Regional Response Plan for Programmatic Management of Drug-resistant Tuberculosis

Report of meeting of WHO country offices' focal points
SEARO, New Delhi, 4–6 April 2011

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Abbreviations

ACSM	advocacy, communication and social mobilization
AFB	acid-fast bacilli
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
CPT	co-trimoxazole preventive therapy
CXR	chest X-ray
DOT	directly observed therapy
DOTS	The internationally recommended strategy for TB control and the foundation of the new Stop TB Strategy introduced in 2006
DRS	drug resistance surveillance
DR-TB	drug-resistant tuberculosis
DST	drug susceptibility testing
FDC	fixed-dose combination
GDF	Global (TB) Drug Facility
GLC	Green Light Committee
GLI	Global Laboratory Initiative
Global Fund (GFATM)	Global Fund to Fight AIDS, Tuberculosis and Malaria
HRD	human resource development
IC	infection control
ISTC	International Standards of TB Care
LFT	liver function test
LPA	line probe assay
MDR-TB	multidrug-resistant tuberculosis
MIC	minimum inhibitory concentration

NTP	national TB control programme
NRL	national reference laboratory
PMDT	programmatic management of drug-resistant tuberculosis
QA	quality assurance
R&R	recording and reporting
SCC	short-course chemotherapy
SNRL	supranational reference laboratories
STB	WHO Stop TB Department
TB	tuberculosis
TB/HIV	HIV-related TB
TSH	thyroid-stimulating hormone
USP	United States pharmacoepia
UVGI	ultraviolet germicidal irradiation
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis

1. Background

The 60th World Health Assembly passed a resolution in 2007 requesting WHO to strengthen its support to countries affected by tuberculosis (TB), in particular, those heavily affected by multidrug-resistant and extensively drug-resistant TB (MD/XDR-TB) as well as HIV-related TB (TB/HIV). The 60th SEA Regional Committee, following the ministerial meeting of countries with a high MDR-TB burden in Beijing, China in April 2009, and the 62nd World Health Assembly, endorsed resolutions urging all Member States to achieve universal access to diagnosis and treatment of DR-TB, and monitor achievement in the sphere of prevention and control of DR-TB.

2. Objective of the meeting

The overall objective of the meeting was to strengthen the regional response plan for MDR-TB and draw a road map for country-specific plans.

2.1 Specific objectives of the consultation meeting

(1) Discuss plans for strengthening priority areas in the Region as per the areas identified in the response plan

(2) Discuss country-specific issues and plans and get contextual comments

(3) Share experiences to reach the common goals

(4) Strengthen and streamline data reporting on MDR-TB from the country offices to the Regional Office and headquarters

(5) Discuss technical assistance needs for programmatic management of drug-resistant tuberculosis (PMDT)

3. Regional situation and progress

Well-functioning national TB control programmes in the Region have led to low levels (range: 1.7%–4.2%) of multidrug-resistance (MDR) among newly detected cases. Among previously treated cases in the Region, MDR-TB

rates range from 10.0% to 34.7%. However, given the large numbers of TB cases in the SEA Region, this translates to 130 000 MDR-TB cases (110 000–170 000), which account for nearly one third of the world's MDR-TB cases.

During the past few years, steady progress has been made in the Region in initiating treatment in MDR-TB cases. The Green Light Committee (GLC) had approved the case management of patients with MDR-TB under national programmes in 10 countries. Bangladesh, India, Indonesia and Myanmar are in the process of expanding these services, while Nepal has already established ambulatory case management services for MDR-TB throughout the country. Maldives continues to treat the few cases that occur on a case-by-case basis. Bhutan and Sri Lanka began enrolling cases later, in 2010, while DPR Korea will apply to the GLC to establish MDR-TB case management under its national programmes in early 2012. Until the end of 2010, more than 5000 patients with MDR-TB had been registered for treatment in the Region. XDR-TB has also been reported from five countries in the Region. MDR-TB could potentially replace drug-susceptible TB and constitutes a threat to global public health security. In areas with a high prevalence of HIV, the potential for increased transmission of MDR-TB is also high.

Considerable efforts are required to expand the capacity of countries, which would have to strengthen their planning to adequately respond to this challenge. Further, all activities need to be in alignment with the latest WHO guidelines. A regional response plan has been developed and there is a need to discuss this with all country focal points to foster a common understanding of the activities to be undertaken and to scale up the MDR-TB response so that the goals of universal access for all MRD-TB patients can be reached.

4. Technical sessions

4.1 Overview of regional status and progress on M/XDR TB

MDR-TB in the SEA Region

Nearly 130 000 cases, equivalent to around one third of the global burden, emerged in the Region in 2010. India is estimated to have the second

highest number globally. XDR-TB has been reported from five countries (Bangladesh, India, Indonesia, Nepal and Thailand) in the Region.

Capacity for diagnosis

Countries with culture and DST facilities: Bangladesh, Bhutan, DPR Korea, India, Indonesia, Myanmar, Nepal, Sri Lanka and Thailand

Countries without culture and DST facilities: Maldives and Timor-Leste

Even countries with DST facilities need to have more quality-assured laboratories to offer the test to all those who need to be tested for drug-resistant forms of TB.

There are only two supra-national reference laboratories (SNRLs) in the Region. These are overstretched and cannot meet all their mandated functions for the entire Region. The SNRLs in the Region and those outside the Region but linked to the SEA Region are:

Within the Region

SNRL Bangkok, Thailand: Bhutan, Myanmar, Thailand
SNRL Chennai, India: India, Maldives, Sri Lanka

Outside the Region

SNRL Adelaide, Australia: Indonesia, Timor-Leste
SNRL Antwerp, Belgium: Bangladesh
SNRL Gauting, Germany: Nepal
SNRL China, Hong Kong Special Administrative Region (Hong Kong SAR)

In general, most countries have developed plans for roll-out, while national laboratory networks remain weak. The countries have, therefore, adopted different approaches to detecting MDR-TB cases. For example, Bangladesh and Myanmar are targeting all patients who fail Category 2 regimens; and India and Nepal are looking to identify cases among Category 1 and 2 failures, close contacts of MDR-TB cases, and other re-treatment and chronic cases.

Managing MDR-TB: Recommendations of Regional Working Group on MDR and XDR-TB to stop development of drug resistance and manage existing cases

It is of foremost importance for the countries to determine how/where MDR-TB is being generated. For ongoing TB services, while achieving good cure rates under DOTS, the countries should also focus on reasons for default in treatment and other unfavourable outcomes. For many countries, the question arises whether, given good cure rates under DOTS, most MDR-TB cases are arising from unsupervised treatment, through unsustainable out-of-pocket expenditure, outside of DOTS programmes?

All causes of adverse treatment outcomes would need to be addressed. There is a definite need to enhance the involvement of the private sector and unlinked public health facilities, and promote wider acceptance and application of the International Standards of TB Care (ISTC).

For scaling up PMDT, the countries would need to set feasible targets based on national capacity and more ambitious plans for expansion. They would need to follow principles of DOTS expansion: ensure diagnostics, secure supply lines for drugs, properly equipped facilities and trained staff, and provide DOT and psychosocial support. Member States would need to exercise caution against rapid and improperly executed expansion; expansion should be undertaken following successful cross-over of at least two cohorts of patients from the intensive to the continuation phase. They would need to be careful about decentralizing below the district level as such level of decentralization may not be advisable in most countries of the Region.

For proper implementation of PMDT services, the countries would need to monitor progress internally every six months; external monitoring could be done once a year initially and once in two years, as part of the reviews of the national TB control programmes (NTPs), thereafter. The countries should aim for a national consensus statement endorsed by nationally recognized experts and professional societies.

SEA Region: Priorities for M/XDR-TB

The priorities for M/XDR TB in the SEA Region include to:

- Strengthen basic DOTS
- Scale up programmatic management of MDR-TB and XDR-TB
- Build laboratory services for timely diagnosis of MDR-TB and XDR-TB
- Expand drug resistance surveillance to better understand the magnitude and trends of drug resistance to first- and second-line anti-TB drugs
- Foster sound infection control (IC) measures to avoid MDR-TB and XDR-TB transmission, especially in settings with a high prevalence of HIV
- Pursue resource mobilization at global, regional and country levels
- Promote research on new diagnostics and drugs, and field-testing under programmatic conditions.

4.2 Regional laboratory status, plans and recommendations on newer diagnostics

A rapid scale-up of laboratory capacity is crucial, both to diagnose MDR-TB cases and conduct surveillance. National reference laboratories (NRLs) in all Member States (with the exception of Maldives and Timor-Leste) have capacity for mycobacterial culture. However, this capacity is limited. In Nepal, culture and DST facilities are being provided through an NGO-run laboratory, quality-assured by the SNRL at Gauting, Germany. An NRL is in the process of being established. The NRLs in Bangladesh, Indonesia and Myanmar have been accredited for quality assurance for culture and drug susceptibility testing, while Sri Lanka is in the process of upgrading the NRL for TB.

Status of laboratory networks in SEA Region

Activity	Status
Smear microscopy network	All countries (QA partial /complete)
National reference laboratory	Functional (except Maldives and Timor-Leste)
Linkage to supranational laboratory network	All countries
Culture and DST facility either in NRL or other sectors	All (except Maldives and Timor-Leste)
Introduction of newer tools	India (2011), Myanmar (2009)
Newer tools to be introduced	Bangladesh, Indonesia, Sri Lanka
Supranational reference laboratories (SNRLs) of SEA Region	TRC Chennai and NTRL Bangkok
Other SNRLs	SNRL Hong Kong (SAR), Adelaide, Gauting and Antwerp

Status of NRLs/RRLs in SEA Region

Country	Status
Bangladesh	1 QAed NRL (FLD) 6 regional reference laboratories (RRLs) (in process) 2 QAed RRLs in NGO sector
Bhutan	1 NRL 2 regional laboratories (QA in process)
DPR Korea	1 NRL (QA in process)
India	4 QAed NRLs (FLD and SLD) 14 state, 7 NGO/private, 2 MC, 3 other government
Indonesia	3 QAed NRLs (FLD, SLD) 5 RRLs (2 QAed, 3 in process)
Myanmar	1 QAed NRL and 1 QAed RRL
Nepal	1 QAed NRL
Sri Lanka	1 NRL (in process on QA)
Thailand	1 QAed NRL (FLD and SLD), RRLs in all regions
Maldives and Timor-Leste	NRLs not established

On the basis of the status assessment, the needs of the Region include to:

- Continue to perform quality-assured microscopy
- Improve TB case finding by use of LED-based systems in appropriate settings based on local needs
- Develop infrastructure and local capacity for C & DST for management of MDR-TB
- Improve capacity for second-line DST in SNRLs
- Improve collaboration and liaising with SNRLs of WPRO assisting SEA Region countries
- Assist countries to develop national strategic plans for increasing laboratory capacity
- Provide information to NTPs on the use of newer tools within the programme
- Evaluate the operational use of liquid culture and molecular line probe assay (LPA) for rapid diagnosis of MDR-TB as a means of expediting the detection and referral of patients eligible for MDR-TB treatment
- Conduct training workshops—continuing medical education (CME), newer tools, biosafety, IC
- Technical assistance for the implementation of biosafety and IC in laboratories at all levels
- Facilitate the participation of institutions and national programmes in the Region in global operations research
- Conduct field testing of newer diagnostics to generate evidence base and to guide policy and strategy formulation for the management of MDR-TB.

Introduction of newer diagnostics is being facilitated by the Global Laboratory Initiative (GLI) through the EXPAND TBx project (implementing partner FIND). There is a plan for phased introduction of LED FM in all settings (as per the needs of different countries). The introduction of LPA

and automated liquid culture is also envisaged. However, both these tests have specific infrastructure needs, which include strict infection control in the laboratories performing the tests. The capacity for these tests must thus be built before they are introduced. GeneXpert was endorsed by WHO in December 2010. Evidence collection is ongoing/ planned in India, Indonesia, Myanmar and Sri Lanka. However, all operational challenges will have to be sorted out before this rapid test is rolled out on a large scale.

Advantages and requirements of newer tools

Technology	Requirements, technical expertise and cost
Automated liquid culture	Requires directional airflow (Neg Pr), extensive training and technical expertise. Moderate cost.
Line probe assay (LPA)	BSCs for sputum processing, Requires three clean rooms, moderate technical expertise and training. Moderate cost.
GeneXpert (automated NAAT)	No biosafety requirements, one-step processing, 90-minute computer-based readout results for TB and RIF resistance, multi-disease platform, district level or even subdistrict level
LAMP	No biosafety requirements, multi-step manual processing, results read visually, to be introduced in microscopy level—only TB detected, multi-disease platform

4.3 Monitoring and evaluation of PMDT

Monitoring is done because more information is needed for project management than is needed at the national or international level. Thus, the number of indicators for which data are collected should decrease substantially from the subnational to the national and international levels. Some indicators are, however, useful at all levels of the system. It is very important to select a limited number of indicators that programme implementers and managers will actually use for effective decision-making. In addition, monitoring is used for measuring trends over time, and the methods used thus need to be consistent and rigorous to ensure appropriate comparison.

The objectives of the monitoring process are to ensure that activities are undertaken as planned; to reveal the progress towards identified targets

and goals; and to identify problem areas and ensure that corrective action is developed and taken.

At the same time, evaluation is the rigorous, scientifically based collection of information on a programme or intervention activities, characteristics and outcomes that determines the merit or worth of the programme or intervention. Assessing the impact of a programme requires extensive investment in monitoring and evaluation (M&E) efforts.

The minimum indicators for PMDT are grouped in four categories:

- Detection
- Enrolment
- Interim results
- Final outcomes.

In the 2010 annual WHO data collection for the 2010 WHO Annual Global TB Control Report, for the first time, outcomes for MDR-TB patients who had started treatment two years before the year of the report were requested for patients enrolled both in GLC-approved cohorts and non-GLC cohorts

The five MDR-TB indicators for the GF 2010 (SDA 2.2. MDR-TB) are:

(1) New and retreatment of TB patients receiving diagnostic DST for MDR-TB among the patients eligible for DST according to national policy (number and percentage) during the specified period of assessment (six-monthly and annually)→ Detection

(2) Number of sputum smear-positive TB patients confirmed as MDR-TB by the laboratory during the year of assessment among all new and re-treatment sputum smear-positive TB patients reported by the programme in the same period who, based on drug resistance studies or other estimates, would be expected to have MDR-TB (Annually) → Detection

(3) Laboratory-confirmed MDR-TB patients enrolled on second-line anti-TB treatment (number and percentage) during the specified period of assessment (six-monthly and annually) → Enrolment

(4) Percentage of MDR-TB cases initiated on a second-line anti-TB treatment who have a negative culture at the end of six months of treatment during the specified period of assessment (six-monthly and annually) → Interim outcome

(5) Laboratory-confirmed MDR-TB patients successfully treated (cured plus completed treatment) among those enrolled on second-line anti-TB treatment during the year of assessment (number and percentage) (annually) →Final outcome

4.4 Management of second-line anti-TB drugs

The Global (TB) Drug Facility (GDF) supports the procurement of SLD for GLC-approved projects for nine Member States of the SEA Region (2007). This helps to provide uninterrupted supply of SLD, provide access to quality-assured and concessionally priced products, and ensure timely delivery (average lead time 103 days in 2010 versus 113 days in 2008).

The GDF quality assurance (QA) policy is harmonized with QA standards for the selection of medicines and manufacturers with the Global Fund and partners (2010). The GDF and the Global Fund have also synchronized their selection processes (combined Expression of Interest (EoI) for TB manufacturers is undertaken every six months for ERP (expert review panel) review/ sampling and testing capabilities and pooling QC testing activities with the Global Fund (GFATM) and partners).

The GDF encourages countries to establish quality monitoring and control systems, if these are not already in place. This includes testing of finished pharmaceutical products in ISO -17025 certified or WHO PQ laboratories (GFATM requirements). In some cases, mobile quality laboratories (minilabs) are used to detect basic quality issues, but this should not replace full quality control (QC) testing.

The challenges faced at country level are:

- Long port clearances
- Delayed disbursement and transfer of funds
- Delayed NTP response on queries
- Slow enrolment of patients

- Short shelf-life
- Inadequate management of SLD

The challenges faced globally are:

- Limited number of Active Pharmaceutical Ingredient (API) producers
- Limited number of PQed TB medicines
- Inadequate demand forecast
- Market-specific issues for some product areas
- Need to reduce lead times for ordering process and delivery
- Need to formalize rapid response capabilities to respond to emergency situations and stock-outs
- Need to build sustainable capacity in drug management and monitoring at country level with partners

The GDF intends to expand market dynamics. For this, a meeting of Indian anti-TB drug manufacturers was organized in New Delhi in March 2011. The objective of the meeting was to sensitize/make aware/get on board potential suppliers. The meeting was also intended to bring together manufacturers and partners and assist with the provision of TA through various sources, such as UNITAID, USP, WHO, the GF and the GDF. The meeting met with a huge response and a follow-up meeting is planned for August 2011.

Another meeting of anti-TB drug manufacturers from the SEA Region and WP Region was organized by the GDF/USP in Jakarta, Indonesia in March 2011. The objective of the meeting was to make the participants aware of free-of-charge technical assistance in preparation for the dossier for WHO pre-qualification (PQ). The participants included representatives from government and private companies of Bangladesh, Indonesia, Myanmar, Nepal and Thailand.

A current challenge for the GDF in the context of MDR-TB market dynamics is to attract new suppliers to submit dossier for WHO prequalification process. The Market Allocation System is a tool that

envisages the allocation of the market share to all eligible suppliers of the same medicine based on a combination of quality, price and registration status criteria.

A forecasting tool for second-line anti-TB medicines has been developed jointly by the GDF and Clinton Foundation (CHAI) for country forecasting to be further improved for global forecasting needs. Five to six pilot countries are expected to be engaged by December 2010 in the task of comparing the Global Fund targets with the actual enrolment rates so as to have accurate forecasts at six months and one year. By the end of 2011, the second phase will be implemented. This would determine when the project will be rolled out to more countries. It is planned to adopt another approach to the issue—the dual approach. This would entail one system for the short term (years 1 and 2), and one outlining trends for the longer term (years 3 to 5). Both systems are being updated every six months.

There is a plan for strengthening in-country procurement and supply management (PSM) systems specifically for second-line drugs. A global workshop is planned for August. According to the agenda, MDR-TB logistic focal persons of WHO/NTP/implementing partners would and could attend. During the meeting, plans for strengthening PSM will be developed and followed up for implementation. The workshop is expected to be followed up by roll out of basic trainings at the country level.

5. Outline of the regional response plan

Considerable efforts are required to expand the capacity of countries and these would include strengthening of planning to adequately responding to the M/XDR-TB challenge. All activities also need to be in alignment with the latest WHO guidelines. Keeping this in mind, the SEA Region has developed a response plan to draw a road map for regional contribution to the achievement of the global targets set forth for M/XDR-TB in the Global Plan to Stop TB, 2011–2015. The plan will also act as a guiding tool for the Member States in the development of strategic and operational plans for PMDT, and serve as a reference document and tool of communication for regional priorities while addressing the challenges related to M/XDR-TB in the Region.

The plan calls for a comprehensive approach to address the MDR-TB burden by preventing the emergence of new MDR-TB cases, and emphasizes early diagnosis and treatment of the existing cases. All sectors will need to be involved to mobilize the available resources. The activities would need to be supported by advocacy, communication and social mobilization. While scaling up MDR-TB services, the health systems would also need to be strengthened in accordance with the needs. Appropriate operational research for diagnosis and models of care will help countries quickly adapt new tools and technologies to local needs.

Relevant global targets

	Baseline (2008-2009)	**Target (2015)**
Drug-resistant TB/Laboratory strengthening		
Percentage of previously treated TB patients tested for MDR-TB	5%	100%
Percentage of new TB patients tested for MDR-TB	2%	20%
Number of countries among the 22 HBCs and 27 MDR-TB HBCs with ≥1 culture laboratory per 5 m population	18–21	36
Percentage of confirmed cases of MDR-TB enrolled on treatment according to international guidelines	28%	100%
Number of confirmed cases of MDR-TB enrolled on treatment according to international guidelines	11 000	~270 000
Treatment success rate among confirmed cases of MDR-TB	60%	≥75%

Purpose of the document

- To provide an overview of planned regional response to M/XDR-TB
- To draw a road map for regional contribution to the achievement of global targets set forth for M/XDR TB in the Global Plan, 2011–2015
- To act as a guidance tool for Member States for developing strategic and operational plans for PMDT

- To serve as a reference document and tool of communication for regional priorities while addressing the challenges related to M/XDR TB in the Region.

Goal of the response plan

In tandem with the regional strategic plan for TB control 2006–2015, the overall goal for TB control is to reduce morbidity, mortality and transmission of TB until it is no longer a public health problem in the Region.

Component strategies

- Preventing the emergence of resistance through sustained and enhanced efforts to reach all TB patients with quality care
  - Strengthening basic TB control services to improve case notification and treatment success
  - Promoting adoption of ISTC by all care providers
  - Promoting rational use of drugs and pharmacovigilance
  - Strengthening TB-HIV collaboration
- Scaling up programmatic management of drug-resistant TB (PMDT)
  - Screening and testing for resistance to first- and second-line drugs, as well as HIV testing among confirmed cases of MDR-TB
  - Providing access to effective treatment for drug-resistant TB
  - Providing patient-centric care and promoting adherence
- Implementing TB IC in health-care facilities and congregate settings
- Strengthening surveillance, including recording and reporting of drug-resistant TB
- Strengthening health systems to ensure capacity for PMDT integrated with primary health care
- Forging partnerships and ensuring coordination with stakeholders to mobilize requisite resources

- Supporting PMDT through advocacy, communication and social mobilization (ACSM)
- Undertaking research.

With the implementation of this response plan, it is expected that the Region will strengthen the laboratory capacity through the introduction of newer tools for diagnosis, such as the GeneXpert and LPA. This will help initiate at least 55 000 MDR-TB cases on treatment with quality-assured second-line anti-TB drugs by 2015. It is expected that out of these, at least 75% will be treated successfully.

The plan is expected to contribute to the overall regional plan to stop TB by reducing the morbidity and mortality due to the disease.

6. Conclusion and recommendations

Conclusion

Although steady progress has been made in the Region in addressing the problem of MDR-TB, the activities need to be further accelerated through strengthened country capacity. All countries would need to have a costed expansion plan in alignment with the recommended guidelines of WHO. Sufficient resources need to be mobilized for the purpose. Newer tools and technologies need to be quickly rolled out after collecting in-country evidence on their operational feasibility. The Regional Office would need to facilitate the roll out of technologies through guidance and workshops for the dissemination of knowledge. The countries will also need to integrate PMDT in regular programme delivery. System strengthening, along with recording and reporting of all cases initiated on treatment, would help this integration.

Recommendations

The meeting concluded with the following recommendations and action points for follow-up.

(1) There is a need to strengthen regional activities and the response to MDR-TB in order to reach the global targets for universal access by 2015.

(2) The headquarters should let the revised structure of MDR-TB support for countries be known as early as possible.

(3) There is a need for a regional workshop on newer diagnostics for

- Planning introduction
- Operational challenges
- Technical guidance.

(4) Regional support is required for the development of a network for the transportation of samples from NRLs to SNRLs.

(5) There is a need to improve the quality of training in the Region through

- Training of trainers (TOT) for PMDT to improve the quality of facilitators
- Monitoring quality of training through follow-up.

(6) Country support for Global Fund Round 11 would be required for some Member States.

(7) There is a need for regional support for small countries with limited human resources. This could be done through

- Mentorship programmes—both remote and on-site
- Online support

(8) There is a need to strengthen ACSM for PMDT

(9) There is a need to address country-specific requirements, which include the following.

- Additional resources should be mobilized for countries such as Bhutan and DPR Korea.
- DPR Korea should be supported through the launch of PMDT services and scale-up.
- Thailand should receive in-country technical assistance for PMDT services.

Annex 1

Key achievements, plan and challenges for expansion of PMDT in the Member States of the SEA Region

Bangladesh

Achievements in PMDT

A DOTS-Plus Coordination Committee has been providing direction for overall implementation. There is a functional Clinical Management and Social Support Committee. The MDR-TB management guidelines have been developed. The first nationwide drug resistance survey (DRS) has been in progress since December 2010. This can provide realistic data on the situation of drug resistance in Bangladesh.

A PMDT expansion plan has been developed, as have TB-IC strategies and guidelines. Training of trainers (ToT) has been completed. A second MDR-TB treatment unit was functionalized in the Chest Diseases Hospital, Chittagong in February 2011. In addition, the second GLC mission has been conducted.

PMDT expansion plans

The expansion plan aims to achieve 'universal access', which the Global Plan to Stop TB defines as 'diagnosis and treatment of 80% of the estimated number of smear+ and/or culture+ cases of MDR-TB by 2015, in programmes following the international guidelines for the management of drug-resistant TB'.

The other approach is to make use of the estimate made by WHO in its 2010 report, of a total of 9800 MDR cases on the basis of mathematical modelling. Almost half (53%, or 5194) will be assumed to be pulmonary-positive. Eighty per cent of this would be 4155. For purposes of the expansion plan, pending DRS results, the 2010 WHO estimate will be used as a reference, with a target of 4155 MDR-TB cases to be treated by 2015.

Targets as per expansion plan

	2008–2009 Baseline	2010	2011	2012	2013	2014	2015
Estimated MDR-TB cases	Annual estimated target = 9800 MDR-TB cases (all cases), of which 53% (5194) is assumed to be pulmonary-positive. Universal access aims at 80% (4155) by 2015.						
Target number of patients to be treated	283	779	1 558	2 597	3 116	3 636	4 155
% treated among incident cases	5%	15%	40%	50%	60%	70%	80%

Challenges
Laboratory aspects

There are limited laboratory facilities. They are available only in Dhaka (NTRL, NIDCH), Chittagong and Rajshahi (where there are RTRLs). There is no new laboratory technology and conventional culture and DST (C&D) is being used.

The capacity for the maintenance of equipment is limited. Further, the fund flow for routine activities is interrupted. There is a shortage of microbiologists and other human resources.

Implementation of laboratory expansion plan (due to lack of funds and commitment) and introduction of newer technologies.

Treatment

- The duration of treatment is long, i.e. 24 months.
- Hospitalization is necessary during the intensive phase, as per the policy.
- The number of hospital beds is limited. The facility for admission is available only in Dhaka, Chittagong and Rajshahi.
- There are difficulties in treatment in special situations and situations requiring referral linkages, e.g. with ENT, psychiatry, nephrology and gastroenterology.

- Ancillary tests (baseline eudiometry, LFT, RFT, TFT, CXR and some biochemical tests, pregnancy test for women of childbearing age, HIV screening test) also pose a problem.
- Implementation of community-based MDR-TB management is problematic.
- There is a lack of skilled and committed human resources.
- The default rate is high.

Bhutan

Achievements

- MDR-TB guidelines have been developed.
- An IC plan has been developed.
- Two medical specialists have received training in MDR-TB management.

C&DST facilities and laboratory networks

- Culture facilities are available at three regional referral hospitals.
- DST facilities are available at the PHL, Thimphu.
- The PHL is linked with the SNRL in Thailand.

SLD status and source

- Procurement of SLD has been initiated through the GDF.
- Funding is being supported through the Global Fund, Round 6.
- There is an adequate stock of SLD.

PMDT expansion plans

- MDR-TB treatment will be limited to 3 RR hospitals only.
- Decentralization is planned during the continuation phase.

- Doctors will be trained in the management of MDR-TB.
- Laboratory technicians will receive international training on DST in the SNRL.

Challenges

The joint review of the National TB Control Programme in Bhutan, 9–18 June 2010, and other reviews have identified the weaknesses and challenges in following areas:

- Planning, management, coordination and supervision
- Access to services
- Laboratory services
- Treatment services
- Human resource
- Management of drugs and supplies
- Paediatric TB
- MDR-TB
- TB/HIV
- IC
- Community involvement.

DPR Korea

Achievements

- A national TB reference laboratory (NTRL) was established at the Central TB Preventive Institute (CTPI) in October 2010.
- WHO extended technical assistance in January 2011 to review and build the capacity of the NTRL.
- Fifty samples collected from Category 1 and 2 failures were sent to the Hong Kong STRL to determine the extent and pattern of

MDR-TB in DPR Korea, and the DST is ongoing; the results of 39 samples have already been interpreted.

C&DST facilities and laboratory networks

- The NTRL has been upgraded for C&DST and has been operational since October 2010.
- Workflow in the NTRL is state-of-the-art, as per the international recommendations.
- The staff capacity is improving.
- A regional C&DST laboratory will be established in South Hamgyong province.
- A national laboratory network for TB exists from the central to the county level.
- Quality control and EQA are being conducted on a regular basis.

PMDT expansion plans

- There is a tentative plan to initiate two PMDT pilot sites.
- Approximately 50 MDR cases are to be registered for treatment per year initially.
- Plans to be prepared by the end of April 2011.
- Expansion plans will be submitted early in the third quarter of 2011.

Challenges

- The technical capacity of the peripheral staff is limited.
- There are gaps in infrastructure, and all operational costs are not being met.
- Data management is still poor.
- Financial gaps exist in spite of Round 8.

- Pharmacovigilance is not in place.
- There is a lack of expertise in technical areas, e.g. in the management of paediatric and MDR-TB, culture and DST.
- Exposure to international best practices and standards for TB care is insufficient.
- No services are in place for the management of MDR-TB.
- Implementing of IC activities in all hospitals

India

RNTCP response to MDR-TB

Strategy to scale up laboratory services

- It is planned to scale up the number of culture and DST laboratories nationwide to at least 43 by 2013.
- The throughput per laboratory is to be increased by investment in sputum processing capacity and the introduction of high-throughput molecular DST.
- Automated liquid culture systems shall be established.
- Specimen transport systems and electronic results reporting are to be strengthened.
- Reference laboratories shall be strengthened.
- Training capacity is to be scaled up.
- It is planned to engage private sector and medical college contractual laboratory services.

Achievements

Laboratories

A total of 25 laboratories have been accredited for C&DST out of which 4 are NRLs and 12 are IRLs.

LPA services are available in four laboratories.

DOTS-Plus status (December 2010)

DOTS-Plus was initiated in 2007 in Gujarat and Maharashtra, and has been expanded in a phased manner. At present, 12 states are implementing basic DOTS-Plus services in some districts. Six states are to initiate services shortly. The remaining states will initiate basic services by the end of 2011. A total of 288 million people (24% of the population) have access to DOTS-Plus services in India.

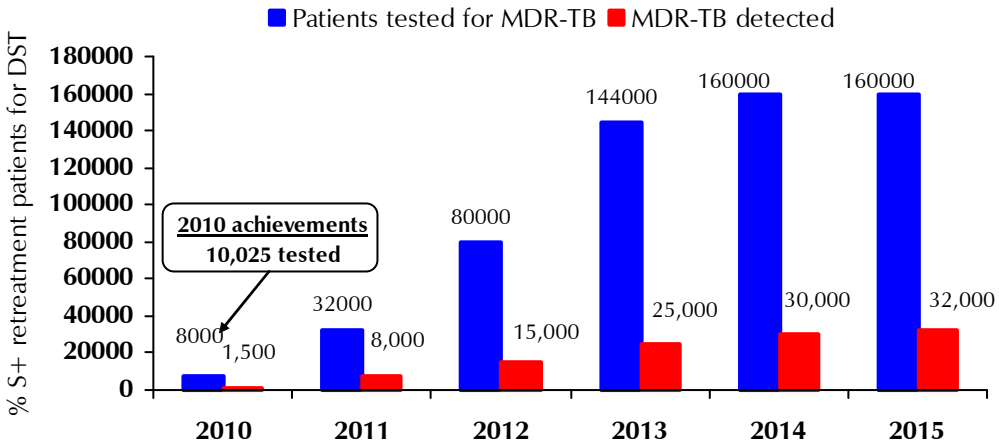
In all, 19 178 MDR suspects have been examined and treatment has been initiated in 3605 patients.

PMDT expansion plans

Laboratory scale-up plan

Forty-three laboratories are to be established and strengthened. The capacity for sputum processing (staff, centrifuges, BSC) shall be enhanced. All laboratory units shall have capacity for solid culture and DST. Further, all laboratories are to have facilities for LPA, while 33 will have facilities for liquid culture.

Plan for testing and treating patients for MDR-TB



Challenges

There are delays in the establishment and accreditation of laboratories.

The conventional method is associated with diagnostic delays (3–4 months' turn-around time).

There are certain special requirements for the introduction of newer rapid diagnostics (laboratory infrastructure and training).

There is a need to improve the efficiency of the identification and referral of MDR suspects.

Efficiently starting treatment on diagnosed MDR-TB patients.

Deaths, refusals because of long delay in diagnosis.

Ensuring uninterrupted supply of second-line drugs.

Cost escalation (US$ ~2100) of SLDs reduces the number of patients.

Extensive training, supervision and monitoring are needed at all levels, nationwide.

Dramatic demand for local programme staff for supervision, ensuring treatment adherence and timely follow-up.

Indonesia

Achievements

Five sites (networks) are providing services (East Jakarta, Surabaya city, Malang city, Solo, Makassar).

Out of 788 MDR-TB suspects, 574 completed DST, and in 254 cases MDR-TB (44.2%) was confirmed. Of the 254 confirmed MDR-TB cases, 179 (70.4%) were enrolled, 16 pre-enrolled, 4 excluded, 16 (6.2%) died before enrolment, 17 (6.7%) lost, and 22 (8.6%) refused treatment.

At 6-month follow-up, the interim results among 79 cases, 61 converted, 18 not converted, yet

Treatment outcome of 21 cases: 1 cured, 9 died, 9 defaulted, 7 failed

Category MDR/XDR	Regimen	Estimated % of cases
Standardized regimen for MDR TB suspects	Km Lfx Eto Cs (E) Z	75 %
Standardized regimen for XDR TB suspects (chronic cases and treated in private sector with non-DOTS SLD)	Cm Lfx (high dose) Eto Cs PAS (E) Z	25 %

Challenges

- Complicated treatment delivery structure and ongoing decentralization of services
- Weak technical capacity in medical management and programme management in provinces/ districts

- Laboratory network: baseline infrastructure and capacity, long-term commitment for maintenance of equipment is not there
- R&R: e-TB manager, challenges in scaling up and linkage
- Availability of SLDs: dependent on GF, drug shortage from GDF, long time in custom clearance
- ACSM and specifically community-based DOT for MDR-TB: not yet community involvement
- Involvement of other sectors: need orientation/ role clarification/ trainings
- Infection control: IC emphasize renovation, limited scale, coordinated by Department of Medical Service
- Undertaking DRS: sentinel sites follow DST laboratory and PMDT
- Pharmacovigilance and promoting rational drug use: big issue, weak hospital involvement on DOTS, use of quinolone with FLD in new TB cases, private sector: unknown
- Human resource: zero growth, high turnover, motivation
- Financial: Global Fund dependent
- Commitment from provinces/ districts: weak

Myanmar

Achievements

- Expert committees and coordination bodies have been set up.
- The MDR-TB pilot project, ending in June 2011, has been successful.
- Two state-of-the-art reference laboratories have been established.
- A massive programme for capacity-building has been undertaken.

- A social support system for patients has been developed.
- Health care workers have been provided incentives.
- IC is adequate in MDR-TB hospitals.

MDR-TB expansion plan

A draft MDR-TB expansion plan to supplement the National Strategic Plan for TB 2011–2015 is to be finalized in Q2 2011. It includes:

- Revisions to the present model of care on the basis of the experience with the pilot project
- National goals for expansion over a five-year period (including roll-out of Xpert)
- Revisions to the existing operational procedures for MDR-TB
- A plan for funding and support

Draft MDR-TB expansion plan

Year	Reference laboratories	Number of centres with Xpert	Number of states/ Divisions with TB/MDR-TB hospital	Number of townships with MDR-TB treatment	Percentage of townships covered	Percentage of population covered
2010	2	0	2	10	3%	2%
2011	2	4	2	22	7%	
2012	2	7	5	37	11%	
2013	2	12	10	77	24%	
2014	2	12	10	100	31%	**Goal > 50%**
2015	2	19	10	100	31%	

Main challenges

The main challenges are in the areas of human resources, basic health staff, motivation, financial resources, infrastructure and communication, monitoring and management of adverse events in remote areas, and organization of community support and volunteers.

Nepal

Key achievements

- A total of 894 drug-resistant TB (880 MDR-TB and 14 XDR-TB) cases were registered for treatment by the end of December 2010.
- The programme has been expanded to allow for nationwide coverage.
- A five-year expansion plan has been developed as part of the National Strategic Plan.
- Treatment of XDR-TB has commenced (14 patients on treatment).
- The drug-resistant TB manual was revised in 2010–2011.
- Funding is available through the GFATM NSA grant till 2015.
- The public–private partnership is excellent, with 50% of treatment centres and sub-treatment centres in the private sector.
- A survey to gauge the prevalence of XDR-TB among registered MDR-TB patients has been completed (5%)

Other achievements

- Socioeconomic support is being provided by the Government of Nepal and through a GFATM grant—$19 per month has been allocated for transportation expenses.
- A full-time coordinator has been appointed at the Central level.
- There is a plan to set up 10 hostels (funded through the GFATM NSA grant), starting from the latter half of 2011.
- An infection control plan has been developed. Funding has been approved through the GFATM NSA grant, and the

implementation of the plan was to start in early 2011 there is some delay.

- Funding has been approved for 'hazard allowance' for staff involved in the MDR-TB management programme
- The programme has been expanded to manage cases as per the estimates of the WHO 2010 Global Report Surveillance and Response.

Challenges

- The decreasing cure rate (71% in 2005, 64% in 2006, 63% in 2007) is due mainly to the high default rate (17% cumulative for five years).
- There are no culture facilities at the regional level.
- There is no provision of hospital beds or hostels for MDR-TB patients.
- Supervision is inadequate.
- There is a lack of IC in the health care setting.
- The NTP central laboratory still needs to take up full responsibility for the NRL.
- There is a lack of electronic data management.

Plans for 2010–2015

- It is planned to treat 1500 cases during the 2010–2015 period (300 per year).
- The NTP has agreed in principle with the GLC 2011 mission to aim for treating 60% of the estimated cases.
- The number of MDR-TB programme sites is to be expanded to 80.
- There are plans for the provision of hostel accommodation (10 hostels).

- The central NTP laboratory shall be upgraded to an NRL.
- Culture facilities are to be established at the regional level (3) and DST (1 region).
- There are plans to continue to expand partnership with the public and private sectors.

Sri Lanka

Achievements

- There is strong political commitment.
- Global targets have been achieved and sustained.
- DOTS coverage is high.
- There has been a downward trend in defaulter rates.
- Drugs being purchased from GDF and GLC (unclear)
- A good social marketing programme is in existence.
- The surveillance network is strong.

TB laboratory network, culture and DST facilities

- There are two culture facilities, while three are planned.
- There is one DST facility.
- The total number of TB laboratories is 178.
- The total number of laboratory staff is 242.
- There are 26 district laboratories.
- There are 151 peripheral microscopic centres.

PMDT expansion plans

- There are plans to upgrade culture and DST facilities at the NRL.

- Quality-assured culture facilities are to be established in selected districts.
- Formal links shall be maintained with the SNRL.
- Periodic DRS will be conducted.
- The management of MDR-TB patients with second-line drugs shall be integrated with routine TB control activities.

Challenges have been identified in following areas

- R&R
- ACSM and specifically community-based DOT for MDR-TB
- Implementation of IC plan
- Undertaking DRS
- Human resources
- Financial resources

Thailand

Achievements

- Guidelines for the treatment of MDR-TB were developed and launched in 2009.
- Standard first- and second-line drugs have been made available through allocation from the national budget and with significant contribution from the GF and GLC/GDF for model development.
- MDR-TB treatment is available at teaching, regional and provincial hospitals
- Among the other parties involved are the World Vision Foundation and Raks Thai Foundation.
- TB culture is available.

- DST is available in approximately 15 sites for first-line drugs. There are plans to scale up the capacity.

Challenges

- The strategic plan must be translated into action to ensure achievement.
- Rights of patient, involvement of affected persons needs to be ensured
- Technical capacity needs to be strengthened
- Psychosocial support needs to be provided to TB and MDR-TB patients and their families.
- Coverage should be ensured for non-Thai and other vulnerable groups.
- Scaling up of culture and DST is a must to increase request. Expansion of laboratories (GeneXpert) is required to support increasing need.
- Prescription of standard regimen by all providers.
- IC: at beginning phase needs to be expanded.
- Pharmacovigilance.

Annex 2

Agenda

(1) Global and regional situation of MDR/XDR TB and progress

(2) Regional laboratory status, plans and recommendations on newer diagnostics

(3) Systems strengthening and HR issues in the context of PMDT

(4) Monitoring and evaluation of PMDT

(5) Second-line TB drug management

(6) Country presentations – progress, plans and challenges to scale up programmatic management of drug-resistant TB (PMDT)

(7) Country-specific progress, plans and challenges to scale up programmatic management of drug-resistant TB (PMDT)

(8) Plenary discussions - country experience sharing on success and desired external support in 1: Laboratory strengthening, networks and expansion 2:Treatment organization and models of care being used in country 3:Recording and reporting paper based and electronic systems 4:Second-line drug management how the countries have avoided stock outs

(9) Country experience sharing on success in 1:Human Resource Development – motivation of staff and retention and 2.Monitoring and Evaluation – organization of monitoring missions

(10) Video Conference with HQ

(11) Draft regional response plan

(12) Discussions on the Regional plan

(13) Country contextual comments on plan in 1. Setting country targets in accordance with Global and regional plans and 2. technical assistance needs; and financial requirements for various activities

(14) Summarizing and closing

Annex 2

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Well-functioning national TB control programmes in the Region have resulted in low levels (Range: 1.7- 4.2%) of multidrug-resistance (MDR) among newly detected cases. Among the previously treated cases in the Region, MDR-TB rates range from 10.0 - 34.7%. However, given the large numbers of TB cases in the SEA Region, this translates to 130 000 MDR-TB cases (110 000–170 000) accounting for nearly one third of the world's total.

During the past few years, steady progress has been made in the Region in initiating MDR-TB cases on treatment. The Green Light Committee had approved the case management of patients with MDR-TB under national programmes in 10 countries. Until the end of 2010, more than 5000 patients with MDR-TB had been registered for treatment in the Region. Extensively drug-resistant TB (XDR-TB) has also been reported from five countries in the Region. MDR-TB could potentially replace drug-susceptible TB and constitutes a threat to global public health security. In areas of high HIV prevalence, the potential for increased transmission of MDR-TB is high.

Considerable efforts are required to expand the capacity of countries, including strong planning to adequately respond to this challenge. All activities need to be in alignment with the latest WHO guidelines. A regional response plan has been developed with all country focal points to have a common understanding of activities to be undertaken and scale up MDR-TB response to reach the goals of universal access for all MRD-TB patients.

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