Stop TB Working Group on DOTS-Plus for MDR-TB
Strategic Plan 2006-2015

Background

Current threat and status of the global epidemic of multidrug resistant tuberculosis (MDR-TB)

Along with HIV/AIDS, MDR-TB is the most important threat to TB control. Countries with a high MDR-TB prevalence generally have a history of poor TB control. There are both preventative and restorative strategies to combat resistance - DOTS and DOTS-Plus. The major barrier to MDR-TB treatment is the high cost of second-line drugs which are at least 300 times more expensive than first-line drugs based on Green Light Committee (GLC) prices and between 1000-3000 times more expensive when market prices are used. Additional barriers include extensive laboratory requirements to conduct culture and drug susceptibility testing (DST), severe adverse events associated with second-line drugs and fear of development of resistance to second-line drugs. Consequently, most National TB Programmes (NTPs), excluding those in established market economies and the former Soviet Union, choose to focus on prevention of drug resistance to the exclusion of diagnosis and treatment of MDR-TB. This means that MDR-TB sufferers are left with little or no hope of recovery and that MDR-TB continues to spread. At the same time, private practitioners and public providers not linked to the NTP, diagnose and treat MDR-TB patients in many countries including China and India which account for 35% of the global TB case-load, and treatment practices often fail to meet acceptable standards. The misuse of second-line drugs could lead to the creation of TB strains resistant to all known anti-TB drugs. The control of MDR-TB requires sound implementation of DOTS to prevent the development of new cases, and a careful introduction of second-line drugs with adequate laboratory support to stop the amplification and circulation of resistant strains.

An estimated 273,000 new cases of MDR-TB occurred worldwide in 2000 or 3.2% of all new TB cases. Among previously treated cases, the prevalence of MDR-TB was seven times higher than in new cases. The high proportion of re-treatment cases reported by countries, particularly in high MDR-TB prevalence countries, is a sign that drug-resistant forms of TB are more common than currently estimated. New estimates suggest that there are about half a million MDR-TB cases per year including new and previously treated cases, half of them in China and India.

Though the global median of resistance remains low, several regions of the world are experiencing severe epidemics that threaten the control of TB and that translate into low cure rates. The low cure rates mean that high MDR-TB prevalence countries will not reach the target of curing 85% of infectious TB cases by 2005 set by the World Health Assembly. DOTS alone is not sufficient to curb the TB epidemic in countries with high rates of MDR-TB and large proportions of re-treatment cases. The highest prevalences of MDR-TB have been observed in countries of the former Soviet Union and provinces of China. However most regions have reported one or more countries with an MDR-TB

prevalence of 5-6% among new cases. Drug resistance in countries of the former Soviet Union is more severe than in other regions. For example, 50% of MDR-TB cases detected in these countries are resistant to all four first-line drugs compared to only 12% in the rest of the world. Though surveillance is not yet standardized, many countries of the former Soviet Union report high levels of second-line drug resistance as well.

Overall, a major concern is that the reported drug resistance surveillance (DRS) data represent areas with the minimum infrastructure and political commitment to conduct surveillance. It is expected that many of the areas not yet reporting data and with chequered histories of TB control have even more severe epidemics. Another area of concern is the trend in resistance. The few trends available from high MDR-TB prevalence and high TB burden countries are worrying.

Measures of surveillance and control of MDR-TB

In 1994, the WHO/IUATLD global project on anti-TB DRS began with the objective of standardizing a methodology for surveillance to compare results between and within countries. The project allows a country to estimate the magnitude of drug resistance, particularly MDR-TB, assist in programme planning and policy development and increases the capacity of the laboratory to conduct culture and DST.

In 1999, WHO and partners launched "DOTS-Plus for MDR-TB" to manage MDR-TB with second-line drugs in resource-limited settings. In the absence of data, this new approach needed rapid assessment of its feasibility and effectiveness under programme conditions. As part of this strategy, a novel partnership known as the Green Light Committee (GLC) was created to foster access to, and rational use of, second-line drugs. By July 2005, 36 DOTS-Plus pilot projects[1] have been established in 27 countries for the treatment of more than 10,000 MDR-TB patients to evaluate the feasibility and cost-effectiveness of diagnosis and treating MDR-TB patients in resource-limited settings. Projects approved by the GLC have access to quality-assured and reduced-priced second-line drugs and benefit from technical assistance.

Achievements against the first Global Plan to Stop TB (2000-2005)

Challenges identified for MDR-TB control 2000-2005

In the first Global Plan to Stop TB, four reasons were mentioned for why MDR-TB presents a threat to TB control:

1. Standardized short-course chemotherapy does not yield acceptable cure rates for MDR-TB

[1] Azerbaijan, Bolivia, Costa Rica, El Salvador, Egypt, Estonia, Georgia, Haiti, Honduras, India, Jordan, Kenya, Kyrgyzstan, Latvia, Lebanon, Malawi, Mexico, Moldova, Nepal, Nicaragua, Peru, Philippines, Romania, the Russian Federation, Syria, Tunisia and Uzbekistan.

2. Effective therapy for MDR-TB is currently more expensive than short-course chemotherapy for pan-susceptible TB
3. Without effective treatment, transmission of MDR-TB and drug-resistant TB will continue - indeed, the rates of spreading may increase
4. Most ominously, MDR-TB threatens the potential salutary impact of DOTS programmes.

Three areas needing more investment were identified: 1) strengthening laboratory capacity, 2) defining and operationalizing programmes that can effectively deliver MDR-TB therapy and 3) providing treatment for MDR-TB patients.

Achievements in surveillance and control of MDR-TB 2000-2005

Five years after the compilation of the first Global Plan, the threat of MDR-TB persists. Although MDR-TB prevalence data from more geographical settings are available, it is still not known whether MDR-TB rates are increasing or decreasing at global and national levels. Of the three areas identified for investment, the second - defining and operationalising programmes for MDR-TB therapy - has been accomplished while the two other remain priorities.

A significant number of activities has been carried out to improve MDR-TB control from 2000 to 2005. Drug resistance surveillance data are now available from 90 countries and trends are available from 26 countries. Quality-assurance of National Reference Laboratories (NRLs) has expanded along with surveillance. Since 1994, more than 100 NRLs have participated in the international quality assurance scheme undertaken by the Supranational Reference Laboratory Network (SRLN), and 60% of these laboratories participate annually.

In 2000, the Stop TB Working Group on DOTS-Plus for MDR-TB was created. In addition, the GLC for access to quality-assured and reduced-priced second-line drugs was set-up. Through negotiations with pharmaceutical manufacturers, the prices of some second-line drugs were reduced by 95%. In 2000, the first DOTS-Plus pilot projects were launched. In 2002, the board of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) decided that requests for second-line drugs for the management of MDR-TB should go through the GLC in order to prevent the misuse of second-line drugs. As a result of additional financial resources for MDR-TB control, there has been a rapid increase in the number of countries implementing DOTS-Plus. Today the piloting phase of DOTS-Plus has been successfully accomplished and there is evidence that MDR-TB management is feasible and effective in resource-limited settings. Among 1047 MDR-TB patients evaluated from the first five GLC-approved DOTS-Plus projects, 70% were successfully treated. Out of these patients, more than 50% were previously treated with first and second-line drugs and 65% were resistant to both first and second-line drugs. On average 3.2% of patients stopped treatment due to adverse reactions.

In May 2005, a resolution by the World Health Assembly encouraged all Member States "to ensure that all tuberculosis patients have access to the universal standard of care" and

requested the Director-General "to implement and strengthen strategies for the effective control of, and management of persons with, drug-resistant tuberculosis". This resolution is in line with the new vision of TB control and the new "International standards of TB care", encompassing all TB patients including those with MDR-TB and TB/HIV. To complement these developments, the WHO "Treatment of tuberculosis: guidelines for national programmes" were revised in 2004 to include standard care for MDR-TB patients. In addition, and based on evidence from the first DOTS-Plus pilot projects and consensus within the GLC, DOTS-Plus guidelines for resource-limited settings were developed in 2004 and are currently being finalized.

Studies of the cost and cost-effectiveness of DOTS-Plus have been completed in Estonia, the Russian Federation (Tomsk), the Philippines (Manila) and Peru. The cost per patient treated was about US$ 2,500 to US$ 3,500 in Peru and the Philippines, and about US$ 9,000 to US$ 10,000 in Estonia and the Russian Federation. The cost per DALY (disability adjusted life year) gained was about US$200 in Peru and the Philippines, and higher at about US$ 500-1,000 in Estonia and the Russian Federation. These cost per DALY gained figures compare favorably with benchmarks that are widely used for assessing whether a health intervention is cost-effective (for example, average income per capita), suggesting that DOTS-Plus can be considered a cost-effective strategy. It should be stressed that these costs are derived from the implementation of DOTS-Plus in populations characterized by high proportions of severe chronic cases with difficult drug resistant patterns. In other areas of the world treating MDR-TB may pose fewer challenges and therefore the costs may be lower.

Challenges ahead

With the evidence of DOTS-Plus as an effective, feasible and cost-effective intervention in resource-limited settings, the main challenges today are to expand surveillance and monitor trends of global anti-TB drug resistance, and to scale-up DOTS-Plus implementation beyond the pilot phase as an integrated component of DOTS. The delivery of sound MDR-TB diagnostic and treatment services is, however, severely limited by lack of political will, public health infrastructure (particularity laboratory capacity), organization and management of health care delivery and, perhaps most importantly, lack of qualified human resources.

Strategic vision 2006-2015

The vision of the Stop TB Working Group on DOTS-Plus for MDR-TB is to integrate drug resistance surveillance (DRS) and the management of MDR-TB as routine components of TB control providing access to diagnosis and treatment for all TB patients and by all health care providers. This is in line with the new comprehensive approach to global TB control. As a result, all MDR-TB management measures will be implemented in collaboration with DOTS expansion and strengthening activities and also in line with the activities of the other Stop TB Working Groups.

Objectives, targets and indicators

Currently, less than 2% of the total number of estimated culture-positive MDR-TB patients are treated according to WHO recommendations. With the planned expansion of DOTS-Plus, it is envisaged that by 2015, 56% of culture-positive MDR-TB patients will be detected and treated under DOTS-Plus. During the 10 year period of the Global Plan to Stop TB 2006-2015 a cumulative 23% of all culture-positive MDR-TB patients will be treated under DOTS-Plus.

During the planning period, it is estimated that 778,000 MDR-TB cases will be treated according to WHO guidelines, 53% of them being from the Eastern European Region, 19% from the Southeast Asian Region and 16% from the Western Pacific Region (Figure 1). Of these, an average of 75% or 587,000 will be treated successfully. With the implementation of DOTS and DOTS-Plus, it is expected that the estimated global proportion of re-treatment cases will decrease from 20% in 2005 to 11% in 2015. Most importantly, it is expected that the number of MDR-TB cases will be reduced from an estimated 533,000 in 2005 to 193,000 in 2015, mainly as a result of a reduction in incidence and proportion of re-treatment cases and as a combined effect of all TB control interventions. With the expansion of DOTS-Plus, it is expected that 142,000 deaths from MDR-TB will be averted from 2006-2015 (Tables 1 and 2).

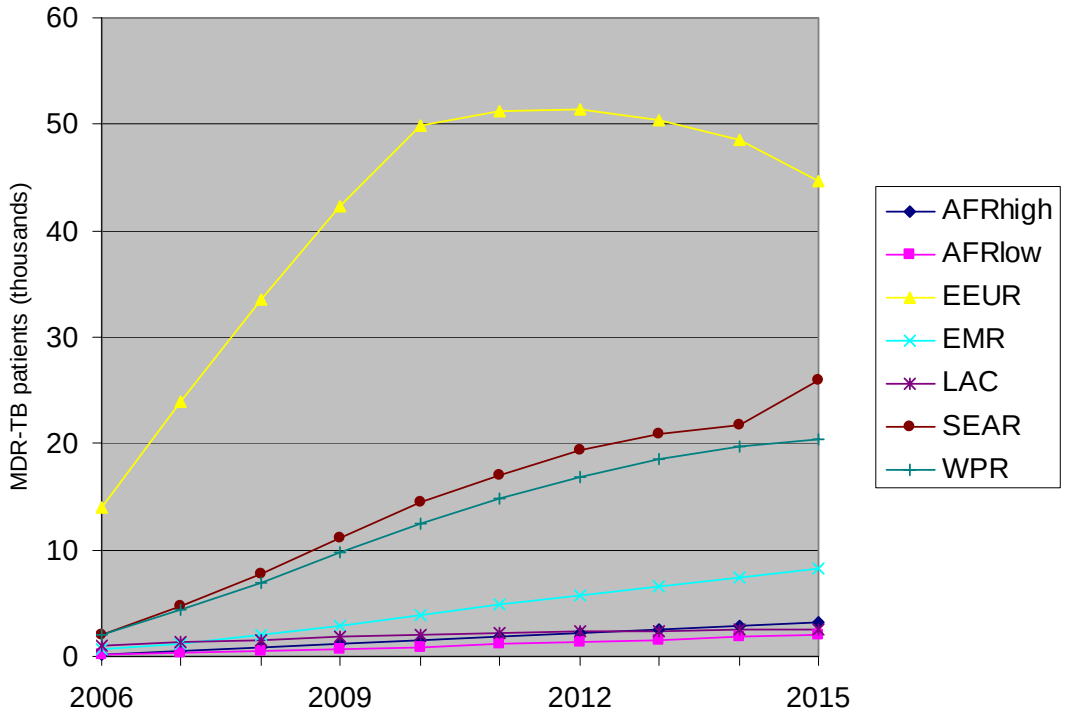

Figure 1. Number of MDR-TB patients to be treated per year under DOTS-Plus by Region, 2006-2015

To obtain these above-mentioned goals, the priorities for the next decade are to expand DRS, monitor trends and regularly update the global MDR-TB estimates, strengthen capacity to perform quality-assured culture and DST, scale up MDR-TB treatment according to WHO guidelines, create a healthy and competitive market of quality-assured second-line drugs and finally provide technical and global coordination to accomplish the goals. For the above, the strengthening of health systems and the workforce to deliver sound diagnostic and treatment practices to all MDR-TB patients are key and crosscut all areas.

The work to be delivered is grouped into the below five objectives:

1. By 2015, representative data on the global magnitude of MDR-TB, reliable trends from high MDR-TB prevalence countries and data on the relationship between MDR-TB and HIV/AIDS should be available.
2. By 2015, all Regions should provide DST for all previously treated TB patients. In the eastern European Region, DST will also be provided for all new cases and in the Latin American, Southeast Asia and Western Pacific Regions, DST should be provided for 20% of new TB patients, targeting those people at increased risk of having MDR-TB.
3. By 2015 all detected MDR-TB patients should be treated with quality-assured second-line drugs in line with WHO guidelines (17% of the estimated culture-positive MDR-TB cases in 2010 and 56% in 2015).
4. By 2015 further reduce the price of second-line drugs and secure additional production of quality-assured second-line drugs by manufacturers based in high-MDR-TB burden countries.
5. Provide technical direction and strategic planning for the management and coordination of global MDR-TB surveillance and control through the Stop TB Working Group on DOTS-Plus for MDR-TB, in close collaboration with the other Stop TB Working Groups including those on new drugs and diagnostics.

Activities, timelines and milestones

The key milestones of the plan are indicated below.

<u>By the end of 2006</u>

Objective 1:

- Drug resistance data available from more than 110 countries for analysis and publication including data from additional areas of China, India and the Russian Federation, new data from high-burden countries including Bangladesh and Indonesia, and from new suspected high-MDR-TB burden countries including Ukraine and Kyrgyzstan.

- Data available from three new priority settings (i.e. high MDR-TB or HIV settings) combining DRS and HIV surveillance among TB patients.

Objective 2:

- Laboratory assessments and proficiency testing of 20 new NRLs.

Objective 3:

- DOTS-Plus expansion in India and the Russian Federation and pilot projects established in six new countries including China and the high MDR-TB burden country Kazakhstan.

Objective 4:

- Meetings conducted with second-line drug manufacturers in China, India and the Russian Federation in order to increase the number of manufacturers on the WHO white-list of prequalified second-line drugs.
- The white-list of prequalified second-line drug manufacturers containing at least two manufacturing sources per drugs published.
- An inventory of global second-line drug use published.
- A buffer stock of second-line drugs created enabling the GLC to deliver drugs in a timely fashion.

Objective 5:

- The structure and functions of the Stop TB Working Group on DOTS-Plus for MDR-TB and its subgroups including the GLC reviewed and adapted to the new challenge of scaling-up the diagnosis and treatment of MDR-TB reaching beyond the initial phase of piloting MDR-TB management. DRS included in the Working Group.
- All WHO Regions to have strategic plans for DRS and DOTS-Plus and two Regions to have developed regional GLCs.
- Capacity building: two DOTS-Plus capacity building centres set-up in the Western Pacific Region, key NTP staff trained in DOTS-Plus from the countries of the former Soviet Union and from the WHO African, American, Southeast Asian and Western Pacific Regions. Training manual on DOTS-Plus developed and additional TB consultants trained in DOTS-Plus.
- The new DOTS-Plus and the DRS guidelines printed and disseminated in Chinese and Russian.
- Development of guidelines for DOTS-Plus management in the private sector and establishment of DOTS-Plus projects in additional private sector TB control programmes.
- Sub-meeting of the Stop TB Working Group on DOTS-Plus for MDR-TB conducted.
- Annual SNRL meeting held.
- Finalization of the standardization of DST to second-line drugs.

By the end of 2007

Objective 1:

- Drug resistance data available from seven new countries with high TB burden, expected high MDR-TB prevalence or high HIV prevalence.
- Data on the relationship between HIV and MDR-TB available from two new settings.
- Data on trends in drug resistance available from three new settings.

Objective 2:

- All countries with high MDR-TB prevalence and high TB burden having NRLs performing quality-assured culture and DST and collaborating with a supranational TB reference laboratory (SRL).

Objective 3:

- DOTS-Plus expansion in India and the Russian Federation and pilot projects established in six new countries including the high-burden countries Bangladesh, Myanmar, Tanzania and Viet Nam.

Objective 5:

- Meeting of the Stop TB Working Group on DOTS-Plus for MDR-TB conducted.
- Annual SNRL meeting held.
- DRS, MDR-TB management and second-line drug management built into general TB management courses.
- Evaluation of feasibility, effectiveness and cost-effectiveness of standardized treatment approaches to MDR-TB control.

By the end of 2008

Objective 1:

- Drug resistance data available from seven new countries with high TB burden, expected high MDR-TB prevalence or high HIV prevalence.
- Data on relationship between HIV and MDR-TB available from two new settings.
- Data on trends in drug resistance available from five new settings.

Objective 3:

- DOTS-Plus expansion in India, China and the Russian Federation and pilot projects established in six new countries including the high-burden countries Indonesia and Pakistan.

Objective 5:

- All WHO Regions having regional GLC mechanisms reviewing applications and ensuring that DOTS-Plus is monitored regularly as part of routine TB control missions.
- Sub-meeting of the Stop TB Working Group on DOTS-Plus for MDR-TB conducted.
- Annual SNRL meeting held.

By the end of 2009

Objective 1:

- Drug resistance data available from ten new countries with high TB burden, expected high MDR-TB prevalence or high HIV prevalence.
- Data on relationship between HIV and MDR-TB available from two new settings.
- Data on trends in drug resistance available from seven new settings.

Objective 5:

- Meeting of the Stop TB Working Group on DOTS-Plus for MDR-TB conducted.
- Annual SNRL meeting held.

By the end of 2010

Objective 1:

- Drug resistance data available from ten new settings with high TB burden, expected high MDR-TB prevalence or high HIV prevalence. Data from 130 countries ready for publication, with half of them reporting trend data with three or more data points.
- Data on relationship between HIV and MDR-TB available from two new settings.
- Revision of estimates on the global MDR-TB burden published.

Objective 2:

- All countries having NRLs performing quality-assured culture and DST and collaborating with an SRL.
- DST expanded to cover 92% of all new and previously treated cases in eastern Europe. All other Regions performing DST to approximately 60% of targeted previously treated patients and the Latin American, Southeast Asia and Western Pacific Regions, also performing DST to at least 10% of targeted new cases.

Objective 3:

- Between 40-70% of detected MDR-TB patients in all Regions should have access to adequate MDR-TB treatment according to WHO guidelines.

Objective 4:

- Quality-assured production of second-line drugs in high-MDR-TB burden countries including China, India, the Russian Federation and South Africa.

Objective 5:

- Meeting of the Stop TB Working Group on DOTS-Plus for MDR-TB conducted.
- Annual SNRL meeting held.

By the end of 2015

Objective 1:

- Drug resistance data available representing 90% of settings with expected high MDR-TB prevalence or high HIV prevalence settings. 70% of settings reporting trend data with three or more data points. Reliable trends available from key high MDR-TB and HIV prevalence settings.
- Data on relationship between HIV and MDR-TB established.
- Revision of estimates on the global MDR-TB burden published.

Objective 2:

- All countries having NRLs performing quality-assured culture and DST and collaborating with an SRL.
- All Regions should provide DST for all previously treated TB patients. In the eastern European Region, DST will also be provided for all new cases and in the Latin American, Southeast Asia and Western Pacific Regions, DST should be provided for 20% of targeted new cases.

Objective 3:

- All detected MDR-TB patients to have access to adequate MDR-TB treatment according to WHO guidelines.

Objective 5:

- Capacity building: all Regions and countries including DRS and MDR-TB management in regular TB courses and workshops.

Resource needs

The funding needed for DOTS-Plus implementation at country level during the period 2006-2015 is US$ 5.8 billion (table 3). More than two-thirds of the funds - US$ 3.9 billion - are needed for the eastern European Region.

Costs for each region are based on multiplying the estimated cost per MDR-TB patient treated in a DOTS-Plus programme by the estimated number of patients to be treated. The cost per patient treated is considered from a provider perspective and based on costing studies undertaken in Estonia, the Russian Federation, the Philippines and Peru (described above), with appropriate adjustments for income level and, sometimes, to the drug regimen to reflect the regional drug resistance pattern. All relevant costs are incorporated, including second-line drugs, hospitalization (for some Regions), DOT visits, laboratory tests, training, infection control, programme and data management, food parcels and management of adverse events (Table 1).

For coordination of the Working Group and its subgroups, US$ 11 million are needed for the 10-year period of the Strategic Plan.

Technical support and capacity building will be undertaken jointly for DOTS Expansion, TB/HIV and DOTS-Plus. The reason is that technical staff, especially in regions and countries, will share their time for various activities under the different Working Groups. Furthermore, cross-cutting technical assistance for activities under the different Working Groups will be coordinated within and between partner organizations in order to improve efficiency and reduce duplication of work. The annual total cost for technical cooperation ranges from US$ 220 millions to US$ 280 millions and is reflected in the budget of the DOTS Expansion Working Group Strategic Plan.

Monitoring and evaluation

The global MDR-TB situation is monitored by the WHO/IUATLD global DRS project and data are published every three years. In addition, MDR-TB estimates have been published and are being updated regularly. DOTS-Plus programme performance is currently monitored by WHO and the GLC. An inventory of second-line drug use in public and private sectors will be conducted in 2005.

The SNRL started in conjunction with the WHO/IUATLD global DRS project and is composed of twenty-three TB laboratories conducting annual proficiency testing on itself. This network is also responsible for the quality-assurance of DST in NRLs worldwide.

A DOTS-Plus recording and reporting system has recently been developed which allows managers at different levels of NTPs to monitor overall DOTS-Plus programme performance. In the future, elements of this system will also be included in the DOTS recording and reporting system at district level.

As the DOTS strategy is evolving to include all TB patients, MDR-TB notifications and treatment outcomes should become part of the annual WHO report: Global Tuberculosis Control: surveillance, planning and financing.

Monitoring to evaluate progress in MDR-TB control will also be performed in collaboration with partners and WHO Region and Country staff during routine technical missions.

Finally, annual or semi-annual meetings of the Stop TB Working Group on DOTS-Plus for MDR-TB will take place to review the progress made in global DRS and MDR-TB control and give strategic direction on future activities. The Working Group will also monitor funding and expenditure on the global coordination costs for DOTS-Plus scale-up during the planning period.

Key risk factors

Deterioration in the global MDR-TB situation and continued misuse of second-line drugs

Should DOTS-Plus not be promoted and scaled-up by all health care providers diagnosing and treating MDR-TB (including private practitioners), there is a risk of the creation and circulation of TB strains resistant to all known anti-TB drugs. In addition, the potential for the joint impact of HIV and MDR-TB in resource-limited settings cannot be overstated and requires urgent attention. The combination of a rapidly increasing HIV epidemic in the countries of the former Soviet Union, the extended hospitalization of MDR-TB patients in these settings and high levels of TB, MDR-TB and HIV in prisons combined with poor infection control measures, could have a significant impact on the incidence of MDR-TB.

Poor quality drugs may favor the emergence of additional drug-resistance. Second-line drug manufacturers must be mobilized to apply to the WHO prequalification system for second-line drugs, especially as some countries may not be interested in purchasing drugs from the GLC (mainly countries producing second-line drugs). In order to ensure the use of quality-assured drugs, WHO and partners should advocate for NTPs and funding agencies to purchase drugs from the WHO white-list of prequalified manufacturers.

Lack of well-functioning laboratory networks providing culture and drug susceptibility testing (DST).

Currently one of the biggest obstacles to monitoring drug resistance and implementing DOTS-Plus programmes is the lack of well functioning culture and DST laboratories. A massive influx of both technical and financial resources is required to scale up laboratory services in order to expand DRS and DOTS-Plus globally. Services should start with a well equipped, safe, and highly performing central laboratory and expanded as needed while maintaining quality. Improvement in laboratory networks would include both the optimal utilization of existing tool and development and implementation of new technology. Both the working group on new diagnostics and the DEWG laboratory strengthening subgroup have accounted for scale up within the global plan.

Lack of political will

Lack of national policies on MDR-TB control and of leadership to engage all health care providers present threats to the global MDR-TB situation. Future success will depend on the political commitment and stability of countries, the donor community and technical agencies to scale-up and strengthen DOTS-Plus programmes. Political commitment is key for any DOTS-Plus programme and must translate into financial and human resources.

At country level, financial resources are needed for all aspects of DOTS-Plus implementation. The GFATM now plays a major role in the financing for MDR-TB control, contributing to funding for almost half the current GLC-approved projects. In addition, it is envisaged that a significant number of high TB and MDR-TB burden countries will include MDR-TB control in their 5th round of GFATM proposals. For countries that have secured funds for MDR-TB control, the key question is whether the NTP can spend the money effectively. Guidance is needed to guarantee a rational use of funds.

Strengthening the workforce to deliver sound MDR-TB control is a priority for the next decade and countries must have clear plans for human resource development and financial resources to realize the plans.

Lack of global coordination efforts

At global level, a number of activities are needed in order to ensure a smooth scale-up of DRS and DOTS-Plus. Resources are needed for the monitoring of the global MDR-TB epidemic and for DOTS-Plus programme performance. Continued policy development and dissemination of guidelines are key for success. As at country-level, human resource are needed to provide technical assistance for countries to plan, monitor, expand and evaluate DOTS-Plus.

The GLC mechanism needs to be reformed to allow for the increasing demand of quality-assured second-line drugs and technical assistance. This could be done by decentralizing the functions of reviewing and monitoring DOTS-Plus implementation to WHO Regional level. In addition, the GLC should converge with the Global TB Drug Facility (GDF) to ensure a reliable and experienced bundling mechanism for anti-TB drugs.

Table 1. Estimated number of MDR-TB patients, number of patients treated under DOTS-Plus, deaths averted, cost per treated MDR-TB patient and total costs, 2006-2015, by Region.

	Estimated number of culture-positive MDR-TB cases (thousands)	Number of patients treated under DOTS-Plus (thousands)	Number of patients successfully treated (thousands)	Deaths averted (thousands)	Cost per patient treated under DOTS-Plus (US$)	Total costs (million US$)
African - high HIV/AIDS	147	18	13	3	2273	46
African - low HIV/AIDS	58	11	8	2	1979	26
Eastern Europe	858	410	315	72	8196	3928
Eastern Mediterranean	407	48	36	6	3897	226
Latin America	72	20	15	3	5189	121
Southeast Asia	1021	145	107	31	3908	678
Western Pacific	809	126	93	25	5197	782
TOTAL	**3372**	**778**	**587**	**142**	**-**	**5806**

Table 2. Regional scale-up of DST and DOTS-Plus by Region

	DST coverage in new cases (%)			**DST coverage in previously treated cases (%)**			**DOTS-Plus coverage among detected MDR-TB patients (%)**		
	2005	*2010*	*2015*	*2005*	*2010*	*2015*	*2005*	*2010*	*2015*
African - high HIV/AIDS	0	0	0	0	60	100	0	50	100
African - low HIV/AIDS	0	0	0	21	60	100	8	54	100
Eastern Europe	83	92	100	83	92	100	5	70	100
Eastern Mediterranean	0	0	0	21	60	100	17	58	100
Latin America	12	16	20	42	71	100	29	65	100
Southeast Asia	3	12	20	18	59	100	1	43	100
Western Pacific	0	10	20	10	55	100	8	54	100

Table 3. DOTS-Plus for MDR-TB Working Group costs, 2006-2015

WG cost 2006-2015 (US$ millions)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years
COUNTRY NEEDS											
All regions	**142**	**258**	**383**	**510**	**634**	**700**	**752**	**788**	**811**	**828**	**5806**
AFR- high	0.5	1.1	1.9	2.8	3.8	4.8	5.9	7.1	8.3	9.5	46
AFR low	0.3	0.6	1.0	1.5	2.1	2.7	3.3	4.0	4.7	5.4	26
EEUR	114	202	291	379	461	487	504	508	504	478	3928
EMR	2.9	5.5	9.0	14	19	24	30	35	41	47	226
LAC	5.7	7.2	8.7	10	12	13	14	16	16	17	121
SEAR	7.9	19	32	47	64	77	90	100	107	133	678
WPR	11	23	38	55	73	90	105	118	130	138	782
EXTERNAL AGENCY NEEDS											
Technical Cooperation*	*	*	*	*	*	*	*	*	*	*	*
WG Operational Needs	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**11**
TOTAL	**143**	**259**	**384**	**511**	**635**	**701**	**753**	**789**	**812**	**829**	**5,818**

*: Some aspects of technical cooperation will be undertaken jointly for DOTS Expansion, TB/HIV and DOTS-Plus.
Since it is difficult to identify what share of these costs applies to each WG, the total is shown in the budget for DOTS Expansion.
Annual total cost ranges from US$ 220 millions to US$ 280 millions.