

# **Tuberculosis: International Efforts and Issues for Congress**

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May 1, 2008

Congressional Research Service 7-5700 www.crs.gov RL34246

## 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.

Non-health officials are becoming increasingly aware of the threat that infectious diseases pose. An event that illuminated the issue occurred in May 2007, when a man known to be carrying a drug-resistant form of 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 2006, an estimated 14.4 million people were living with TB globally, including 9.2 million who contracted the disease that year. About 1.7 million people carrying TB died in 2006, including 200,000 people co-infected with HIV/AIDS. About 80% of all estimated new TB cases arising in the world each year occur in 22 high-burden countries (HBCs).

WHO indicates that the global incidence of TB per capita peaked around 2003 and since then, incidence per 100,000 population stabilized in Europe and declined in all five WHO regions, although the absolute number of new cases increased between 2005 and 2006 in Africa, the Middle East, Europe, and Southeast Asia. In sub-Saharan Africa, weak health systems, minimal access to health facilities, insufficient staffing and little human resource development, ill-equipped and substandard laboratories, and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) co-infection have limited countries' ability to contain TB.

In FY2008, Congress funded U.S. global TB operations at unprecedented levels. Through FY2008 Consolidated Appropriations, Congress provided \$162.2 million to international TB programs and an additional \$840.3 million for a U.S. contribution to the Global Fund to Fight HIV/AIDS, TB, and Malaria (Global Fund). The House passed and the Senate Foreign Relations Committees reported out companion TB bills, Stop TB Now Act (H.R. 1567 and S. 968) 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. The Administration requested \$97.1 million for FY2009 global TB efforts, some \$55 million less than appropriated in FY2008. This report, which will be updated periodically, 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."<sup>1</sup> NIC cited a number of factors that 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, infected more than 8,400 people, and killed 813 of those who contracted it. In 2003, when the disease was ultimately contained, scientists called the agent severe acute respiratory syndrome (SARS).<sup>2</sup> That same year, Influenza A/H5N1 (bird flu) reemerged and spread to more than 50 countries. As of April 17, 2008, 381 people have contracted H5N1, 240 of whom died.<sup>3</sup> About 63% 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 contracts TB every second and that about one-third of all people in the world are currently infected with TB; most of these cases, however, are latent.<sup>4</sup> 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.<sup>5</sup> TB 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).

<sup>&</sup>lt;sup>1</sup> National Intelligence Council, *The Global Infectious Disease Threat and Its Implications for the United States*. January 2000, at http://www.dni.gov/nic/PDF\_GIF\_otherprod/infectiousdisease/infectiousdiseases.pdf, visited on January 29, 2008.

<sup>&</sup>lt;sup>2</sup> For more information on SARS, see CRS Report RL32072, *Severe Acute Respiratory Syndrome (SARS): The International Response*, by (name redacted) and (name redacted).

<sup>&</sup>lt;sup>3</sup> 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, by (name redacted) and CRS Report RL33871, Foreign Countries' Response to the Avian Influenza (H5N1) Virus: Current Status, by (name redacted) et al.

<sup>&</sup>lt;sup>4</sup> People who have latent TB infection do not feel sick, do not have any symptoms, and cannot spread TB to others. Latent TB becomes active when the host becomes infectious and begins to feel ill.

<sup>&</sup>lt;sup>5</sup> Information in this paragraph was summarized from WHO's fact sheet on tuberculosis, at http://www.who.int/ mediacentre/factsheets/fs104/en/, visited on March 5, 2008.

#### **Global TB Statistics**<sup>6</sup>

Although TB is curable, WHO estimates that in 2006 (the year for which the most current data are available), there were 14.4 million prevalent cases of TB, including some 9.2 million people who contracted the disease that year.<sup>7</sup> About 80% of annual TB cases occur in 22 high-burden countries (see **Figure A-1** in the **Appendix**).<sup>8</sup> All but two of those high-burden countries were in Africa or Asia.<sup>9</sup> More than 50% of all new TB cases occurred in five countries (in descending order of TB cases): India, China, Indonesia, South Africa, and Nigeria. The disease killed an estimated 1.7 million people in 2006, including 230,857 who were also infected with HIV/AIDS (see **Table A-1** in the **Appendix**).

Although southeast Asia had the highest number of new TB cases, incidence and mortality per capita rates were considerably higher in sub-Saharan Africa. Among the 15 countries with the highest estimated TB incidence rates, 13 were in Africa, due in part to relatively high rates of HIV co-infection (see **Table A-2** in the **Appendix**).<sup>10</sup> In 2006, about 3.10 million people in Southeast Asia were newly infected with TB (109 per 100,000 people) and about 2.81 million in sub-Saharan Africa (363 per 100,000). The actual number of TB-related deaths and the mortality per capita rates were higher in sub-Saharan Africa than in Southeast Asia. About 514,699 people died of TB in southeast Asia (30 per 100,000 infected), while some 639,089 people died of TB in sub-Saharan Africa (83 per 100,000 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 health facilities, insufficient staffing and other human resource constraints, ill-equipped and substandard laboratory services, and little collaboration between TB and HIV programs.

#### HIV/AIDS and TB

In areas with significant HIV/AIDS prevalence, the virus is contributing to rising TB prevalence.<sup>11</sup> People living with HIV/AIDS are at greater risk of contracting TB because of their weakened immunity. Each disease accelerates the advancement of the other. TB considerably shortens the survival of people with HIV/AIDS and quickens the progression of HIV into AIDS. Meanwhile, HIV/AIDS is the most potent risk factor for converting latent TB into active TB. 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

<sup>9</sup> Of the high burden-countries, Brazil and Russia are not in Africa or Asia.

<sup>&</sup>lt;sup>6</sup> Data in this section was compiled by CRS from WHO, 2008 Global Tuberculosis Control Report, at http://www.who.int/tb/publications/global\_report/2008/pdf/fullreport.pdf.

<sup>&</sup>lt;sup>7</sup> 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 report.

<sup>&</sup>lt;sup>8</sup> The 22 high-burden countries, in descending order of absolute TB case numbers, were India, China, Indonesia, South Africa, Nigeria, Bangladesh, Ethiopia, Pakistan, Philippines, Democratic Republic of Congo, Russia, Vietnam, Kenya, Tanzania, Uganda, Brazil, Mozambique, Thailand, Burma, Zimbabwe, Cambodia, and Afghanistan.

<sup>&</sup>lt;sup>10</sup> The 15 countries with the highest TB incidence per capita rates (in order from highest to lowest rates) were Swaziland, South Africa, Djibouti, Namibia, Lesotho, Zimbabwe, East Timor, Zambia, Botswana, Sierra Leone, Cambodia, Mozambique, Cote d'Ivoire, Congo, and Rwanda.

<sup>&</sup>lt;sup>11</sup> Information in this paragraph was compiled by CRS from WHO, *Frequently asked questions about TB and HIV/AIDS*. http://www.who.int/tb/hiv/faq/en/.

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-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 2006, about 85% of all HIV-positive people with TB were found in Africa.<sup>12</sup> That year, an estimated 709,000 people were co-infected with HIV/AIDS and TB, some 606,000 of whom were African. About 205,000 of the 231,000 co-infected patients who died from TB were African, representing 89% of those deaths. In countries with high HIV/AIDS prevalence, HIV/TB co-infection poses a significant health challenge. In Swaziland, for example, 75% of TB patients were HIV-positive.<sup>13</sup> South Africa, with 0.7% of the world's population and the most number of people living with HIV/AIDS, had 28% of all HIV/TB co-infection cases and 33% of HIV-positive cases in sub-Saharan Africa.

In many high-burden countries, particularly in sub-Saharan Africa, TB patients are not yet routinely tested for HIV, and HIV patients are not yet routinely tested for TB.<sup>14</sup> HIV testing for TB patients has increased, however, between 2002 and 2006. In 2002, nine countries reported testing 21,806 TB cases for HIV, representing less than 1% of notified TB cases. By 2006, 112 countries had reported testing 687,174 patients for HIV, equivalent to about 12% of notified TB cases. In Africa, 287,945 patients were tested for HIV—some 22% of all notified TB cases. In Africa, HIV testing of TB patients increased from 7.5% to 35% from 2004 to 2006. The testing increase was driven primarily by Kenya and South Africa. In spite of improvements in HIV testing in Africa, the region still lagged behind other countries. On average, 56% of TB patients were tested for HIV outside of Africa.

## **Drug Resistance to TB Treatments**

## Multi-Drug Resistant TB (MDR-TB)

MDR-TB are TB organisms that do not respond to at least two first-line drugs.<sup>15</sup> Drug resistance mostly arises from poor treatment adherence or incorrect drug usage. Adherence means taking

<sup>&</sup>lt;sup>12</sup> Unless otherwise noted, information in this paragraph was compiled by CRS from WHO, 2008 Global Tuberculosis Control Report, at http://www.who.int/tb/publications/global\_report/2008/pdf/fullreport.pdf.

<sup>&</sup>lt;sup>13</sup> WHO, 2007 Global Tuberculosis Control: Surveillance, Planning, Financing, at http://www.who.int/tb/publications/global\_report/en/index.html.

<sup>&</sup>lt;sup>14</sup> Information in this paragraph was compiled by CRS from WHO, 2008 Global Tuberculosis Control Report, p. 48, at http://www.who.int/tb/publications/global\_report/2008/pdf/fullreport.pdf.

<sup>&</sup>lt;sup>15</sup> Unless otherwise specified, data on MDR-TB was compiled by CRS from WHO, *Tuberculosis Infection Control in the Era of Expanding HIV/AIDS Care and Treatment*, 2007, at http://whqlibdoc.who.int/hq/1999/ (continued...)

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 patients do not take their medicine for the full term, TB may become resistant to the drugs.

The development of MDR-TB is particularly troubling to scientists, because MDR-TB carriers can transmit resistant forms of TB to others. MDR-TB is transmissible, even among those who have never had TB. Research has indicated that patients are less likely to complete regimens for treatment-resistant forms of TB, in part, because resistant forms take longer to cure. Non-resistant forms of TB take between six and nine months to cure, while MDR-TB takes about two years to cure. MDR-TB treatments are also more toxic, more expensive, often of limited availability in resource-limited settings, and generally less effective, especially among HIV-positive people. If patients adhere to treatment regimens, cure rates for non-resistant TB range between 80% and 95%; cure rates for MDR-TB range between 50% and 60%.

WHO advises that health care providers treat MDR-TB patients in separate facilities than those with HIV/AIDS. Separating MDR-TB patients from HIV/AIDS

patients can be particularly challenging in resource-limited settings, where hospitals are frequently overcrowded, ill-equipped, and unable to house individuals for the entire treatment term. In areas with high HIV-prevalence, efforts to care for MDR-TB patients separately from HIV/AIDS patients are often complicated by the high proportion of hospital beds filled with HIV/AIDS patients.

In February 2008, WHO released a report on TB drug resistance that summarized findings from surveys conducted between 2002 and 2006 in 81 countries.<sup>16</sup> Based on those surveys, WHO estimates that almost 490,000 MDR-TB cases emerged in 2006, representing about 5% of all new TB cases—though MDR-TB rates varied widely from 0% in some western European countries to over 35% in some former Soviet states. Among the 490,000 MDR-TB cases, 285,718 were new cases and 203,230 had been previously treated.

WHO estimated that, of the countries for which adequate data exist, China, India, and Russia are estimated to have the highest number of MDR-TB cases. China and India hold about 50% of all MDR-TB cases and Russia comprises another 7%. Russia has the greatest proportion of MDR-TB cases among new ones, however. About 13% of all new TB cases were MDR-TB, 19% of all TB cases were MDR-TB, and almost 50% of previously treated TB cases were identified as MDR-TB.<sup>17</sup> Although no other HBC reported equally high MDR-TB rates, a number of Eastern European countries are estimated to have greater proportion of MDRT-TB prevalent rates. WHO has identified 27 countries, which together account for about 86% of all global MDR-TB cases; 15 of them are in Eastern Europe (see **Figure A-1** and **Table A-3** in the **Appendix**).

<sup>(...</sup>continued)

WHO\_TB\_99.269\_ADD\_eng.pdf and WHO, *Anti-Tuberculosis in the World*, 2008, at http://www.who.int/entity/tb/ publications/2008/drs\_report4\_26feb08.pdf. General TB statistics included throughout this report were mostly taken from WHO's 2007 *Global Tuberculosis Control Report*. Data in this paragraph may vary slightly from those, as they were taken from WHO's 2008 report, *Anti-Tuberculosis in the World*, which included more recent statistics on drug resistance but did not provide analysis on TB generally.

<sup>&</sup>lt;sup>16</sup> Unless otherwise indicated, data included in this section was taken from WHO, *Anti-Tuberculosis in the World*, 2008, pp. 73 and 82.

<sup>&</sup>lt;sup>17</sup> WHO, 2008 Global Tuberculosis Control Report, p.51.

Although WHO's report provided greater insight into the prevalence of drug resistant forms of TB, little is known about resistance in Africa. The findings included in the report were estimated to have measured about one-half of all drug-resistant TB cases, because the surveys were conducted only in those countries with the capacity to conduct drug resistance surveys. Such capacity remains limited in Africa. Findings from six countries in sub-Saharan Africa were included in the analysis (Cote d'Ivoire, Ethiopia, Madagascar, Rwanda, Senegal, and Tanzania). Data from South Africa were included in the illustrations and tables throughout the report, but not in the analysis, because WHO used a different methodology to analyze data previously collected from South Africa.

Based on available data, WHO estimates that in 2006, some 2% of all TB cases were MDR-TB in Africa, 7% in the Western Pacific Region, and 19% in Eastern Europe (see **Table A-4** in the **Appendix**). WHO asserts that although it can use available data to approximate the global burden of MDR-TB, it cannot detect global changes in MDR-TB prevalence, because data in many high-burden countries are unavailable, incomplete, and/or have only recently begun to be compiled. The organization can, however, extrapolate trends in key areas. WHO found that MDR-TB cases declined in China and the United States; were stable in Thailand, some parts of Vietnam, and three Baltic countries; and increased in the Republic of Korea and Peru. In Peru, a decline in TB notification rates suggests weaknesses in TB control. In Korea, the TB burden is shifting to the elderly and the number of MDR-TB cases among new TB cases is increasing. Two regions in the Russian Federation are showing increases in the proportion of MDR-TB among new cases at a very rapid rate, while the TB notification rate in those regions is falling slowly.

WHO has indicated that similar outbreaks of drug resistance with associated high mortality are likely occurring in other African countries but are going undetected because of insufficient laboratory capacity.<sup>18</sup> MDR-TB patients are not yet routinely checked for HIV/AIDS in Africa, though they are extremely susceptible to the disease. Botswana, Mozambique, and South Africa are reportedly the only countries in sub-Saharan Africa that routinely test drug-resistant TB cases for HIV.<sup>19</sup> According to the latest available data, in 2006, almost 90% of new MDR-TB cases that occurred in the three countries were found in high HIV-prevalent settings.

## **Extensive Drug Resistant (XDR)-TB**

MDR-TB is considered XDR-TB when it becomes resistant to three or more of the six classes of second-line drugs. In high-quality health facilities, XDR-TB treatment is successful in 30% of the cases. In low-resource settings, XDR-TB is almost always fatal. WHO is uncertain about the extent of XDR-TB prevalence, in large part because drug resistance testing to second-line drugs is not available in most high-burden countries.<sup>20</sup> The majority of countries that reported XDR-TB cases to WHO were low-burden countries and do not reflect the global magnitude of the phenomenon. WHO estimates that XDR-TB is widespread, with 45 countries having reported at least one case.

<sup>&</sup>lt;sup>18</sup> Unless otherwise noted, information in this paragraph was compiled by CRS from WHO, *Anti-Tuberculosis Drug Resistance in the World*, 2008, p. 91, at http://www.who.int/tb/publications/2008/drs\_report4\_26feb08.pdf, and Sello Motseta, "Botswana Confirms Cases of Resistant TB." *Associated Press*, January 16, 2008.

<sup>&</sup>lt;sup>19</sup> Information in this paragraph was compiled by CRS from WHO, *Anti-Tuberculosis in the World*, 2008, at http://www.who.int/tb/publications/2008/drs\_report4\_26feb08.pdf, visited on March 5, 2008.

<sup>&</sup>lt;sup>20</sup> Ibid, p. 78.

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.<sup>21</sup> 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.

Concern about the spread of XDR-TB rose in May 2006 when an outbreak caused several deaths in Kwazulu-Natal, South Africa. Many health experts were alarmed by the high mortality rates. South African officials invited CDC and WHO to assess the situation. Five hundred forty-four patients were studied; 221 were diagnosed with MDR-TB, including 53 cases determined to be 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 has indicated that similar outbreaks of drug resistance with associated high mortality are taking place in other African countries, but going undetected because of insufficient laboratory capacity.<sup>22</sup> HIV/AIDS patients are not yet routinely checked for TB in Africa (except in Botswana, Mozambique, and South Africa), though they are extremely susceptible to the disease. According to latest estimates, 996 of 17,615 MDR-TB cases in South Africa were identified as XDR-TB, representing some 5.6% of all MDR-TB cases. XDR-TB cases were considerably higher in Kwazulu-Natal, with some 14% (656 cases) of all MDR-TB cases identified as XDR-TB. Some observers believe more undetected cases may exist in the country, asserting that testing results are often inaccurate, testing methods are outdated, and many patients die before they are diagnosed.

On January 16, 2008, the Government of Botswana confirmed that 100 people were diagnosed with MDR-TB and an additional two were diagnosed with XDR-TB.<sup>23</sup> Botswana's Ministry of Health officials are urging those with chronic coughs and all who have been exposed to patients with active TB to go to their nearest health facility to be tested.

WHO has ramped up its XDR-TB efforts in southern Africa.<sup>24</sup> A delegation of WHO officials and its partners visited Lesotho early 2008 to help plan XDR-TB surveillance and treatment, as well as improve basic TB control. Similar missions were also held in Malawi and Swaziland in February 2008. In March 2008, a team of WHO officers began to assist KwaZulu-Natal authorities investigate the origin and spread of XDR-TB in the province. The team is expected to remain in the country for several months. Botswana, Lesotho, Malawi, Mozambique, Swaziland, and Zimbabwe have reportedly submitted national XDR-TB response plans to WHO. Lesotho has reportedly completed a rapid survey on suspected XDR-TB cases; Botswana has started one; and Malawi, Mozambique, Namibia and Swaziland intend to start surveys within a few months.

<sup>&</sup>lt;sup>21</sup> WHO, "WHO concern over extensive drug resistant TB strains that are virtually untreatable." September 5, 2006, at http://www.who.int/mediacentre/news/notes/2006/np23/en/index.html.

<sup>&</sup>lt;sup>22</sup> Information in this paragraph was compiled by CRS from WHO, *Anti-Tuberculosis in the World*, 2008, p.91 and Sello Motseta, "Botswana Confirms Cases of Resistant TB." *Associated Press*, January 16, 2008, at http://ap.google.com/article/ALeqM5hPwuo15khre\_PPVZtGZ72KZSj9pAD8U76PIO0, visited January 18, 2007.

<sup>&</sup>lt;sup>23</sup> "Drug resistant TB hits Botswana." *Botswana Press Agency*, January 16, 2008, at http://www.gov.bw/cgi-bin/ news.cgi?d=20080116&i=Drug\_resistant\_TB\_hits\_Botswana, visited January 18, 2007.

<sup>&</sup>lt;sup>24</sup> Information in this paragraph was compiled by CRS from WHO, "XDR-TB: Extensively Drug -Resistant Tuberculosis." March 2008. At http://www.who.int/tb/challenges/xdr/news\_mar07.pdf, accessed on February 4, 2008.

Madagascar, Mozambique, and Tanzania have ongoing anti-TB drug resistance surveys; Angola, Lesotho, Malawi, Namibia, South Africa, and Zimbabwe plan to start surveys by the end of 2008.

## **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. Congress designates funds for global TB interventions only to the U.S. Agency for International Development (USAID), while other agencies and departments draw from general funds (see **Table A-5** in the **Appendix**). Because agencies and departments might use discretionary funds to support global TB initiatives, some U.S. international TB activities might not be included here, such as research conducted by the National Institute of Health (NIH) to develop a new TB drug with a shorter treatment regimen.<sup>25</sup>

## **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. In FY2004, Congress provided \$85.1 million to USAID for international TB efforts, \$92.0 million in FY2005, \$91.5 million in FY2006, \$94.9 million in FY2007, and \$162.2 million in FY2008.<sup>26</sup> The Administration requested \$97.1 million for USAID's FY2009 international TB interventions.

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

CDC supports global TB efforts by providing epidemiologic, laboratory, and programmatic support to USAID, WHO, and the International Union Against TB and Lung Diseases.<sup>27</sup> 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 fiscal year since FY2004, it has spent on average some \$2 million of its TB appropriation on global TB efforts and anticipates spending the same amount on global TB in each of FY2008 and FY2009.

USAID also transferred \$3.4 million in each of FY2006 and FY2007 to CDC in support of CDC's technical efforts in other countries. Through its Global AIDS Program (GAP), CDC supports the Global Fund (the Global Fund is discussed more comprehensively in the "International TB

<sup>&</sup>lt;sup>25</sup> The program descriptions below were compiled from interviews with Administration officials.

<sup>&</sup>lt;sup>26</sup> Reported to CRS by USAID's Budget Office on March 15, 2008.

<sup>&</sup>lt;sup>27</sup> 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

Efforts" section below) and has technical staff assigned to positions in the Office of the Global AIDS Coordinator (OGAC), USAID, the HHS Office of Global Health Affairs and WHO.

### **Department of State**

On January 28, 2003, during 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 through an initiative he called the President's Emergency Plan for AIDS Relief (PEPFAR). The initiative, authorized in May 2003 by P.L. 108-25, the U.S. Leadership Against HIV/AIDS, Tuberculosis, and Malaria Act, anticipates channeling \$10 billion through the Global HIV/AIDS Initiative (GHAI) to 15 Focus Countries; directing \$4 billion to global TB programs, international HIV/AIDS research, and bilateral HIV/AIDS programs in more than 100 additional non-Focus Countries; and reserving \$1 billion for U.S. Global Fund contributions.<sup>28</sup>

Congress appropriates the bulk of PEPFAR funds to the GHAI account, which 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, and international partnerships, such as the Global Fund. OGAC reports that, in FY2006, it transferred \$48.4 million to implementing agencies for TB projects in the 15 Focus Countries and \$131.0 million in FY2007. The Administration did not request any funds for TB activities for FY2008, though Congress directed OGAC to provide not less than \$150 million for joint HIV/TB programs through FY2008 Consolidated Appropriations, Division J, Foreign Operations Appropriations.

## **International TB Efforts**

A number of organizations collaborate to combat TB globally. Most of these 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)—WHO's decision making body composed of delegations from all 193 member countries—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,<sup>29</sup> and cure of 85% of such cases, by the year 2000.<sup>30</sup> In 1994, WHO and

<sup>&</sup>lt;sup>28</sup> For more information on PEPFAR, see CRS Report RL33771, *Trends in U.S. Global AIDS Spending: FY2000-FY2008*, and CRS Report RL34192, *PEPFAR: Policy Issues from FY2004 through FY2008*, by (name redacted), and White House Fact Sheet, "The President's Emergency Plan for AIDS Relief," January 29, 2003, at http://www.state.gov/p/af/rls/fs/17033.htm, visited on January 29, 2008.

<sup>&</sup>lt;sup>29</sup> 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 (continued...)

global health experts developed and recommended that all health practitioners use the Directly Observed Treatment, Short-course (DOTS) strategy to combat TB.<sup>31</sup> 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 to 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 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 that advocated 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).<sup>32</sup> 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 estimates that \$56 billion would be needed from 2006 through 2015 to implement its Global Plan to Stop TB (see **Table A-6** in the **Appendix**).<sup>33</sup> Of the estimated \$56 billion needed to reverse the incidence of TB, WHO suggests that \$28.9 billion be spent on expanding DOTS,

<sup>(...</sup>continued)

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

<sup>&</sup>lt;sup>30</sup> Resolution WHA44.8. Tuberculosis control program. In: *Handbook of resolutions and decisions of the World Health Assembly and the Executive Board*. Volume III, 3<sup>rd</sup> ed. (1985-1992). Geneva, World Health Organization, 1993 (WHA44/1991/REC/1):116.

<sup>&</sup>lt;sup>31</sup> See WHO's website on DOTS, at http://www.who.int/tb/dots/en/index.html.

<sup>&</sup>lt;sup>32</sup> 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/.

<sup>&</sup>lt;sup>33</sup> Figures in this section were compiled from *The Global Plan to Stop TB: 2006-2015*. http://www.stoptb.org/globalplan/plan\_main.asp

\$5.8 billion be spent on DOTS-Plus initiatives, \$6.7 billion be spent on treating people coinfected with HIV/AIDS and TB, and \$9.0 billion be spent on research and development. WHO estimates that 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.

#### 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<sup>34</sup> reviews requests for treatments through DOTS-Plus projects and determines whether it can provide the medication in compliance with international standards of care.<sup>35</sup>

#### 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.<sup>36</sup> 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;

<sup>&</sup>lt;sup>34</sup> 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.

<sup>&</sup>lt;sup>35</sup> 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

<sup>&</sup>lt;sup>36</sup> For more on the Stop TB Partnership, see http://www.stoptb.org/stop\_tb\_initiative/.

- expand the availability, affordability and quality of TB drugs;
- 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.<sup>37</sup> 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.<sup>38</sup> The Fund is a financing vehicle, not a development agency, and its grants are intended to complement existing efforts rather than replace them. As of March 4, 2008, the Fund approved more than \$10 billion in support of nearly 500 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.<sup>39</sup> About 17% of Global Fund grants are targeted at TB control and treatment. According to the Fund's website, it has helped to detect 5 million TB cases, supported treatment for 3 million TB cases using the DOTS strategy, and administered treatment for 24,000 MDR cases.<sup>40</sup>

## Bill and Melinda Gates Foundation

Since the Gates Foundation funded its first grant in 1999, the foundation has provided \$781 million to combat TB globally.<sup>41</sup> The foundation has pledged an additional \$650 million to the

<sup>&</sup>lt;sup>37</sup> http://www.stoptb.org/gdf/

<sup>&</sup>lt;sup>38</sup> Information in this paragraph was summarized from Global Fund, *Monthly Progress Update*, January 31, 2007, at 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, 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.* 

<sup>&</sup>lt;sup>39</sup> Global Fund, "Grant Commitments & Disbursements." February 1, 2008, at http://www.theglobalfund.org/en/ funds\_raised/commitments/, accessed on March 6, 2008.

<sup>&</sup>lt;sup>40</sup> Global Fund webpage on tuberculosis, at http://www.theglobalfund.org/en/about/tuberculosis/, accessed on March 6, 2008.

<sup>&</sup>lt;sup>41</sup> Correspondence with Gates Foundation officials on February 4, 2008. Also see Gates Foundation's list of TB grants and announcements, at http://www.gatesfoundation.org/GlobalHealth/Pri\_Diseases/Tuberculosis/, accessed on January 30, 2008.

Global Fund to Fight AIDS, Tuberculosis, and Malaria, of which \$350 million has been paid to date.<sup>42</sup> 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.<sup>43</sup>

## **Issues for Congress**

Since PEPFAR was launched in FY2004, overall U.S. spending on international TB initiatives has hovered around \$90 million (see **Table A-5** in the **Appendix**). In FY2004, Congress appropriated \$85.1 million to USAID for global TB efforts, \$92.0 million in FY2005, \$91.5 million in FY2006, and \$94.9 million in FY2007. In FY2008, Congress significantly boosted support for global TB programs, providing \$162.2 million to USAID for international TB efforts and directing OGAC to provide not less than \$150 million for joint HIV/TB programs. 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.

## **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. More than a century after its development, in most developing countries, TB is primarily identified through microscopic examination of sputum. This tool, however, only detects from 40% to 60% of TB cases, and as little as 20% of HIV co-infected cases.<sup>44</sup> Although sputum testing has limited reliability, this procedure is the most widely used in developing countries and is usually performed only after TB treatment has failed—after which the patient could have transmitted the disease to others. About 85% of all countries who reported TB testing practices to WHO indicated that all suspected pulmonary TB cases undergo sputum testing. Of the 22 HBCs, 7 did not meet the minimum requirement of at least one sputum testing laboratory per 100,000 persons (see **Table A-7** in the **Appendix**).

<sup>&</sup>lt;sup>42</sup> Global Fund, *Pledges and Contributions*, March 4, 2008, at http://www.theglobalfund.org/en/files/ pledges&contributions.xls, accessed on March 6, 2008.

<sup>&</sup>lt;sup>43</sup> Gates Foundation, "Grantmaking priorities for Tuberculosis," accessed on March 6, 2008, at http://www.gatesfoundation.org/GlobalHealth/Pri\_Diseases/Tuberculosis/TB\_Grantmaking.htm.

<sup>&</sup>lt;sup>44</sup> Gates Foundation, "Tuberculosis Backgrounder," accessed on March 6, 2008. http://www.gatesfoundation.org/ GlobalHealth/Pri\_Diseases/Tuberculosis/TB\_Backgrounder.htm

Health experts also advocate for improved access to advanced testing technology, because sputum tests do not reliably detect smear-negative TB cases, particularly among HIV-positive patients.<sup>45</sup> Culturing, a process requiring laboratory diagnosis, is the most definitive method of detecting TB, particularly in smear-negative cases. WHO recommends that countries have at least one laboratory per 5 million people that is capable of culturing samples. Seven of the 22 high-burden countries meet this minimum requirement: Brazil (5.1), Cambodia (1.1), China (1.4), Russia (34.0), South Africa (1.3), Thailand (5.1), and Vietnam (1.0) meet this criteria. South Africa is the only country in sub-Saharan Africa that meets this criteria.

In order to prescribe medications properly, laboratories must be capable of conducting drug susceptibility tests (DST). Prescribing the wrong medication or dosage not only minimizes the effectiveness of TB treatments, but can also lead to drug resistance. WHO recommends that countries have at least one DST lab per 10 million people. Of the 22 high-burden countries, Bangladesh and Nigeria have no DST labs, nine countries have one DST lab to serve their entire population (about one-third of high-burden countries), and nine meet the minimum of one per 10 million people: Brazil, Cambodia, China, Indonesia, Russia, South Africa, Thailand, Uganda, and Vietnam.

In many countries, patients might experience lapses in TB treatments, because clinics might not have the medicines in stock. Irregular drug deliveries are often caused by poor data collection, deficient road and transport conditions, and poor-quality 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.

The African Health Capacity Investment Act of 2007 (H.R. 3812/S. 805) aims to address some of these issues. The bills authorize funds to improve health care capacity on the continent. Related activities include training African health care workers, providing incentive to retain health worker, and establishing off-site HIV/AIDS testing and treatment facilities for health care providers. The bill also requires the President to develop a strategy that would coordinate health-related strategies with other donors.

## Address Health Worker and Health Center Shortages

Shortages of properly trained health care workers and sufficiently equipped health centers in high-burden countries, particularly in Africa, complicate efforts to properly contain and treat TB cases. Most of the 22 high-burden countries do not have enough health workers to meet the most

<sup>&</sup>lt;sup>45</sup> 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 TB outside 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

basic health care needs, including identifying and treating TB cases and monitoring drug usage (see **Table A-8** in the **Appendix**).<sup>46</sup> In addition, many health centers are unable to contain airborne infections like TB.<sup>47</sup>

High HIV prevalence in some parts of Africa further complicates shortage issues, because HIV and TB patients are usually housed within close proximity of each other in poorly equipped facilities. WHO maintains that in order for countries to effectively control TB and prevent increases in MDR-TB and XDR-TB cases, HIV/AIDS and TB patients should be housed separately and teams of health workers should be trained specifically to manage drug resistance and work in hospitals or isolation units dedicated to TB patients. Another challenge is that in some countries with high HIV prevalence, a significant number of health workers are HIV-positive, posing a risk to themselves and their patients. WHO contends that all of these issues converge to cause the extremely high mortality in KwaZulu-Natal.<sup>48</sup>

It is widely understood that MDR-TB is caused in large part by poor treatment adherence. Health worker shortages lessen the likelihood that the dispensing of medication 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.<sup>49</sup> 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.

## 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 has expressed concern that HIV patients are not yet routinely tested for TB in most high-burden countries. WHO asserts that countries could significantly improve TB case identification if health professionals would routinely test all those newly diagnosed with HIV for TB. 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 spent nearly \$50 million on TB efforts in the 15 Focus Countries and about \$120 million on addressing HIV/TB co-infection in FY2007. Health advocates urge Congress to increase funding for programs that integrate HIV/AIDS and TB responses. Congress directed OGAC to spend not less than \$150 million of the \$4.7 billion appropriated to OGAC on joint HIV/TB programs through FY2008 Consolidated Appropriations, Division J, Foreign Operations Appropriations.

<sup>&</sup>lt;sup>46</sup> WHO, 2006 World Health Report: Working Together for Health, at 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.

<sup>&</sup>lt;sup>47</sup> WHO, 2007 World Health Report, A Safer Future: Global Public Health Security in the 21<sup>st</sup> Century. http://www.who.int/whr/2007/whr07\_en.pdf

<sup>&</sup>lt;sup>48</sup> *Ibid*.

<sup>&</sup>lt;sup>49</sup> WHO, 2007 World Health Report, A Safer Future: Global Public Health Security in the 21<sup>st</sup> Century. http://www.who.int/whr/2007/whr07\_en.pdf

## **Provide Additional Funds for Research**

#### Treatments

Many health experts urge Congress to increase support for TB research that 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. WHO and others are seeking to develop new TB treatments that will be effective against MDR-TB, can cure patients between one and two months, and will cure latent TB infection. Researchers are also attempting to develop drugs that will be affordable and easily managed in resource-limited settings.

#### Vaccines

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 support organizations like Aeras Global TB Vaccine Foundation, which are seeking to develop a vaccine that protects the innoculated throughout their lives.<sup>50</sup>

#### **Diagnostic Tools**

TB experts stress the need for new 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.<sup>51</sup>

In 2007, Representatives Gene Green and Sherrod Brown introduced H.R. 1532 and S. 1551, the Comprehensive Tuberculosis Elimination Act of 2007. The bills amend Section 317E of the Public Health Service Act (42 U.S.C. 247b-6) to authorize funds for the research and development of TB vaccines, new treatments, and more effective diagnosis tools that could be used in low-resource settings. In October 2007, the House passed and the Senate Foreign Relations Committees reported out companion TB bills, S. 968 and H.R. 1567, the Stop Tuberculosis (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.

<sup>&</sup>lt;sup>50</sup> See Aeras Global TB Vaccine Foundation, http://www.aeras.org/about-tb/need.php.

<sup>&</sup>lt;sup>51</sup> For more information on TBDI, see http://www.who.int/tdr/diseases/tb/tbdi.htm. Other TB research initiatives include 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/; Global Tuberculosis Research Initiative (GTRI) at WHO, http://www.who.int/tdr/diseases/tb/gtri.htm; and The Action TB Program at University of Cape Town, http://web.uct.ac.za/depts/mmi/lsteyn/glaxo.html.

They also authorize \$70 million in FY2008 and \$100 million in FY2009 for anti-TB programs at CDC.

## **Consider Involuntary Detention**

Debate about whether to forcefully detain those infected with XDR-TB has intensified, particularly in South Africa. In January 2007, WHO issued a statement indicating that "if a patient wilfully refuses treatment and, as a result, is a danger to the public, the serious threat posed by XDR-TB means that limiting that individual's human rights may be necessary to protect the wider public."<sup>52</sup> Forcefully detaining people carrying XDR-TB has a number of human rights implications. The low quality of some health facilities in high-burden countries complicates arguments about involuntary detention. A number of individuals being forcefully isolated in South African health centers reportedly held protests and walked out of facilities, complaining of poor treatment and prison-like conditions. One patient was reportedly shot while attempting to leave the premises.<sup>53</sup> Several provinces in South Africa have reportedly taken legal action to force drug resistant TB patients to stay in hospitals in isolation units surrounded by wire fences and protected by guards.<sup>54</sup>

The South African Medical Research Council (MRC) asserts that forcibly quarantining individuals is a complicated issue, because MDR- and XDR-TB patients might never be cured (MDR- and XDR-TB are difficult to cure in low-resource settings), forcing the patients to be confined until death. MRC does not support coerced treatment, because of "the lower success rate of [resistant forms of TB] and the reduced life expectancy of MDR-TB patients."<sup>55</sup>

Some observers point out that forced isolation is also complicated by socio-economic factors.<sup>56</sup> About 10 million South Africans—about 25% of the population—receive some form of social welfare. South African policy mandates that those who are hospitalized at the country's expense lose their government assistance. Many MDR-TB patients choose not to stay in hospitals, in part because they can not earn money or receive assistance while hospitalized and MDR-TB treatment takes between 18 and 24 months.

## **Address Poverty**

Tuberculosis experts are increasingly studying the intersection of poverty and tuberculosis. The Stop TB Partnership has recently commissioned the World Bank to study the economic impacts of

<sup>&</sup>lt;sup>52</sup> WHO, "WHO Guidance on Human Rights and Involuntary Detention for XDR-TB Control." Press Release. January, 24, 2007, at http://www.who.int/tb/xdr/involuntary\_treatment/en/print.html, visited on January 31, 2008.

<sup>&</sup>lt;sup>53</sup> Adele Baleta, "Forced Isolation of Tuberculosis Patients in South Africa." *The Lancet*. Volume 7, Number 12, December 2007, at http://download.thelancet.com/pdfs/journals/1473-3099/PIIS1473309907702815.pdf, visited on January 31, 2008.

<sup>&</sup>lt;sup>54</sup> Jerome Sing et al., "XDR-TB in South Africa: No Time for Denial or Complacency." *PLoS Medicine*. Volume 4, Issue 1, January 2007, at http://medicine.plosjournals.org/perlserv?request=get-document&doi=10.1371/journal.pmed.0040050, visited on January 31, 2008.

<sup>&</sup>lt;sup>55</sup> MRC, "Managing Multi-Drug Resistent Tuberculosis: Legal Implications." Policy Brief. January 2006, at http://www.mrc.ac.za/policybriefs/managingTB.pdf, visited on January 31, 2008.

<sup>&</sup>lt;sup>56</sup> Information in this paragraph was compiled by CRS from, Jerome Sing et al., "XDR-TB in South Africa: No Time for Denial or Complacency." *PLoS Medicine*. Volume 4, Issue 1, January 2007, at http://medicine.plosjournals.org/ perlserv?request=get-document&doi=10.1371/journal.pmed.0040050, visited on January 31, 2008.

TB at the household and macro level in Africa. At the household level, some analysts contend that people sickened by TB experience reduced earning potential, which in impoverished areas might induce them to avoid or discontinue treatment as soon as symptoms abate. At the macro level, observers assert that the crowded, poorly planned, unsanitary conditions that often characterize urban slums facilitate transmission of TB. Some 1 billion people are believed to live in urban slums, and the figure is expected to reach 2 billion in the next 30 years. In the world's poorest countries, about 80% of the urban population live in slums. Some health advocates are beginning to argue that TB control should be considered an integral part of poverty reduction strategies.

## **Appendix.** Tables and Figures





Source: Map Resources. Adapted by CRS April 2008.

	New T		New TB Cases			TB-Related Deaths		
Country	Number	# per  00,000	% HIV-Positive	% MDR-TB	Percentage of Previously Treated TB Cases MDR-TB	Number	# per 100,000	
India	I,933	168.0	1.2	2.8	17.0	325.0	28.0	
China	1,311	99.0	0.3	5.0	26.0	201.0	15.0	
Indonesia	534	234.0	0.6	2.0	9.0	88.0	38.0	
South Africa	454	940.0	44.0	1.8	6.7	105.0	218.0	
Nigeria	450	311.0	9.6	1.9	9.3	117.0	81.0	
Bangladesh	351	225.0	0.0	3.6	19.0	70.0	45.0	
Ethiopia	306	378.0	6.3	1.6	12.0	68.0	83.0	
Pakistan	292	181.0	0.3	3.4	36.0	55.0	34.0	
Philippines	248	287.0	0.1	4.0	21.0	39.0	45.0	
DR Congo	237	392.0	9.2	2.4	9.1	51.0	84.0	
Russia	53	107.0	3.8	13.0	49.0	24.0	17.0	
Vietnam	49	173.0	5.0	2.7	19.0	20	23.0	
Kenya	4	384.0	52.0	0.0	0.0	26.0	72.0	
Tanzania	123	3   2.0	18.0	1.1	0.0	26.0	66.0	
Uganda	106	355.0	16.0	0.5	4.4	25.0	84.0	
Brazil	94.0	50.0	12.0	0.9	5.4	7.6	4.0	
Mozambique	93.0	443.0	30.0	3.5	3.3	24.0	117.0	
Thailand	90.0	142.0	11.0	1.7	35.0	3.0	20.0	
Burma	83.0	171.0	2.6	4.0	16.0	6.	3.0	
Zimbabwe	74.0	557.0	43.0	1.9	8.3	17.0	131.0	
Cambodia	71.0	500.0	9.6	0.0	3.1	3.0	92.0	
Afghanistan	42.0	161.0	0.0	3.4	37.0	8	32.0	

Table A-1. Tuberculosis Cases in the 22 High-Burden Countries, 2006

Source: WHO, 2008 Global Tuberculosis Control Report

	New TB	Cases	TB-HIV/AIDS O	Co-infected		ТВ	Related Deaths	
Region	Number	# per 100,000	Number	# per 100,000	Number	# per 100,000	Number TB- HIV/AIDS Co-infected	# TB-HIV/AIDS Co-infected per 100,000
Africa	2,807,688	363	605,989	78.0	639,089	83.0	204,559	26.0
The Americas	330,724	37	21,265	2.4	40,600	4.5	3,876	<1.0
Eastern Mediterranean	569,708	105	6,538	1.2	107,895	20.0	2,737	<1.0
Europe	433,261	49	l 2,842	1.4	62, 197	7.0	2,335	<1.0
Southeast Asia	3,100,355	180	39,556	2.3	5   4,699	30.0	10,805	<1.0
Western Pacific	1,915,285	109	22,823	1.3	291,240	17.0	6,545	<1.0
Global	9,   57,02	139	709,0 3	11.0	1,655,720	25.0	230,857	4.0

### Table A-2. Global Tuberculosis Cases (Regional), 2006

**Source:** WHO, 2008 Global Tuberculosis Control Report

Country	Percentage of All TB Cases with MDR-TB	Number of MDR-TB Cases	
China	8.3	l 30,548	
India	4.9	0, 32	
Russia	19.0	36,037	
Pakistan	5.0	١5,233	
Bangladesh	4.0	l 4,583	
South Africa	2.6	l 4,034	
Ukraine	22.0	l 3,429	
Indonesia	2.2	12,142	
Philippines	4.6	I I,848	
Nigeria	2.3	11,171	
Uzbekistan	24.0	9,829	
DR Congo	2.8	7,044	
Kazakhstan	25.0	6,608	
Vietnam	4.0	6,421	
Ethiopia	1.9	5,825	
Burma	4.8	4,25	
Tajikistan	20.0	3,204	
Azerbaijan	29.0	2,397	
Republic of Moldova	27.0	2,035	
Kyrgyzstan	18.0	l,368	
Belarus	16.0	I,096	
Georgia	12.0	652	
Bulgaria	13.0	45	
Lithuania	17.0	425	
Armenia	14.0	381	
Latvia	14.0	218	
Estonia	20.0	128	
Global MDR-TB Priority Countries	5.6	421,490	
Global	4.8	489,   40	

Table A-3. MDR-TB Cases in 27 Global Priority Countries, 2006

Source: WHO, 2008 Global Tuberculosis Report, p. 51.

WHO Region	Percentage of all TB Cases	Percentage of MDR-TB Cases	% MDR-TB
Established Market Economies	105,795	1,317	1.2
Central Europe	50,502	1,201	2.4
Eastern Europe	4 6,3 6	80,057	19.2
Latin America	349,278	12,070	3.5
Eastern Mediterranean	601,225	25,475	4.2
Africa (low HIV incidence)	375,801	8,415	2.2
Africa (high HIV incidence)	2,656,422	58,296	2.2
Southeast Asia	3,464,313	149,615	4.3
Western Pacific	2,173,333	152,694	7.0
All Countries	10,192,985	489,140	5.1

Source: WHO, Anti-Tuberculosis in the World, 2008, p. 73.

#### Table A-5. U.S. International Tuberculosis Spending: FY2004-FY2009

(current U.S. \$ millions)

Agency or Department	FY2004 Actual	FY2005 Actual	FY2006 Actual	FY2007 Estimate	FY2008 Request	FY2008 Estimate	FY2009 Request
USAID	\$85. I	\$92.0	\$91.5	\$94.9	\$89.9	\$162.2	\$97. I
Department of State	n/a	\$26.2	\$48.4	\$ 3 .0	\$0.0	\$150.0	\$0.0
CDC	\$2.0	\$2.3	\$2.2	\$1.9	\$0.0	\$2.0	TBD

**Source:** Appropriations legislation and interviews with Administration officials. The State Department reports that in FY2004, it did not collect data on TB/HIV funding in FY2004.

	Sub-	Saharan Africa		
Program	Needs (thousands)	Estimated Results		
DOTS expansion	\$I3,278	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		
	Ea	stern Europe		
Needs Program (thousands)		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		
	So	utheast Asia		
Needs Program (thousands)		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	2 31.0 thousand treated for HIV/AIDS/AIDS		
Other Programs	\$631			
Southeast Asia Total	\$6,199	Avert 5.1 million deaths		

#### Table A-6. Global TB Financing Needs and Outcomes: 2006-2015

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

Country	– Population (thousands)	Laboratory Diagnostic Services						
		Sputum Smear		Culture		DST		
		# of Labs	# per 100,000	# of Labs	# per 5 <b>M</b> illion	# of Labs	# per I <b>0 M</b> illion	
India	1,151,751	11,968	1.0	8	0.03	8	0.07	
China	l,320,864	3,010	0.2	360	1.40	90	2.70	
Indonesia	228,864	4,858	2.1	41	0.90	11	1.80	
South Africa	48,282	143	03	13	1.30	8	2.70	
Nigeria	144,720	694	0.5	0	0.00	0	0.00	
Bangladesh	155,991	687	0.4	3	0.10	0	0.20	
Ethiopia	81,021	713	0.9	I	0.10	I	0.10	
Pakistan	l 60,943	<b>9</b> 82	0.6	3	0.10	I	0.20	
Philippines	86,264	2,374	2.8	3	0.20	3	0.30	
DR Congo	60,644	I,069	1.8	I	0.10	I	0.20	
Russia	143,221	4,953	3.5	978	34.00	302	68.00	
Vietnam	86,206	874	1.0	18	1.00	2	2.10	
Kenya	36,553	770	2.1	2	0.30	2	0.50	
Tanzania	39,459	690	1.7	3	0.40	I	0.80	
Uganda	29,899	726	2.4	3	0.50	2	1.00	
Brazil	l 89,323	4,044	2.1	193	5.10	38	10.00	
Mozambique	20,97 I	250	1.2	I	0.20	I	0.50	
Thailand	63,444	937	1.5	65	5.10	18	10.00	
Burma	48,379	391	0.8	2	0.20	I	0.40	
Zimbabwe	3,228	180	1.4	I	0.40	I	0.80	
Cambodia	4,   97	186	1.3	3	1.10	I	2.10	
Afghanistan	26,088	500	1.9	İ	0.20	I	0.40	

Table A-7. Laboratory Ca	pacity in High	-Burden Countries.	2006
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Source: WHO, 2008 Global Tuberculosis Control Report.

	Population, 2005 (thousands)	Physicians		Nurses		Pharmacists			
Country		Number	# per 1,000	Number	# per 1,000	Number	# per 1,000	Year Data Collected	
India	١,103,371	645,825	0.60	865,   35	0.80	592,577	0.56	2003	
China	1,315,844	l,364,000	1.06	l,358,000	1.05	359,000	0.28	2001	
Indonesia	222,781	29,499	0.13	135,705	0.62	7,580	0.03	2003	
South Africa	47,432	34,829	0.77	l 84,459	4.08	2,52	0.28	2004	
Nigeria	131,530	34,923	0.28	210,306	١.70	6,344	0.05	2004	
Bangladesh	141,822	38,485	0.26	20,334	0.14	9,411	0.06	2004	
Ethiopia	77,431	I,936	0.03	l 4,893	0.21	I,343	0.02	2003	
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	
DR Congo	57,549	5,827	0.11	28,789	0.53	I,200	0.02	2004	
Russia	143,202	60,9043	4.25	1,153,683	8.05	11,404	0.08	2003	
Vietnam	84,238	42,327	0.53	44,539	0.56	5,977	0.08	2001	
Kenya	34,256	4,506	0.14	37,113	1.14	3,094	0.01	2004	
Tanzania	38,329	822	0.02	l 3,292	0.37	365	0.01	2002	
Uganda	28,816	2,209	0.08	16,221	0.61	688	0.03	2004	
Brazil	186,405	198,153	1.15	659,111	3.84	51,317	0.30	2000	
Mozambique	19,792	514	0.03	3,954	0.21	618	0.03	2004	
Thailand	64,233	22,435	0.37	171,605	2.82	15,480	0.25	2000	
Burma	50,519	17,791	0.36	19,254	0.38	127	0.00	2004	
Zimbabwe	13,010	2,086	0.16	9,357	0.72	883	0.07	2004	
Cambodia	4,07	2,047	0.16	8,085	0.61	564	0.04	2000	
Afghanistan	29,863	4,104	0.19	4,752	0.22	525	0.02	2001	
United States	295,410	730,801	2.56	2,669,603	9.37	249,642	0.88	2000	

Table A-8. Health Workers in High-Burden Countries and the United States

Source: WHO, 2006 World Health Report.

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