,863	435	1.5	0	0	0	0
Bangladesh	141,822	635	0.4	2	0.1	0	0.1
Brazil	186,405	4,000	2.1	187	5.0	33	10
Burma	50,519	310	0.6	2	0.2	1	0.4
Cambodia	14,071	186	1.3	3	1.1	1	2.1
China	1,315,844	3,240	0.2	327	1.2	187	2.5
DR Congo	57,549	1,041	1.8	1	0.1	1	0.2
Ethiopia	77,431	607	0.8	1	0.1	1	0.1
India	1,103,371	11,813	1.1	5	0.02	5	0.05
Indonesia	222,781	3,320	1.5	41	0.9	22	1.8
Kenya	34,256	619	1.8	3	0.4	3	0.9
Mozambique	19,792	252	1.3	1	0.3	1	0.5
Nigeria	131,530	598	0.5	3	0.1	3	0.2
Pakistan	157,935	982	0.6	3	0.1	0	0.2
Philippines	83,054	1,858	2.2	3	0.2	3	0.4
Russia	143,202	4,953	3.5	not available	not available	not available	not available
South Africa	47,432	143	0.3	18	1.9	18	3.8
Tanzania	38,329	690	1.8	3	0.4	1	0.8
Thailand	64,233	846	1.3	40	3.1	8	6.2
Uganda	28,816	465	1.6	2	0.3	2	0.7
Vietnam	84,238	875	1.0	30	1.8	2	3.6
Zimbabwe	13,010	167	1.3	1	0.4	1	0.8

Source: WHO, *2007 Global Tuberculosis Control Report*

Table 5. Distribution of Health Workers in 22 High Burden Countries and the United States

Country	Population Thousands (2005)	Physicians		Nurses		Pharmacists		Year Data Collected
		Number	Number per 1,000	Number	Number per 1,000	Number	Number per 1,000	
Afghanistan	29,863	4,104	0.19	4,752	0.22	525	0.02	2001
Bangladesh	141,822	38,485	0.26	20,334	0.14	9,411	0.06	2004
Brazil	186,405	198,153	1.15	659,111	3.84	51,317	0.30	2000
Burma	50,519	17,791	0.36	19,254	0.38	127	0.00	2004
Cambodia	14,071	2,047	0.16	8,085	0.61	564	0.04	2000
China	1,315,844	1,364,000	1.06	1,358,000	1.05	359,000	0.28	2001
DR Congo	57,549	5,827	0.11	28,789	0.53	1,200	0.02	2004
Ethiopia	77,431	1,936	0.03	14,893	0.21	1,343	0.02	2003
India	1,103,371	645,825	0.60	865,135	0.80	592,577	0.56	2003
Indonesia	222,781	29,499	0.13	135,705	0.62	7,580	0.03	2003
Kenya	34,256	4,506	0.14	37,113	1.14	3,094	0.01	2004
Mozambique	19,792	514	0.03	3,954	0.21	618	0.03	2004
Nigeria	131,530	34,923	0.28	210,306	1.70	6,344	0.05	2004
Pakistan	157,935	116,298	0.74	71,764	0.46	8,102	0.05	2004
Philippines	83,054	44,287	0.58	127,595	1.69	2,482	0.03	2000
Russia	143,202	60,9043	4.25	1,153,683	8.05	11,404	0.08	2003
South Africa	47,432	34,829	0.77	184,459	4.08	12,521	0.28	2004
Tanzania	38,329	822	0.02	13,292	0.37	365	0.01	2002
Thailand	64,233	22,435	0.37	171,605	2.82	15,480	0.25	2000
Uganda	28,816	2,209	0.08	16,221	0.61	688	0.03	2004
Vietnam	84,238	42,327	0.53	44,539	0.56	5,977	0.08	2001
Zimbabwe	13,010	2,086	0.16	9,357	0.72	883	0.07	2004
United States	295,410	730,801	2.56	2,669,603	9.37	249,642	0.88	2000

Source: WHO, *2006 World Health Report*