

**Global MDR-TB and XDR-TB
Response Plan 2007 - 2008**

DRAFT
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Executive summary

An estimated 424,000 multidrug resistant TB (MDR-TB) cases emerge every year as a result of misuse of anti-TB drugs and transmission of drug resistant strains. From 2000 to 2005, national TB control programmes, in close collaboration with WHO, partners and the Green Light Committee, established that treatment of MDR-TB is efficacious, feasible and cost-effective in low-income settings. At the beginning of 2006, the new Stop TB Strategy¹ was launched, which includes MDR-TB management as a basic component of TB control. The Global Plan to Stop TB, 2006–2015,² was also launched in 2006 and provides a consensus view of what the Stop TB Partnership can achieve by 2015, provided the resources are mobilized to implement the Stop TB Strategy.

Following the launch of these two documents, extensively drug resistant TB (XDR-TB) was reported from all regions of the world and was heightened as a serious, emerging threat to public health. XDR-TB raises concerns of TB epidemics with severely restricted treatment options that can jeopardize the gains made not only in global TB control but also in the progress towards universal access to HIV treatment and prevention.

As a result of the XDR-TB threat, the international community decided to take more urgent measures to scale-up sound TB control to prevent the onset of new MDR-TB and XDR-TB cases while at the same time accelerating treatment of resistant cases. The MDR-TB component of the Global Plan has been provisionally revised to reach universal access to sound MDR-TB and XDR-TB management globally by 2015, and entails the treatment of 1.5 million MDR-TB and XDR-TB cases by 2015 instead of 800,000 MDR-TB cases in the original Global Plan.

This document draws on the global framework for WHO and partners' response to MDR-TB and XDR-TB, presented in the accelerated Global Plan, and on the recommendations of the Global XDR-TB Task Force which met at WHO in Geneva in October 2006. The purpose is not to discuss the rationale or technical aspects of the global response to drug resistant TB, but rather to set out the main activities to be conducted at global, regional and country level in 2007 and 2008 to operationalize the accelerated drug resistance component of the Global Plan, and to mark an end to the XDR-TB emergency phase by starting to mainstream MDR-TB and XDR-TB response activities into day-to-day TB control activities. There is still an urgent need to gather additional information on the XDR-TB magnitude, distribution, trends, treatment practices and outcomes; WHO will publish in 2007 guidelines on XDR-TB diagnosis and treatment practices; and international consensus will be sought on the revised MDR-TB component of the Global Plan, which includes additional investment needs to prevent and control XDR-TB. Nonetheless, response activities, including budgeting and planning, must now be mainstreamed into a comprehensive and sustainable TB control package as outlined in the Stop TB Strategy.

¹ *The Stop TB Strategy*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.368).

² *The Global Plan to Stop TB, 2006–2015*. Geneva, World Health Organization, 2006 (WHO/HTM/STB/2006.35).

Budget needs globally for the accelerated response in 2007 - 2008 are estimated at US\$ 1.3 billion. It should be noted that although these budgets include the costs of diagnosing MDR-TB and XDR-TB patients, these requirements do not account for establishing and sustaining laboratories, nor do they include budget requirements for basic TB and TB/HIV control, overall health system strengthening and human resources requirements as these elements are outlined elsewhere.

I Background on MDR-TB and XDR-TB

While the MDR-TB definition has been established and widely accepted for a long time, the debate around XDR-TB is more recent. In 2005, the United States Centres for Disease Control and Prevention (CDC), WHO and 14 Supranational TB Reference Laboratories (SRLs) initiated a study to determine the extent to which resistance to second-line anti-TB drugs had emerged among MDR-TB isolates. The data were published by WHO and CDC in March 2006 in an article in which XDR-TB was first defined.^{3,4} The study analysed 17,690 isolates from 49 countries showing 20% of all isolates collected were MDR-TB and 2% were XDR-TB. XDR-TB was identified in all regions. Latvia and the United States were able to provide drug susceptibility data on their entire TB populations showing that 4% and 19% of their MDR-TB cases had XDR-TB, respectively. South Korea reported on the majority of their TB cases showing that 15% of their MDR-TB cases had XDR-TB. The total number and proportion of XDR-TB isolates observed in this study increased from 5% of MDR-TB isolates in 2000 to 7% of MDR-TB isolates in 2004.⁵

XDR-TB was reported as a serious, emerging threat to public health and TB control, raising concerns of TB epidemics with severely restricted treatment options that could jeopardize the gains made in global TB control. Furthermore, XDR-TB poses specific challenges to global control of HIV/AIDS and could compromise the progress already made in many countries towards universal access to HIV treatment and prevention.

In May 2006, the results of an outbreak of HIV-associated XDR-TB in Tugela Ferry, KwaZulu-Natal Province, South Africa, were presented at the PARTNERS⁶ meeting in Atlanta, Georgia, USA. From January 2005 to March 2006, 221 MDR-TB cases were identified in Tugela Ferry, of which 53 were also resistant to kanamycin and ciprofloxacin. Half of the patients had never previously received anti-TB treatment. Out of the 53 patients, 44 were tested for HIV and found to be HIV-positive. Mortality was high: 52 of the patients died within a median range of 16 days of initial sputum collection. Fifteen of the patients who died were receiving antiretroviral drugs (ARV) treatment.

³ Emergence of *Mycobacterium tuberculosis* with extensive resistance to second-line drugs – worldwide, 2000–2004. *Morbidity and Mortality Weekly Report*, 2006, 55(11):301–305.

⁴ XDR-TB was initially defined as MDR-TB with further resistance to three or more of the six main classes of second-line anti-TB drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine and para-aminosalicylic acid).

⁵ Using the initial XDR-TB definition.

⁶ The PARTNERS project was funded by the Bill & Melinda Gates Foundation in 2000 to develop a replicable model for controlling MDR-TB in resource-limited settings. The grant supported a five-year collaborative effort between the Harvard Medical School, CDC, Partners In Health, the Task Force for Child Survival and Development, and WHO.

In June 2006, WHO's strategic and technical advisory group for tuberculosis (STAG) urged WHO to take immediate and effective action to address MDR-TB and XDR-TB in the African Region. Subsequently, in August 2006, the outbreak in Tugela Ferry was discussed at the XVI International AIDS Conference in Toronto, Canada.

From 9 to 10 October 2006, the WHO Stop TB and HIV departments organized a meeting of the Global Task Force on XDR-TB at WHO headquarters in Geneva, Switzerland, in response to the XDR-TB emergency. During this meeting nine recommendations were put forward to the international TB community outlining key areas of response activities, beginning with strengthening of basic TB and HIV/AIDS control and proper management of MDR-TB following WHO guidelines. In addition, the XDR-TB definition was revised.⁷ By the end of January 2007, WHO issued the first update on achievements by the Global Task Force on XDR-TB, outlining more than 80 activities carried out by WHO and partners following the recommendations issued by the task force.⁸

II Goal

The Global MDR-TB and XDR-TB Response Plan has a goal of facilitating immediate strengthening of basic TB control in countries in accordance with the new Stop TB Strategy and the Global Plan to Stop TB, 2006-2015 and in concerted action to accelerate progress towards universal access to diagnosis and treatment of MDR-TB in the high MDR-TB burden countries by 2010.

III Objectives for the response to MDR-TB and XDR-TB in 2007

1. Strengthen basic TB and HIV/AIDS control as detailed in the new Stop TB Strategy and the Global Plan to Stop TB, 2006–2015, to avoid additional emergence of MDR-TB and XDR-TB
2. Scale-up the programmatic management of MDR-TB and XDR-TB to reach the targets set forth in the Global Plan to Stop TB, 2006–2015
3. Strengthen laboratory services for adequate and timely diagnosis of MDR-TB and XDR-TB
4. Expand MDR-TB and XDR-TB surveillance to better understand the magnitude and trends of drug resistance and links with HIV

⁷ XDR-TB is defined as resistance to at least rifampicin and isoniazid (which is the definition of MDR-TB), in addition to any fluoroquinolone, and to at least one of the three following injectable drugs used in anti-TB treatment: capreomycin, kanamycin and amikacin.

⁸ Control of XDR-TB - Update on progress since the Global XDR-TB Task Force Meeting, 9-10 October 2006 (http://www.who.int/tb/xdr/globaltaskforce_update_feb07.pdf).

5. Foster sound infection control measures to avoid MDR-TB and XDR-TB transmission to protect patients, health workers, others working in congregate settings, and the broader community, especially in high HIV prevalence settings
6. Strengthen advocacy, communication and social mobilization
7. Pursue resource mobilization at global, regional and country levels
8. Promote research and development into new diagnostics, drugs and vaccines

IV Partnerships

Prevention and control of MDR-TB and XDR-TB requires a coordinated input from technical and financial agencies. The Stop TB Partnership secretariat, which coordinates over 400 international organizations, countries, donors from the public and private sector, governmental and nongovernmental organizations and people representing the affected TB community and its working groups; the GLC; the SRL network; and TB and HIV/AIDS civil societies are crucial to fighting this emergency.

All seven Working Groups of the Stop TB Partnership: MDR-TB, DOTS Expansion, TB/HIV, ACSM and New TB Diagnostics, Drugs and Vaccines are already incorporating activities related to the MDR-TB and XDR-TB threat. The MDR-TB Working Group is highly involved in policy recommendations and the implementation and scale-up of sound MDR-TB and XDR-TB control practices. The DOTS Expansion Working Group is facilitating work especially in the 22 high TB burden countries and in the areas of health systems and laboratory strengthening, involvement of all health care providers, and Global Fund collaboration and support. The TB/HIV Working Group has established a subgroup on infection control as a result of XDR-TB. The ACSM Working Group has set-up a task force on XDR-TB advocacy and communications. The new tools Working Groups will all be involved in coordinated approaches to enhance research and development.

The main technical partners are all working with WHO, such as the Union, KNCV Tuberculosis Foundation and CDC, and are of vital importance for the delivery of technical assistance and capacity strengthening. Other consultants for different elements of TB control and mainly MDR-TB control have been trained at different consultant courses. An important and underused source for strengthening of MDR-TB and XDR-TB control is also staff working in ongoing GLC approved MDR-TB control programmes. The Eli Lilly MDR-TB partnership is also playing an important role by involving health care professional organizations in the fight against MDR-TB and XDR-TB, and is also since a number of years providing two important second-line anti-TB drugs at concessional price as well as technology transfer of these drugs to high MDR-TB prevalence countries.

WHO will, through its headquarters, region and country offices, provide leadership and coordinate the global response to MDR-TB and XDR-TB. The lead will be taken by the

Stop TB Department in close collaboration with the HIV Department. Moreover, several departments within WHO will contribute to the work including:

- Medicines Policy and Standards of the Health Technology and Pharmaceuticals cluster for rational use and quality-assurance of anti-TB drugs.
- Epidemic and Pandemic Alert and Response of the Communicable Diseases cluster in view of the implications of XDR-TB on the new International Health Regulations.
- Ethics, Trade, Human Rights and Law of the Sustainable Development and Health Environments cluster on policy recommendations on involuntary treatment, use of drugs under development, and human rights of TB patients, including those with MDR-TB and XDR-TB.
- Equity, Poverty and Social Determinants of Health of the Evidence and Information for Policy cluster on poverty and social determinants of TB, including XDR-TB.