
Regional Advisory Committee on MDR-TB
SEAR (r-GLC) Secretariat WHO South East Asia Regional Office

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World Health Organization – Country Office for India, New Delhi
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Programmatic Management of Drug Resistant Tuberculosis

Regional Advisory Committee on MDR-TB SEAR (r-GLC) Secretariat
WHO South East Asia Regional Office

PMDT MONITORING MISSION REPORT
2016

Programme: Country: Democratic People’s Republic of Korea

Lead implementing agency:
National Tuberculosis Programme, Ministry of Public Health, Government of DPR Korea

Inclusive dates of mission:
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- Ministry of Public Health, Government of DPR Korea, Pyongyang
- National TB Programme, Government of DPR Korea, Pyongyang
- WHO Country Office for DPR Korea, Pyongyang and India, New Delhi
- WHO South East Asia Regional Office, New Delhi
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The author extends gratitude to the National Tuberculosis Program (NTP), Ministry of Public Health (MoPH), Government of DPR Korea (GoDPRK) and WHO Representative to DPR Korea and India for their kind support in conducting this mission. Thanks also to NTP staff and officials at the sites visited during the mission for sharing valuable information and contributions to enable comprehensive review of PMDT situation of DPR Korea.

The author acknowledges the leadership, valuable time and insights shared by Dr Ri Chan Hyok, Vice-Director of Department of External Affairs, MoPH, GoDPRK (Global Fund Coordinator) and Dr Choe Tong Chol, NTP manager, Director of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK and his team from Central / Provincial TB Preventive Institutes, National Reference Laboratory, Provincial TB Hospital and TB Sanatoria officials who provided necessary information and directions to the author to focus on specific foreseen challenges and shape up the recommendations to address the felt unmet needs of the NTP DPR Korea for PMDT. Thanks also to Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK for sharing the details of support extended by Eugene Bell Foundation in supporting MDR-TB diagnosis and treatment including the pilot introduction of Bedaquiline containing regimen for XDR-TB patients. Dr Heidi S. Linton, Executive Director and team including Dr Kathlene England, International Consultant from Christian Friends of Korea also graciously discussed the support extended and way forward for laboratory capacity enhancement in DPR Korea in collaboration with the WHO Country Office.

Special appreciations and acknowledgement to Dr Ri Jun Hyok and Dr Ko Jin Hyok from the TB PMU, Pyongyang, MoPH, GoDPRK for their valuable support, care and time given to the reviewer throughout the mission and sharing information on situation, challenges, potential solutions and way forward for TB and MDR-TB interventions in DPR Korea.

The author would also like to thank Dr Thushara Fernando - WHO Representative to DPR Korea for the invitation to conduct the mission and MDR-TB training and discuss specific action points for WHO country office to support DPRK accelerate its response to combat MDR-TB; Mr Thinlay – Administrative Officer for providing organizational support; Dr Gagan Sonal - Technical Officer, Malaria; Dr O Hyang Song - NPO-TB at WHO Country Office in DPR Korea and Dr Partha Mandal - Technical Officer TB at WHO SEARO for their valuable time and guidance on various issues regarding TB and PMDT situation in DPR Korea and the way forward.
## Abbreviations:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADR</td>
<td>Adverse drug reaction</td>
</tr>
<tr>
<td>aDSM</td>
<td>Active drug safety management and monitoring</td>
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<tr>
<td>AO</td>
<td>Administrative Officer</td>
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<tr>
<td>BDQ</td>
<td>Bedaquiline</td>
</tr>
<tr>
<td>BHU</td>
<td>Basic Health Unit</td>
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<tr>
<td>CTPI</td>
<td>Central TB Preventive Institute</td>
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<tr>
<td>CFK</td>
<td>Christian Friends of Korea</td>
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<tr>
<td>DLM</td>
<td>Delamanid</td>
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<tr>
<td>DPRK</td>
<td>Democratic Republic of Korea</td>
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<tr>
<td>MoPH</td>
<td>Department of Public Health</td>
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<tr>
<td>DOT</td>
<td>Directly Observed Treatment</td>
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<tr>
<td>DRTB</td>
<td>Drug Resistant Tuberculosis</td>
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<tr>
<td>DST</td>
<td>Drug Susceptibility Testing</td>
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<td>DVED</td>
<td>Drug Vaccines and Equipment Division</td>
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<tr>
<td>EQA</td>
<td>External Quality Assurance</td>
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<td>EBF</td>
<td>Eugene Bell Foundation</td>
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<td>FLD</td>
<td>First Line Drugs</td>
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<td>GoDPRK</td>
<td>Government of DPR Korea</td>
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<td>GDF</td>
<td>Global Drug Facility</td>
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<td>GF</td>
<td>The Global Fund</td>
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<tr>
<td>GLC</td>
<td>Green Light Committee</td>
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<tr>
<td>HA</td>
<td>Health Assistant</td>
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<tr>
<td>LPA</td>
<td>Line Probe Assay</td>
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<tr>
<td>LT</td>
<td>Laboratory Technologist</td>
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<tr>
<td>LTBI</td>
<td>Latent TB Infection</td>
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<td>MDR-TB</td>
<td>Multi-Drug Resistant Tuberculosis</td>
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<tr>
<td>MoPH</td>
<td>Ministry of Public Health</td>
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<tr>
<td>ND</td>
<td>Newer Drugs</td>
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<td>NFM</td>
<td>New Funding Model</td>
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<tr>
<td>NTP</td>
<td>National Tuberculosis Control Programme</td>
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<tr>
<td>NTRL</td>
<td>National TB Reference Laboratory</td>
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<tr>
<td>PMDT</td>
<td>Programmatic Management of Drug Resistant Tuberculosis</td>
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<tr>
<td>PMU</td>
<td>Programme Management Unit</td>
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<tr>
<td>PSM</td>
<td>Procurement supply chain management</td>
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<tr>
<td>PTH</td>
<td>Provincial TB Hospital</td>
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<td>SCTS</td>
<td>Specimen collection and transport system</td>
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<tr>
<td>SEAR</td>
<td>South East Asia Region</td>
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<tr>
<td>SLD</td>
<td>Second Line Drugs</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>--------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>SL-LPA</td>
<td>Second Line – Line Probe Assay</td>
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<tr>
<td>SMTR</td>
<td>Shorter MDR-TB Regimen</td>
</tr>
<tr>
<td>SNRL</td>
<td>Supranational Reference Laboratory</td>
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<tr>
<td>TBS</td>
<td>TB Sanatorium</td>
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<tr>
<td>TO</td>
<td>Technical Officer</td>
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<tr>
<td>VHW</td>
<td>Voluntary Health Worker</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>XDR-TB</td>
<td>Extensively Drug Resistant Tuberculosis</td>
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</table>
I. Executive summary:

Democratic People’s Republic of Korea is one of the high TB and MDR-TB burden countries in the South-East Asia Region. TB and MDR-TB has been a major public health problem in DPR Korea. DPR Korea initiated PMDT services with external support of Eugene Bell Foundation (EBF) since 2008, technical assistance from WHO Country Office and was complemented by the Global Fund support through UNICEF since 2012. Christian Friends of Korea (CFK) has also been supporting DPR Korea particularly in laboratory capacity development. Progress made in past 4 years in scaling up PMDT services has been slow. At the moment, DPR Korea has covered limited counties in 5 out of 12 provinces with PMDT services under the NTP framework and is currently supported by commodity cum technical support by EBF, CFK and GF-NFM funding through UNICEF and WHO Country Office for DPR Korea.

This is the fifth monitoring mission for Programmatic Management of Drug-Resistant TB (PMDT) component of the National TB Control Program (NTP) of the Government of DPR Korea (GoDPRK) undertaken on behalf of Regional Green Light Committee (r-GLC) of World Health Organization - South East Asia Region (SEAR) from 7 – 18 November 2016.

The two weeks long mission covered briefing meetings with key officials of TB programme management unit (PMU) under NTP, MoPH and WHO DPR Korea (AO, TO-Malaria & NPO-TB), visit to key health care facilities like National TB Reference Laboratory (NTRL) at Central TB Preventive Institute (CTPI), Sadong and Sosong district TB sanatoria (TBS) in Pyongyang city province, specialized provincial TB hospital (PTH) at Kwaksan county of North Pyongan, TB PMU and WHO Country Office of DPR Korea. During the mission, specific meetings were done with key officials from MoPH, GoDPRK viz. Dr Ri Chan Hyok, Vice-Director of Department of External Affairs, (Global Fund Coordinator); Dr Choe Tong Chol, NTP manager, Director of Department of Communicable Disease, Hepatitis and Tuberculosis; Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis (focal person for EBF); the team from TB PMU, CFK and WHO DPR Korea. Discussion could not be arranged with UNICEF and Global Fund representatives during the mission.

The mission also covered a technical training of NTP staff in PMDT at Pyongyang with special focus on the updated WHO PMDT Guidelines – 2016. This training covered updates on Case finding and Diagnostics including Second Line – Line Probe Assay (SL-LPA), updates on treatment including Shorter MDR-TB Regimen (SMTR), introduction of newer drugs (ND) like Bedaquiline (BDQ), Delamanid (DLM) and effective management of adverse drug reactions (ADR) including concepts of active drug safety monitoring (aDSM).
The objectives of the mission were

- To assess the **progress made** in PMDT activities since last rGLC mission in 2015
- To review **status and plans** of PMDT scale up in DPR Korea
- To review **partner’s support** in PMDT and discuss **harmonization** in line with “End TB Strategy” on PMDT
- To provide **recommendations** for implementation and further expansion of PMDT services for next one year in DPR Korea
- To provide **technical training** on PMDT, technical **consultation on WHO recommended shorter regimen** for adaptation and **assess possibility of its roll-out** in DPR Korea

The activities include comprehensive review of services in terms of patient care, programme management, supervision monitoring systems, community engagement, information communication systems for TB/DRTB, interactions with key officials, doctors, staff, specialists, patients, community representatives at the sites visited to analyze the progress made and plans developed for TB and PMDT implementation in light of the last year PMDT mission report, the PMDT expansion plan 2018, the current national PMDT guidelines and the explore the potential for rapid roll-out of the updated WHO PMDT guidelines particularly SMTR and SL-LPA.

The key observations and actionable recommendations based on country’s shared felt needs, observed facts, figures and available evidences from program data and field visits were shared and discussed in details by the author with the key stakeholders of MoPH and WR DPR Korea. The 2016 PMDT mission recommendations revolve around fast-tracking scale-up of PMDT services including laboratory, treatment and aDSM capacity in all remaining provinces of DPRK; minimize diagnosis treatment delays by immediately transitioning to bottom up specimen collection and transport system (SCTS) and a regular supply of second-line anti-TB drugs (SLD) with consumption based rather than cohort based procurement supply chain management system (PSM); initiating better understanding of DR-TB epidemiology; revising the national TB and PMDT guidelines elevating the TB services in DPR Korea from a “Control / passive” mode to a phased “Elimination / active” mode (having achieved the MDG 2015) aligning with the End TB Strategy & Sustainable Development Goals – 2030 by incorporating the updated diagnostic algorithm with rapid molecular diagnostics like Xpert-MTB Rif for diagnosis of TB and RR-TB, SL-LPA, SMTR, aDSM and decentralization of diagnostic, treatment and aDSM services; developing national guidelines for Bedaquiline while strengthening existing implementation pilot; developing next national strategic plan for TB (2018-20) and GF NFM phase II concept note (2018-20) with budgets to aim for universal access to quality TB care across DPRK. The recommendations were gracefully accepted by the top brass as the author exercised transparency and openness to suggestions from them to enable refinement, improvisation and ownership for enactment.
Findings/Observation

a) Progress from the last mission:

The last mission was held in September 2016. The progress was assessed based on observations made and interactions with key NTP stakeholders of DPR Korea.

<table>
<thead>
<tr>
<th>SN</th>
<th>Priority Recommendations</th>
<th>Progress</th>
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<tbody>
<tr>
<td>1</td>
<td><strong>Laboratory strengthening:</strong> Provide close supervision to NRL until consistently proficient in first-line DST; develop an Xpert expansion plan: clarify the role of LPA in the case finding algorithm, and provide assistance to set-up the 1st Regional Reference Laboratory.</td>
<td>Partly met - ongoing</td>
</tr>
<tr>
<td>2</td>
<td><strong>Treatment:</strong> For clinically well patients: urgently discontinue the second-line injectable, if given for &gt;8 months. Adjust drug dosages according to most recent weight-based dosing recommendations (2014 WHO Guidelines).</td>
<td>Met</td>
</tr>
<tr>
<td>3</td>
<td><strong>Shorten the waiting time</strong> of a) presumptive DR-TB patients to diagnosis, and b) confirmed patients to treatment by providing options for sputum transport, and initiation of treatment outside the scheduled visits of the central mobile team.</td>
<td>Not Met</td>
</tr>
<tr>
<td>4</td>
<td><strong>Pharmacovigilance:</strong> Provide a mechanism for PMDT sites to easily request central level for ancillary drugs; Strengthen ADR management by request for technical assistance.</td>
<td>Partly met - ongoing</td>
</tr>
<tr>
<td>5</td>
<td>Strengthen <strong>central leadership</strong> in PMDT implementation and mandate its mainstreaming to routine NTP program: Allow more involvement of provincial level and hospital staff in PMDT case finding, treatment, treatment follow-up, drug management, reporting, monitoring and supervision.</td>
<td>Partly met - ongoing</td>
</tr>
<tr>
<td>6</td>
<td><strong>Harmonization:</strong> Conduct a sit-down meeting with Eugene Bell Foundation, and twice yearly thereafter to consolidate and share country accomplishments, challenges and plans.</td>
<td>Partly Met - ongoing</td>
</tr>
<tr>
<td>7</td>
<td><strong>Case finding:</strong> Expand testing criteria for DR-TB to a) other retreatment cases (relapse, return after loss to follow-up) and b) DOTS non-converters.</td>
<td>Not met</td>
</tr>
<tr>
<td>8</td>
<td><strong>Procurement:</strong> Provide special assistance to DPRK as a member state in the procurement of Xpert and other equipment.</td>
<td>Met</td>
</tr>
<tr>
<td>9</td>
<td>Seek <strong>Technical assistance</strong> for the following: Infection control (priority) ADR management (priority) Conduct of a Training of Trainers in PMDT Electronic R and R Active pharmacovigilance</td>
<td>Partly Met - Ongoing</td>
</tr>
<tr>
<td>10</td>
<td><strong>Drug management:</strong> urgently redistribute the Nov 2015 expiring Cycloserine among PMDT sites to avoid wastage.</td>
<td>Met</td>
</tr>
<tr>
<td>11</td>
<td>Align country <strong>PMDT Report Forms</strong> for Detection and Enrolment with WHO recommended forms.</td>
<td>Not Met</td>
</tr>
</tbody>
</table>
b) Current status of country PMDT implementation:

PMDT services are available in selected county TBS and PTH in 5 out of 12 provinces of DPR Korea. The diagnosis and treatment services are not regular but are provided at intervals of three months with service interruption in between. A team of CTPI visits selected TBS out of the designated DR-TB treatment centers on monthly basis to collect specimen from failures of first line treatment or contacts of MDR-TB cases only and get them to NRL to test mainly on solid culture-DST as the existing Xpert-MTB Rif machine is sub-optimally utilized due to uninterrupted supply of cartridges. A line-list of MDR/RR-TB cases is thus developed and maintained awaiting drugs. Treatment initiation is done in six monthly cohorts whenever SLD are supplied through GDF via UNICEF, the PR of TGF. Intermittently, the non-resident EBF team visits the 12 county TBS under their project area with mobile Xpert-MTB Rif and SLD, tests line-listed presumptive MDR-TB and starts lab confirmed RR-TB cases on MDR-TB treatment. The EBF team visits four times in a year and rest of the time the 4 Xpert machines under their project are not available for routine use. Standard MDR-TB regimen is prescribed after an incomplete set of pre-treatment evaluation by doctors/CTPI/EBF team at TBS/PTH as all investigations are not available at TBS/PTH. All lab confirmed MDR/RR-TB patients are hospitalized for the complete duration of treatment. Patients are provided MDR-TB treatment free of cost, follow up cultures, nutritional support, wages protection and counseling to the patients under NTP DPR Korea as vertical services. aDSM is limited by lack of lab investigations, equipment and clinical capacity. Specialist and emergency consultation is arranged through nearby county general hospital.

In 2015, only 336 (2%) of previously treated cases were tested for RR-TB and 125/209 (60%) lab confirmed RR-TB cases were initiated on standard MDR-TB treatment of 18 month duration. This amounts to treatment coverage of only 3% of 4600 notified and 2% of 6000 incident MDR-TB cases as compared to treatment coverage of >80% incident drug sensitive TB cases estimated in DPR Korea. However, the treatment success in the initial annual cohort of 50 patients has been reported at 86% which is commendable. From mid-2015 to mid-2016, 359 MDR-TB patients (plus 583 MDR-TB patients by EBF) have been initiated on treatment so far leaving behind 25 diagnosed cases as drug courses assigned to a patient is completely reserved and not used in part to initiate any other patient. Further, at Sadong TBS, 11 XDR TB cases diagnosed by EBF through Korea Institute of Tuberculosis (KIT), Seoul, South Korea have been initiated on Bedaquiline with optimized background regimen as a pilot since September 2016.
c) Key challenges identified in this mission (In order of priority):

The key challenges identified in the current mission are enlisted below:

1) PMDT services yet to be available nationwide pending 7 provinces and not yet on a seamless basis in the existing 5 provinces, primarily due to severe resource constraints including funding as a consequence of sanction leading to very low investment in lab infrastructure, equipment, maintaining uninterrupted supplies of diagnostics and second line drugs and capacity building.

2) Limited understanding of epidemiology of TB and DR-TB in the country. Prevalence of RR-TB through a short survey (~400 sample size) conducted in one province using GeneXpert. Extent of H mono/poly, fluoroquinolones (FQ) & second line injectables (SLI) resistance is unknown. Risk groups for active case finding not clearly defined, although the recent national TB prevalence survey offers opportunities.

3) Bedaquiline has been introduced under a pilot project (compassionate use programme) by EBF with UNITAID support and concurrence of NTP after on-site capacity building in Sadong TBS. However, this needs to align with the WHO Interim Guidelines to comply with the five conditions for countries before introduction and policy implementation package for newer drugs. National guidelines for use of Bedaquiline need to be developed with in-country regulatory approvals that are missing elements.

4) Existing integrated TB & PMDT guidelines is too restrictive to offer DST only to TB patients who are failures of first line regimen and contacts of MDR-TB cases. The guidelines are yet to be updated with recent WHO PMDT Guidelines – 2016 that recommends SMTR and SL-LPA.

5) The next one year is critical for planning the new NSP 2018-20, the NFM Phase II proposal and greater political commitment for investment to End TB in DPR Korea.

6) Existing PMDT expansion plan - 2018 needs to be reprogrammed to regularize PMDT services on daily basis and to adjust for revisions anticipated in the PMDT Guidelines.

7) Laboratory capacity is limited (1 solid C/DST & 1 Xpert), constrains PMDT expansion.

8) Sample collection and transport is done by CTPI team during their scheduled monthly visit at selected TBS/PTH with no access to services in the interim period between visits.

9) Unacceptable delays observed in diagnosis & treatment due to systemic PSM issues.

10) Health system strengthening opportunities with PMDT service expansion are missed.

11) PMDT services are completely centralized in all aspects that contributes to system delays and patient inconveniences.
## Conclusion: priority recommendations:

<table>
<thead>
<tr>
<th>SN</th>
<th>Recommendations (preferably not more than 10)</th>
<th>Responsible agency/ Person</th>
<th>Time frame</th>
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<tbody>
<tr>
<td>1</td>
<td>Expedite complete geographical coverage of PMDT services with current DST criteria and expand offer of DST to previously treated cases (including relapse) followed by new cases while enhancing investments in diagnostic and treatment capacity</td>
<td>NTP, PMU with TA from WHO</td>
<td>August 2017</td>
</tr>
</tbody>
</table>
| 2  | Know your TB and DR-TB epidemiology to prompt local epidemiology guided cost-effective strategies  
    - Interim – FL-SL DST to 356 culture positive isolates  
    - Conduct and complete National DRS | NTP, NRL, SNRL TA from WHO                  | Mar 17 Dec 17          |
| 3  | Comply with WHO Interim Bedaquiline Guidelines and Policy Implementation Package for newer drug by developing clear national guidelines, get in-country regulatory approvals and build capacity of Sadong TB Sanatorium for ADR management and monitoring. | NTP, PMU, EBF, WHO                          | June 17                |
| 4  | Revise NTP TB Guidelines with PMDT to align with End TB Strategy and recent WHO PMDT Guidelines 2016 to introduce Shorter MDR regimen and second line LPA in DPR Korea | NTP, PMU with TA from WHO                   | May 17                 |
| 5  | Develop NSP 2018-20 and GF NFM Phase II proposal with budgets to aim for universal access to TB care | NTP, PMU with TA from WHO                   | May 17                 |
| 6  | Update the PMDT Expansion plan – 2018 and re-programme the available resources to regularize PMDT services on daily basis and to adjust for revisions anticipated in the PMDT Guidelines. | NTP, PMU, EBF, WHO                          | Mar 17                 |
| 7  | Expedite laboratory capacity expansion with rapid molecular DST to facilitate faster expansion of PMDT | NTP, NRL, CFK, EBF and WHO                  | May 17                 |
| 8  | Transition to bottom up specimen collection and transport system from Ri and Dong levels to the labs | NTP, NRL, PMU and WHO                       | May 17                 |
| 9  | Minimize delay in diagnosis to treatment pathway and regularize PMDT services by addressing PSM issues | NTP, PMU, UNICEF, WHO                       | May 17                 |
| 10 | Harness the health system strengthening opportunities with PMDT service expansion | NTP, PMU and WHO                            | Nov 17 & ongoing       |
| 11 | Plan for a systematic phased decentralization and expansion of PMDT services | NTP, PMU and WHO                            | Nov 17                 |

The NTP Manager, Vice Director and WR DPR Korea also requested the author to continue providing inputs after the mission on the draft protocol on national drug resistance survey, revision of the national TB and PMDT guidelines, development of the next national strategic plan 2018-20 and the GF NFM Phase II concept note for 2018-20.
II. Detailed report:

A. Introduction/Background

The Democratic People’s Republic of Korea (DPRK) is situated in the north eastern part of Asia; spread over 120 thousand square kilometers, 80% of which are mountains. Administratively, DPRK is divided into 12 provinces with 3 major cities viz. Pyongyang, Rason and Nampo. Provinces are divided into cities (districts) and counties. A county is further subdivided into smaller geographic areas called Ri, (Gu, Dong). County town called Urban Cities (districts); on the other hand, consist of administrative areas known as Dong. In big cities, the dongs are grouped into administrative units called districts. The 2008 census placed the total population at 24.76 million; ~61% percent resides in urban areas.

DPR Korea is one of the high TB and MDR-TB burden countries in the South-East Asia Region. TB and MDR-TB has been a major public health problem in DPR Korea. In 1998, the Ministry of Public Health (MoPH) adopted DOTS and was expanded nationwide by 2003. DPR Korea initiated PMDT services with external support of Eugene Bell Foundation (EBF) in 2008 and technical assistance from WHO Country Office. Since then, EBF, a non-residential international NGO, diagnoses MDR-TB cases using GeneXpert brought into the country during their biannual in-country visits and provide the NTP with Second-Line TB drugs, nutrition supplies and blankets, etc. to support in-patient care in select MDR-TB treatment sites. This effort was further complemented by the Global Fund support through UNICEF since 2012. In 2012, the national PMDT guidelines were finalized through a process of wide stakeholder consultation and expert reviews and updated in 2015. From June 2012, identified cases were enrolled on treatment with second line drugs (SLDs) supported through the Global Fund grant. Christian Friends of Korea (CFK) has also been supporting DPR Korea particularly in laboratory capacity development. In terms of MDR-TB treatment model, the recent multiple platforms, e.g. discussions during JMM, processes for updating the National TB Control Strategy (2015-2018) and inclusive country dialogue for application of GF NFM grant (2015-2018) could have provided the NTP and in-country partners with better understanding and consensus on the most appropriate approaches to maximize the cost-effectiveness of scarce resources for PMDT (Programmatic Management of DR-TB).
To reach appropriate level of condition for quality MDR-TB care with the limited resources, in the end of 2014, Ministry of Public Health made decision to hospitalize MDR-TB patients in a province to its PTH in which adequate human resources and infrastructure to deal with DR-TB patients are available, instead of county TB sanatoria, taking into account the higher benefit of PTHs in the aspect of program management and patient care.

This is the fifth monitoring mission for Programmatic Management of Drug-Resistant TB (PMDT) component of the National TB Control Program (NTP) of the Government of DPR Korea (GoDPRK) undertaken on behalf of Regional Green Light Committee (r-GLC) of World Health Organization - South East Asia Region (SEAR) from 7 – 18 November 2016.

The two weeks long mission covered briefing meetings with key officials of TB programme management unit (PMU) under NTP, MoPH and WHO DPR Korea (AO, TO-Malaria & NPO-TB), visit to key health care facilities like National TB Reference Laboratory (NTRL) at Central TB Preventive Institute (CTPI), Sadong and Sosong district TB sanatoria (TBS) in Pyongyang city province, specialized provincial TB hospital (PTH) at Kwaksan county of North Pyongan, TB PMU and WHO Country Office of DPR Korea. During the mission, specific meetings were done with key officials from MoPH, GoDPRK viz. Dr Ri Chan Hyok, Vice-Director of Department of External Affairs, (Global Fund Coordinator); Dr Choe Tong Chol, NTP manager, Director of Department of Communicable Disease, Hepatitis and Tuberculosis; Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis (focal person for EBF); the team from TB PMU, CFK and WHO DPR Korea. Discussion could not be arranged with UNICEF and Global Fund representatives during the mission.

The mission also covered a technical training of NTP staff in PMDT at Pyongyang with special focus on the updated WHO PMDT Guidelines – 2016. This training covered updates on Case finding and Diagnostics including Second Line – Line Probe Assay (SL-LPA), updates on treatment including Shorter MDR-TB Regimen (SMTR), introduction of newer
drugs (ND) like Bedaquiline (BDQ), Delamanid (DLM) and effective management of adverse drug reactions (ADR) including concepts of active drug safety monitoring (aDSM).

The objectives of the mission were
- To assess the **progress made** in PMDT activities since last rGLC mission in 2015
- To review **status and plans** of PMDT scale up in DPR Korea
- To review **partner’s support** in PMDT and discuss **harmonization** in line with “End TB Strategy” on PMDT
- To provide **recommendations** for implementation and further expansion of PMDT services for next one year in DPR Korea
- To provide **technical training** on PMDT, technical consultation on WHO recommended **shorter regimen** for adaptation and **assess possibility of its roll-out** in DPR Korea

The activities include comprehensive review of services in terms of patient care, programme management, supervision monitoring systems, community engagement, information communication systems for TB/DRTB, interactions with key officials, doctors, staff, specialists, patients, community representatives at the sites visited to analyze the progress made and plans developed for TB and PMDT implementation in light of the last year PMDT mission report, the PMDT expansion plan 2018, the current national PMDT guidelines and the explore the potential for rapid roll-out of the updated WHO PMDT guidelines particularly SMTR and SL-LPA.

### B. Existing TB control program

#### TB Burden:

DPR Korea is listed as a high TB and MDR-TB burden country among the updated list of top 30 highest burden countries of the world to be used by WHO during the period 2016–2020. The TB burden and profile of DPR Korea published in Global TB Report 2016 is annexed with this report. The epidemiological analysis and the national TB prevalence survey conducted by NTP recently were also referred to. The salient observations are as follows:
- In 2015, TB mortality is estimated at 15000 (61/100000 population) while incidence is estimated at 141000 (561/100000 population) for TB in DPR Korea.
- Notification of all forms and all forms of newly notified TB case rate per 100,000 population has increased continuously over the period of 1998-2013 with geographical heterogeneity between provinces. With this impressive increasing trend and 120722 TB patients notified in 2015, DPR
Korea has achieved 80% treatment coverage of 141000 estimated incident TB cases (561/100000) which is commendable, leaving a treatment gap of ~20% based on the reported estimates.

- Preliminary results of the recently conducted national TB prevalence survey by MoPH in DPR Korea reveal a prevalence of ~640/100000 that would enhance the treatment gap for drug sensitive TB.

- Treatment success consistently above 90% among incident TB cases and above 80% among previously treated TB cases as well as MDR TB cases for the cohorts of 2012 and 2013. It is claimed that this is mainly due to early detection through active case finding, high DOT compliance and robust regimen. However, with increasing notification of all types of TB cases particularly relapses (figure below), the trends of treatment outcomes have started to decline in the recent annual cohorts as depicted in the adjoining figure.

- Interestingly over the past few years, newly notified pediatric TB case notification rate for the age group of 0-4 has been shown to be at steady level since 2011 compared to an increasing trend in the age group of 5-14 and peaks in the age group of 45-54. Although this could indicate checked transmission among pediatric TB cases and elderly, it may also point to the need for a higher sensitivity diagnostic test like Xpert-MTB-Rif to be clubbed with active case finding efforts to find more cases among these vulnerable and access restricted groups. This would also provide the opportunity of same day and accurate diagnosis of RR-TB along with M-TB among these groups like those identified through active case finding.

- In absence of the private sector, active case finding for TB, regulated supply of quality assured anti-TB drugs through NTP and government ware-houses supply chain system, ambient temperature favorable for maintaining efficacy of drugs in storage conditions, infection control through separation of infectious cases till rendered non-infectious through prompt treatment, sustained high treatment success rates are factors that could prevent emergence and spread of drug-resistance.
NTP & its structure:

In 1998, the Ministry of Public Health (MoPH) adopted DOTS and was expanded nationwide by 2003. The Department of Communicable Disease, Hepatitis and Tuberculosis is in-charge of policy development and planning, organization of TB services, provision of technical support, communications and international partnerships. The TB services are delivered through the general public health system consisting of health facilities in 10 provinces and 2 major cities, 208 counties and over 7,000 dong/ri units, and TB specific institutes at the central and provincial level, and county levels.

At the central level, the Central TB Preventive Institute (CTPI) is the highest technical unit and provides technical support, laboratory and treatment services, training, M & E, routine programme supervision, recording & reporting and research. A central 100-bed hospital attached to CTPI provides clinical services for TB patients. The National TB Reference Laboratory (NTRL) is part of the CTPI and is responsible for external quality assurance (EQA) for the smear microscopy network, and performance of culture and drug susceptibility testing (DST). The central level works in close collaboration and guidance of MoPH.

At the provincial level, there is a Provincial TB Preventive Institute (PTPI), the Laboratory of the PTPI, and the Regional TB Reference Laboratory (RRL). The county level is represented by the TB section of the County hospital with a laboratory. There are county sanatoria with TB laboratories. The most peripheral units are the Ri (rural PHC) and Dong (urban) clinics manned by TB doctors and household doctors. The TB institutes at provincial and city/county levels works in close collaboration and guidance of Provincial and City/County People’s committee respectively.

The Central Medical Warehouse (CMW) is the central unit of a parallel department within the MoPH that manages the drug supply chain, with corresponding Provincial Medical Warehouses and County Medical Warehouses.

UNICEF is the principle recipient of the Global Fund grants under the New Funding Model with WHO Country office for Korea and NTP being the sub-recipients. There exists a coordinator, an officer for monitoring and evaluation and 4 NPOs appointed through UNICEF for grant management. The Global Fund also supports the Project Management Unit (PMU) that is integrated in the NTP and manages grant implementation. The PMU manages both the TB and malaria programs, including procurement supply chain. A PMDT Officer at the PMU provides assistance to the NTP Manager for the PMDT implementation.
While the health infrastructure and workforce is mainly contributed by the GoDPRK, the global fund supports equipments, lab consumables, drugs, trainings, and technical assistance through PMU for drug sensitive and drug resistant TB.

Observation:

- **Epidemiology of TB and DR-TB is incompletely understood**
  
i. While the national DRS being planned in 2017, the current PMDT Policy & Plans are based on a small scale TB DRS with Xpert conducted in one province
  
  -- MDR-TB is 2.2% in new and 16.3% in previously treated cases
  
  -- No information about H mono/poly or additional second line drug resistance or XDR-TB
  
  ii. National TB Prevalence survey report is expected by Feb 2017 when an epi-analysis by an external expert is proposed which could inflate the estimates of MDR-TB
  
  -- yielded 356 positive cultures stored at NRL Pyongyang
  
  iii. Active case finding approaches need re-designing with clear delineation of vulnerable groups and the effort is compromised with absence of greater sensitivity diagnostic algorithms with new tools like digital chest-X ray and Xpert-MTB-Rif.
  
  iv. Paper based TB/DR-TB surveillance system with aggregated reporting does not serve epidemiological intelligence to the programme for policy refinements.

Recommendations:

- **Know your TB and DR-TB epidemiology to prompt local epidemiology guided cost-effective strategies**

  **Suggested steps:**
  
i. Develop protocol, mobilize resources, complete preparation and initiate the National DR survey in DPR Korea with support from SNRL Hong Kong / Chennai for FL & SL DST on MGIT and whole genome sequencing.
  
  ii. Explore support from SNRL Hong Kong/Chennai to immediately undertake FL & SL DST on MGIT and whole genome sequencing on the 356 positive culture isolates from the Prevalence Survey to get indicative community level prevalence of DR-TB in new and PT cases to facilitate epi-analysis in Feb ‘17 and strategic planning by which time the national DRS results cannot be available to guide strategies.
  
  iii. The clinically and socially vulnerable groups need to be clearly enlisted and defined in the national guidelines to reach the unreached. The data from the national TB prevalence survey and the upcoming national DRS survey must be analyzed carefully to identify these vulnerable groups along with a thorough literature review of published studies among TB patient in DPR Korea. Rational cost-effective active case finding approaches need to be re-designed with high sensitivity screening with symptoms and digital chest X-ray and reliable rapid diagnostic tools like Xpert-MTB-
Rif for same day confirmation for TB and RR-TB could yield the maximum cases missing from treatment.

iv. Initiate the planning for investment in an electronic case-based TB data management and patient tracking system to serve as a robust electronic surveillance system for all forms of TB that could also serve for a dynamic epidemiological intelligence system in the country to identify hot-spots, cold-spots, track migrants and facilitate rational investments in cost-effective strategies to yield maximum outputs within available resources.

Responsibility: NTP, NRL, SNRL, TA from WHO
Timelines: Jan 17 / Dec 17

C. Information on M-/XDR-TB

To get the 1st line drug-resistance profile and assess the feasibility to conduct a countrywide drug resistance survey, a small-scale drug resistance study using Gene Xpert has conducted in 13 cities and counties of North Hwanghae province in November 2013 to February 2014. The result of the small scale drug resistance study was reported as 1.93% MDR-TB cases among new cases and 15.31% MDR-TB cases among previously treated patients. This extrapolates to an estimate of an incident 6000 (24/100000 population) MDR TB emerging in DPR Korea annually. Preliminary results of the national TB prevalence survey would further extrapolate to an estimate of ~8000 MDR-TB emerging annually in DPR Korea.

Increasing trend of previously treated cases particularly relapses, estimated TB cases missing from treatment and negligible levels of access to rapid DR-TB diagnosis with prompt appropriate treatment among all notified TB cases, lack of community level infection prevention practices and model of care balancing infection control with access to DR-TB care at decentralized levels could be potential risk factors to promote propagation of drug resistant TB in DPR Korea.

Progress made in past 4 years in scaling up PMDT services has been slow since its inception in mid-2012. At the moment, DPR Korea has covered limited counties in 5 out of 12 provinces with PMDT services under the NTP framework and is currently supported by commodity cum technical support by EBF, CFK and GF-NFM funding through UNICEF and WHO Country Office for DPR Korea. In 2012, 50 cases were received treatment from two PMDT sites in Pyongyang. In 2013, diagnostic services on solid C/DST results were initiated at the NRL after successful proficiency testing for INH (H) and Rifampicin (R) that formed the basis of treatment initiation. Since then, a total of 507 patients were enrolled on SLD treatment out of which the yearly cohorts of 170, 212 and 125 have been enrolled in 2013, 2014 and 2015 respectively. Currently, the NRL is preparing to initiate line probe assay (LPA)
pending infrastructure updates (3 clean rooms) and equipment installation to initiate DST for first and second line drugs as well as has initiated proficiency testing for second line DST on solid (C-DST).

In 2015, only 336 (only 2%) of previously treated cases were tested for RR-TB and 125/209 (only 60%) lab confirmed RR-TB cases were initiated on standard MDR-TB treatment of 18 month duration as reported in the Global TB Report 2016. This amounts to treatment coverage of only 3% of 4600 notified and 2% of 6000 incident MDR-TB cases as compared to treatment coverage of >80% incident drug sensitive TB cases estimated in DPR Korea. However, the treatment success in the initial annual cohort of 50 patients has been reported at 86% which is commendable. From mid-2015 to mid-2016, 359 MDR-TB patients have been initiated on treatment so far leaving behind 25 diagnosed cases as drug courses assigned to a patient is completely reserved and not used in part to initiate any other patient.

Over and above this, in 2014 & 2015, the EBF enrolled ~900 and ~600 MDR-TB patients on treatment respectively at 9 TB sanatoria and 3 PTHs concentrating around Pyongyang City, South Pyongan, South Hwanghae and North Hwanghae provinces. Further, at Sadong TBS, 11 XDR TB cases diagnosed by EBF through Korea Institute of Tuberculosis (KIT), Seoul, South Korea have been initiated on Bedaquiline with optimized background regimen as a pilot since September 2016. These cases although notified to the NTP, are not yet reported in the WHO Global TB Reports.

In spite of four years of PMDT experience in DPR Korea, only 336 (2%) of previously treated cases and no new cases were tested for Rifampicin Resistance. Also only 125/209 (60%) lab confirmed RR-TB cases initiated on MDR-TB treatment in 2015.

Thus, in contrast to 80% treatment coverage of incident TB cases, the MDR/RR-TB treatment coverage (started on treatment for MDR-TB) is only 3% of 4600 estimated MDR among notified pulmonary TB cases and only 2% of 6000 incident MDR-TB cases, the lowest among the 30 high MDR-TB burden countries and WHO regions of the world (figure enclosed)

Treatment success rates of MDR TB was observed to be 86% (2012 cohort of 50 patients) that has dropped to 84% (2013 cohort of 170 patients) which needs to be checked.
Observations:

- **PMDT services yet to be available nationwide (5/12 provinces)**
  i. PMDT services initiated in 2012 in 2 sites, but till date only 5/12 provinces have interrupted PMDT case finding strategies. This is primarily due to very low investment in capacity building and maintaining uninterrupted supplies of diagnostics and drugs.
  ii. PMDT trainings of key staff of PTH and TB Sanatorium of remaining provinces and counties ongoing
  iii. Remaining preparatory activities to be completed are
    - Establish PMDT committees in the remaining PTPI
    - Cascade PMDT training of staff up to Ri/Dong level in all provinces and counties
    - Arrangement for line-listing suspects, sample collection and transport, lab linkage for DST and follow up culture, pre-treatment and follow-up investigations, IC compliant wards, supply of SLD with ancillary drugs for AE management, referral linkage and record-report format distribution

Recommendations:

- ** Expedite complete geographical coverage of PMDT services with current DST criteria and expand offer of DST to previously treated cases (including relapse) followed by new cases while enhancing investments in diagnostic and treatment capacity**
  **Suggested steps:**
  i. Guide the PTPIs to develop an operational PMDT rapid expansion micro-plan to roll-out services with current DST criteria and monitor its implementation monthly over next 9 months
  ii. Complete PMDT training of all staff at remaining PTH and TB Sanatorium and ensure funding for cascade trainings
  iii. Complete all the pending preparatory activities listed above in all PTH and selected TB Sanatorium in each province to begin with
  iv. All provinces to roll-out PMDT diagnosis and treatment services
  v. Forecast the numbers of Xpert-MTB Rif, LPA labs, treatment centers with IC required, DST demand, RR-TB treatment demand, SL-LPA demand, social protection cost required to test all previously treated cases in year one and embark on all new TB cases in next two years across DPR Korea and enhance investments for these to ensure uninterrupted supplies of X-pert cartridges, C-DST consumables and second line drugs (initially through re-programming existing funds and remainder through next GF NFM II proposal). Aim to achieve 90% treatment coverage of estimated MDR/RR TB patients by 2020.
  **Responsibility:** NTP, PMU with TA from WHO
  **Timelines:** August 2017
D. Government commitment

The MoPH and NTP are committed to implementation of Programmatic Management of Drug Resistant TB (PMDT) and incorporating the WHO recommendations. This commitment translates into the high quality coverage and performance of the NTP in dealing with drug sensitive TB described above. However, the pace of expansion and MDR TB treatment coverage is the lowest among the 30 high burden countries of the world in 2015 as described above. PMDT service expansion is severely constrained by lack of resources to invest in diagnostics and treatment expansion across the country. In 2016, of the total national TB budget of around 30 million USD, only 19% and 27% were reported to be funded by domestic and international funding sources while 54% remained unfunded, the largest funding gap faced by the country in the past five years. This funding gap is exponentially increasing as the domestic and international funding continues to decline since 2014. However, it was learnt during interaction with stakeholders that the government acts humble in completely reporting the expenditures particularly in infrastructure, human resources etc. leading to a larger funding gap and magnified contribution from international agencies to address the funding gap. The MoPH has developed a PMDT expansion plan however; most of it is not yet completely budgeted under the GF NFM or the domestic sources and need to be revisited. The major areas of funding gap identified include diagnostic capacity expansion (equipment, consumables, training, sample transport); treatment capacity (decentralized IC complaint DR-TB treatment centers with aDSM capacity, uninterrupted supply of adequate quantities of quality assured second line drugs), ICT interventions for surveillance and adherence monitoring, patient support and enablers (social protection, nutrition, adherence support, travel support) etc. There are country specific limitations learnt in procurement of certain commodities necessary for scale up of PMDT services, while the government is committed in investment towards building capacity of infrastructure, human resource development, social protection to eliminate catastrophic expenditures etc.

Recommendations:

- Keeping in mind the sustainable development goals and end TB strategy targets as well as the country specific limitations, develop an end TB plan for 2030 (with 3 years intensified investment cum operational plan for scale up of epidemiology guided strategies [NSP 2017-20], 5 years strategic plan and 10 years vision documents) with
escalated rational funding requirements to have visibility into the landscape of funding required to guide appropriate fund raising from domestic as well as international sources. A multi-ministerial, multi-stakeholder consultation with technical and developmental partners may be useful to develop this plan.

- GoDPRK to correctly and completely reflect the realistic expenditures made on the TB programme to negotiate for a competitive counterpart international funding to meet the funding gap.
  
  **Responsibility:** NTP, PMU with TA from WHO  
  **Timelines:** March 2017

E. Partnerships within GoDPRK and with private sector

The general health system under the MoPH is the sole providers of services for TB and DR-TB in DPR Korea. It was conveyed that private sector do not exist in DRP Korea.

PMDT implementation commenced in DPR Korea with partnership through Eugene Bell Foundation since 2008, subsequently with CFK for laboratory strengthening, the Global Fund grant recipients like UNICEF, WHO Country office for DPR Korea etc. Apart from these there are smaller community level support groups who are engaged for patient care and support for ambulatory cases as well as for active case finding efforts.

There are numerous medical colleges across all provinces of DPR Korea, however, apart from academic activities there were no concrete evidences of their active engagement in PMDT service delivery and patient care.

**Recommendations:**

- Strategically engage all the departments/specialists of various Medical colleges across DPR Korea to capitalize on the strengths of each of them as care providers to TB and DR TB patients, referral centers for difficult cases requiring specialist intervention, as training centers and for research.
  
  **Responsibility:** NTP, PMU with TA from WHO  
  **Timelines:** June 2017
F. Advocacy and community engagement

It was learnt from interaction with the programme staff at national, provincial and county levels that advocacy and engagement efforts at the community level was undertaken by the Ri/Dong level staff particularly the household doctors while conducting active case finding activities and supervision. However, advocacy efforts for fund raising to meet the funding gap requirements after a clear understanding of the strategic plans and budgets developed through a stakeholder consultation process as recommended above.

G. Case finding strategy

DR-TB diagnosis and treatment services are episodic i.e. provided at intervals of three months with service interruption in between. For DR-TB case finding, a team of CTPI visits selected TBS out of the designated DR-TB treatment centers on monthly rotation basis to collect sputum specimen from failures of first line treatment or contacts of MDR-TB cases only and get them to NRL to test mainly on solid culture-DST as the existing Xpert-MTB Rif machine is sub-optimally utilized due to uninterrupted supply of cartridges. Intermittently, the non-resident EBF team visits the 12 county TBS under their project area with mobile Xpert-MTB Rif and SLD, tests line-listed presumptive MDR-TB and starts lab confirmed RR-TB cases on MDR-TB treatment. The EBF team visits four times in a year and rest of the time the 4 Xpert machines under their project are not available for routine use. The following diagnostic algorithm is being followed in the PMDT implementing areas of the country:

Although there exists a functional Xpert-MTB-Rif machine at NRL and incorporated in the diagnostic algorithm of DR-TB as above, most of the diagnosis is still done using solid culture-DST due to limited supplies of Xpert cartridges and LPA yet to be made functional as detailed in the next section.
Observations:

- **Unacceptable delays in diagnosis and treatment initiation is observed due to systemic procurement supply chain management (PSM) issues**
  
  i. The diagnostic algorithm for DR-TB is still being implemented with solid culture-DST offered to majority of the presumptive DR-TB patients leading to inbuilt delays of longer turnaround time.
  
  ii. PMDT services in DPR Korea are supply driven and not demand driven. Bulk diagnosis and treatment initiation in cohorts are done on six monthly basis as and when the SLD tranches arrive. Thus, it’s not a continuous service with prevailing long periods of enrollment interruptions.
  
  iii. Nearly six months are lost between identification of presumptive TB to treatment initiation calculated at TBS/PTH visited from random patient’s records.
  
  iv. Due to limited quantities of lab consumables / SLD courses and the policy of not utilizing available stocks reserved for one patient to treat the others, only women and patients of nearby county are given priority at PTH N. Pyongan.

- **Sample collection and transport done only on monthly basis by CTPI team**
  
  i. Sample collection and transport is done by the CTPI team by scheduled monthly visit to the TB sanatorium and PTH on line-listed presumptive DR TB patients (mainly failures of first line treatment).
  
  ii. This may not be sustainable as the country expands to more DR-TB sites
  
  iii. This leads to prolonged waiting period for presumptive MDR TB cases identified at the TB sanatorium.

Recommendations:

- **Minimize delay in diagnosis to treatment pathway and regularize PMDT services by addressing PSM issues**

  Suggested steps:
  
  i. Consider revision of the diagnostic algorithm for DR-TB to incorporate the strengths of rapid molecular DST using a combination of Xpert-MTB-Rif and second line LPA. The suggested algorithm for DPR Korea is enclosed at annexure 4.
  
  ii. Conduct a quick patient pathway analysis using a small sample size of 30 patients to assess the delays in the diagnosis treatment pathway of presumptive MDR-TB patients and identify interventions to minimize them.
  
  iii. Enhance case finding and treatment enrollments with available drugs and uninterrupted equitable supplies eliminating the waiting lists can be ensured through procurement quantification guided by consumptions.

Responsibility: NTP, PMU, UNICEF and WHO

Timelines: May 17
• Transition to bottom up specimen collection and transport system

**Suggested steps:**
1. Decentralize the sample collection at county level microscopy centers of the TB Sanatorium/PTH DR-TB centers to begin with.
2. Provide necessary training and three layer packaging material with gel packs for bio-safe packaging of specimen collected in cold chain.
3. Identify a focal person to transport the specimen with travel allowance.
4. Develop a regular scheduling system in coordination with NRL for transport as and when a presumptive DR TB case is identified.

**Responsibility:** NTP, NRL, PMU and WHO

**Timelines:** Feb 17

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**H. Laboratory services**

Quality assured microscopy centers are established at CTPI/NRL, at all PTPI/PTH and up to all County TBS levels as a three tier system with immediate higher level provides on-site supervision and external quality assurance to the immediate next level of laboratory. The quality of microscopy and the mechanism of quality assurance for smear microscopy were verified during visit to the microscopy center of North Pyongan PTH at Kwaksan County. Bacteriological confirmation and follow up of drug sensitive TB is primarily based on smear microscopy across DPR Korea since the inception of DOTS strategy in 1998.

DR-TB diagnostic services were introduced since 2008 when EBF provided laboratory services by transporting samples to KIT Seoul, South Korea. CFK brought in technical expertise, equipment and consumables to build capacity of NRL to conduct quality assured culture and DST for first line drugs as well as establishment of LPA lab under supervision and support of the SNRL Hong Kong. In 2013, diagnostic services on solid C/DST results were initiated at the NRL after successful proficiency testing for INH (H) and Rifampicin (R) that formed the basis of treatment initiation. One Xpert-MTB-Rif machine and 1000 cartridges were procured with support of WHO DPR Korea and staff trained jointly by CFK and WHO under periodic monitoring of SNRL Hong Kong. Recently, the FL and SL LPA testing kits as well as the missing rotor of the centrifuge have been supplied to the NRL through CFK support. Currently, the NRL is preparing to initiate line probe assay (LPA) pending infrastructure updates (3 clean rooms) and equipment installation to initiate DST for first and second line drugs as well as has initiated proficiency testing for second line drugs (Amikacin and Ofloxacin) on solid (C-DST).
Since the past few years, EBF brought in 4 Xpert-MTB-Rif machines for primary diagnosis of RR-TB while fresh samples from Sadong TBS are being transported to KIT Seoul for second line DST to FQ and SLI as part of the Bedaquiline pilot project.

Apart from the NRL, one regional reference laboratory at Hamhung City of South Hamyong province has been upgraded for solid C-DST and under proficiency testing for first line drugs while another regional reference laboratory is being developed for solid C-DST at Saiwon City of North Hwanghoe province. There is consideration of upgrading these labs in future with LPA.

On the rapid molecular diagnostic front, 4 additional Xpert-MTB-Rif machines and 6000 cartridges have been procured with support from WHO Country Office for Korea and supplied to Hamhund, Wansan, Chongjin and Nampo cities awaiting installation and training with support from WHO and CFK. Further, there is a plan to procure additional Xpert-MTB-Rif machines through WHO in the next year to cover all provinces with at least one Xpert-MTB-Rif machines at each of the 12 province PTPI/PTH level.

**Observations:**

- **Laboratory capacity constrains PMDT services**
  
  i. National Reference Laboratory that is certified for

  - Solid Culture – DST proficient for SHRE and PT for Am/Ofx initiated
  - 1 Xpert MTB-Rif sub-optimally used due to less cartridges and UPS issues
  - Training for FL-SL LPA conducted with available kits on site by SNRL in Sep ‘16
  - LPA yet to be functional due to

    a. Rotor of micro-centrifuge although arrived in the lab has yet to be fixed
    b. Space for 3 clean rooms for LPA processes yet to be made available as biochemistry and hematology labs are also housed in the same premise.

  - Actions on recommendations of SNRL report is yet to be completed

  ii. Two more regional reference laboratories are yet to be made functional

  - South Hamgyong PTPI, Hamhung - RRL staff retraining and PT in solid culture pending
  - North Hwanghae PTPI, Saiwon – Civil work up-gradation and staff training

  iii. 4 Xpert-MTB/Rif machines procured by WHO are yet to be installed, while 3 more machines planned to be procured this year and more to cover all 12 provinces by next year. Universal DST for ~104000 notified TB cases and ~15000 high risk cases (failures, contacts) for targeted DST is far from reach without further expansion of rapid molecular tests like Xpert-MTB-Rif.
iv. CFK has brought in technical expert for a short time to support laboratory capacity expansion in DPR Korea with limited resources; however, the country would need technical expertise on laboratory expansion for the next few years.

v. 4 additional Xpert-MTB/Rif machines are used by EBF during their quarterly visits

vi. An indigenous molecular technology is developed for H & R resistance in DPR Korea that need to be validated

Recommendations:

- **Expedite laboratory capacity expansion to facilitate faster expansion of PMDT services**
  
  **Suggested steps:**
  
  i. NRL to expedite making LPA operational by fixing micro-centrifuge rotors and placing the equipment in 3 clean rooms to initiate proficiency testing for FL and SL DST. Also fix the UPS issue or arrange for solar panel through partners and comply with recommendations of SNRL report.
  
  ii. NRL to also support the two regional reference laboratories to address bottlenecks in their establishment and proficiency testing. NTP to explore procurement of LPA equipment through reprogramming within the available resources at these two labs over the next one year and seek support from WHO and CFK for capacity building, on-site support and trouble-shooting to expedite its development.
  
  iii. 4 Xpert-MTB/Rif machines procured by WHO to be installed and operationalized at the earliest.
  
  iv. Expedite the procurement and operationalization of at least one GeneXpert machine per province by 2017 end. Further, to achieve universal DST with a benchmark of >90% testing coverage among notified TB cases for MDR/RR-TB diagnosis in DPR Korea would need ~ 50 GeneXpert (4 module machines) to test at least 90% of 141,000 incident TB cases as per 2015 report and 1 or 2 LPA lab (equipped with a twincubator and a high throughput GT blot machine) with first and second line kits supply.
  
  v. Seek support of CFK and WHO to conduct a national workshop on laboratory capacity strengthening to orient all PTPI/PTH lab staff in pre-requisites for development of Xpert-MTB-Rif laboratories, the test SOPs, maintenance, quality assurance and documentation aspects.
  
  vi. Optimally utilize the laboratory technical assistance provided through CFK in expediting the laboratory capacity enhancement endeavors and coordination with SNRL Hong Kong to fast-track recommended technical course corrections while simultaneously explore longer term funding assurance through domestic or international funding sources to sustain availability of such a technical expert till NRL/RRL teams of DPR Korea can confidently take over the laboratory services expansion and sustenance functions independently.
vii. Explore routine utilization of the 4 Xpert-MTB/Rif machines by EBF via WHO
viii. Expedite validation of the indigenous molecular technology of diagnosis of MDR-TB and publish the results

Responsibility: NTP, NRL, CFK, EBF and WHO
Timelines: May 17

I. Treatment strategy

A line-list of MDR/RR-TB cases is developed and maintained through the monthly visits for sample collection and testing at NRL by CTPI team awaiting supplies of next tranche of second line drugs. Treatment initiation is done in six monthly cohorts whenever SLD are supplied through GDF via UNICEF, the PR of TGF. Intermittently, the EBF team starts RR-TB patients on MDR-TB treatment on a three-monthly campaign mode. Standard MDR-TB regimen of 18 months duration is prescribed in accordance to WHO PMDT guidelines (2011) after an incomplete set of pre-treatment evaluation by doctors/CTPI/EBF team at TBS/PTH as some investigations like HIV, ECG, Blood sugar, renal function test and pregnancy test are not available at TBS/PTH. All labs confirmed MDR/RR-TB patients are hospitalized for the complete duration of treatment. Patients are provided MDR-TB treatment free of cost, monthly follow up cultures, six monthly chest X-ray, ADR monitoring/management, nutritional support, wages protection and counseling to the patients under NTP DPR Korea as direct patient support services. aDSM capacity is limited by lack of lab investigations, equipment and clinical capacity. Specialist and emergency consultation is arranged through nearby county general hospital. Surgery is conducted only for EP TB cases (non-thoracic sites) wherever surgeons and surgical facilities are available at PTH level. An operational research is currently ongoing at Pyongyang city province to compare feasibility and cost-effectiveness of three models of care for MDR TB patients viz. i) current model with hospitalization throughout treatment course, ii) part hospitalization with ambulatory care following culture conversion and iii) completely ambulatory model of care. Further, at Sadong TBS, 11 XDR TB cases diagnosed by EBF through Korea Institute of Tuberculosis (KIT), Seoul, South Korea have been initiated on Bedaquiline with optimized background regimen as a pilot since Sep 2016.

The following standard treatment regimens are currently used under NTP PMDT services:
- MDR/RR-TB regimen: (8) Z Km/Am Lfx Eto/Pto Cs ± PAS, (10) Z Lfx Eto Cs
- XDR-TB regimen: the following options are available
  1. Z-Bdq-Lfx-PAS-Lzd-Cfz-Amx/Clv
  2. Z-Mpm-Mfx-PAS-Lzd-Cfz (-Amx/Clv)
  3. Z-Cm-Mfx-PAS-Amx/Clv-Cfz-Lzd
  5. Z-OPC-Lfx-PAS-Lzd-Cfz - High dose H
At present, minor differences in treatment regimen and diagnostic algorithm are primarily due to operational considerations, though both are in line with recommendations of WHO PMDT Guidelines (2011 updates). The Central PMDT committee collects and compiles all information from EBF-supported and GF-supported MDR-TB treatment sites. Upon due comparison, the NTP will consider the appropriate way to define the standard MDR-TB management in the country.

Observations:

- **Existing integrated national TB & PMDT guidelines yet to be updated with recent WHO PMDT Guidelines - 2016**
  i. NTP, MoPH willing to expedite adoption of and invest in rapid molecular DST, SL-LPA, Shorter MDR-TB regimen, newer drugs, aDSM systems in DPR Korea as per WHO PMDT Guidelines – 2016
  ii. However, PMDT sections in NTP TB Guidelines and National Strategic plan are based on the old STOP TB Strategy ‘06
  iii. Case finding strategies are based on passive approach for TB and highly selective criteria for DST offer to patients failing first line treatment and contacts of MDR-TB
  iv. TB/DR-TB diagnostic algorithm based on old low sensitivity smear microscopy and solid culture-DST with long turnaround time to results.
  v. Institutional DR-TB treatment based on conventional long term regimen
  vi. Operational research comparing models of care underway. With existing ~4400 beds at all 110 TBS/PTH (~40 beds per TBSPTH), the policy of hospitalization throughout treatment for DR-TB patient will not be sufficient when the country reaches scale ~7200 (90% estimated RR-TB cases initiated on treatment for 18 months duration).
  vii. No mention of policy on second line DST, shorter MDR regimen, aDSM mechanisms and newer anti-TB drugs
  viii. Patient support does not cover transport cost and diet assessment with supplementation for TB patients and their exposed family.

- **Introduction of Bedaquiline through EBF with UNITAID support in Sadong TB Sanatorium needs to align with the WHO Interim Guidelines and policy implementation package for newer drugs**
  i. Eugene Bell Foundation adopted Sadong TB Sanatorium for a pilot introduction of Bedaquiline for XDR TB patient management with prior consent of NTP (??Compassionate use)
  ii. Samples are sent to KTI Seoul, South Korea for SLDST
iii. 11 XDR TB patient are initiated on BDQ containing regimen with Cm, Cfz, Lzd, Z since Sep ‘15
iv. aDSM system includes daily AE monitoring on clinical basis
v. Bio-chemical investigation and ECG done on monthly basis by CTPI team that visits
vi. 111 AE’s reported in 11 patients to date
   – All 11 had Vomiting, Insomnia, Clinical Arrhythmia, Dyspnoea, Gastritis, Skin pigmentation
   – Specialist consultation, management and monitoring of ADR was challenging for the doctors due to complete dependency on the CTPI team visit
vii. Patient informed consent were not observed to be obtained
viii. Standard protocol for BDQ introduction was not available for review during the mission
ix. NTP proposes to request for regulatory approval of the drug after the results of the pilot

Recommendations:

- Revise NTP TB Guidelines with PMDT with recent WHO PMDT Guidelines 2016 and End TB Strategy

  Suggested steps:
  i. Update DR-TB epidemiology, decentralize and integrate PMDT service organogram with DSTB on ambulatory basis reserving institutional care based on patient condition, ADR occurrence and extent of resistance.
  ii. Update TB/DRTB diagnostic algorithm with rapid molecular Xpert/SL-LPA aiming for universal DST and appropriate treatment
  iii. Reserve CXR for screening and smear/culture for follow up monitoring
  iv. Introduce shorter MDR-TB regimen for RR-TB and longer (20 month) regimen with/without newer drugs like BDQ/DLM for FQ and/or SLI resistant cases as per WHO recommendations
  v. Consider decentralized DR-TB care for ambulatory non-seriously ill cases after culture conversion by utilizing the existing household doctors at Ri/Dong levels for treatment support after a thorough capacity building.
  vi. Introduce active drug safety monitoring and management (aDSM) system to safeguard patients
  vii. Include social protection, nutrition, counseling, transportation to eliminate all anticipated catastrophic cost from the patient

Responsibility: NTP, PMU with TA from WHO
Timelines: March 17
• Ensure compliance to the WHO Interim Guidelines for BDQ and Policy Implementation Package for newer drug and capacity building of Sadong TB Sanatorium for ADR management and monitoring
  i. Review the BDQ protocol if any (not available for review during the mission) used in Sadong TB Sanatorium and align it with the WHO Interim Guidelines and policy implementation package for newer drugs.
  ii. Equip Sadong TB Sanatorium with all laboratory investigations, ECG machine with automatic QTC interval reader, Audiometer, Ophthalmoscope etc.
  iii. Establish a robust aDSM system as per WHO guidelines with specialists, particularly cardiologist on call linked to Sadong TB Sanatorium.
  iv. Ensure all necessary ancillary medicines for AE management are available in adequate quantities in Sadong TB Sanatorium.
  v. Expedite in-country regulatory approval and inclusion of BDQ in essential drug list of the country in light of the growing global evidences on efficacy and safety of BDQ in patients treated for MDR-TB.
  vi. Develop national guidelines for use of BDQ under NTP or integrate BDQ in the revision of national TB and PMDT guidelines.
  vii. Consider accessing avenues for free access to BDQ courses and its systematic introduction by NTP at other sites.

Responsibility: NTP, PMU, EBF and WHO
Timelines: Jan 17

J. Program management and coordination

The MoPH coordinates PMDT management including diagnosis and treatment irrespective of funding sources. The MoPH oversees the whole process and funding for MDR-TB management in the country to avoid any duplication of support from different donors.

Observations:

• PMDT services are centralized in all aspects that contributes to system delays and patient inconveniences
  i. The following PMDT services were observed to be centralized:
     – Sample collection and transport system
     – Drug Susceptibility Testing
     – Pre-treatment evaluation
     – Institutional management of MDR-TB throughout treatment
     – Bio-chemical investigation for ADR Monitoring
ii. With PMDT service expansion in future, decentralization of the above would be necessary for system to cope with the case load

Recommandations:

- Systematically decentralize PMDT services in all aspects that can minimize system delays and patient inconveniences in the diagnostic treatment pathway
  i. Enlist facilities up to which decentralization could be feasibly done for each of the above enlisted service delivery components
  ii. Plan for resource mapping, mobilization and capacity building of the concerned facilities where the above services are proposed to be decentralized.
  iii. Strengthen the supervision and monitoring components from the higher to the immediate next level of service delivery to ensure mentoring, troubleshooting and streamlining of services

Responsibility: NTP, PMU and WHO
Timelines: Nov 17

K. Drug management:

First line anti-TB drugs (4FDC) and all second line anti-TB drugs are centrally procured through GDF using the Global Fund grants by UNICEF. The supplies are in 6 monthly tranches. Apart from these, second line drugs are also brought in by the EBF during their episodic services when patients are initiated on treatment at the selected PTH/TBS they serve. There exists no domestic source of funding for drug procurement. Same is the case with procurement and supply of equipment, lab consumables for drug sensitive as well as drug resistant TB diagnosis

To ensure uninterrupted supply of drugs, the first line drugs (4FDC) are supplied from central to provincial to county warehouses in the form of complete 6 month courses per patients with a stocking norm of 3 months’ supply of complete 6 month courses maintained at the provincial and county warehouses. The Ri/Dong household doctors are provided with complete 6 months’ supply of 4FDC for every patient diagnosed as TB with an average 15 days to actual treatment initiation from county warehouses via TBS/PTH.

On the contrary, the second line drugs constituting the regimen are supplied from central to county warehouses to TBS/PTH with first supply to cover 6 months of all drugs in the intensive phase per patient followed by 3 monthly supplies of all drugs in continuation phase per patient. The stocking norm for county warehouses is 3 months’ supply per patient till end of treatment. Supplies are limited up to the TBS/PTH level as all patients are hospitalized and managed throughout treatment to date. Drugs are supplied in 6 monthly
tranches and utilized within one-two months of supplies to initiate MDR/RR-TB patients as per the wait list developed during the monthly sample collection and testing processes. There remains a lean time with no treatment initiation between these supplies in tranches. Drugs earmarked for one patient is not used to initiate treatment of any wait-listed patient. Thus PMDT services are in reality, supply driven and episodic.

Recommendations:

• Consider transitioning to a demand driven regular uninterrupted procurement supply chain for diagnostics and drugs to enable early diagnosis and prompt treatment initiation giving equal chance to all presumptive DR-TB patients to receive services as early as possible
  i. Forecast and procure sufficient quantities of second line drug courses to treat the patients of DR-TB diagnosed from all provinces as the numbers increase with the expansion of services to all provinces and the DR testing criteria.
  ii. Transition away from cohort based procurement to consumption based procurement of lab consumables and second-line drugs while maintaining stocking norms for regular supply of 3 monthly stocks per patient at provincial and county level. Stocking norm at Ri/Dong level could be considered along with the policy decision of decentralized ambulatory management of DR-TB patients.
  iii. Consider initiating patients in the wait list with drugs available on shelf for the patients already on treatment (of 18 months duration) keeping a 6 months buffer per patient maintained and adjust the quantification of the next drug order to cover for the remaining months of treatment of existing patients along with the full course of treatment for the next patients. This way, the number of patients put on treatment could be more than the number of patient courses ordered eliminating the waiting list and ensuring regular uninterrupted supplies for existing as well as new patients.
  iv. Consider greater investment in second line drugs forecasted balanced with diagnostics demand through the systematic PMDT scale up planning process with donor funding considering the country specific challenges with domestic funds.

Responsibility: NTP, PMU, UNICEF, TGF and WHO

Timelines: Mar 17
L. Recording and reporting, and data management

DPRK maintains a paper based recording and reporting systems. Paper printouts of forms, registers and quarterly reporting formats for case finding, interim culture conversion and final treatment outcome are sent to the TBS/PTH from CTPI. The reports are sent from TBS/PTH to CTPI through the PTPI concerned in aggregate numbers. The NTP also continues to collect and compile the treatment outcomes data from MDR-TB patient cohorts support by GF and compare the results with data from EBF. It is planned that the NTP will report aggregate MDR-TB data, including EBF and GF project data, to WHO, which will be presented in Global TB Report henceforth. Although there is software available at the central level to facilitate data management, this is only for aggregated data and not a case-based web-based data management system.

Recommendations are covered in Section B above.

M. Infection control & health systems

Infection control is an integral part of the PMDT guidelines however, there remains pertinent challenges to infection control posed by need for greater engagement with general health system, the limited access to case finding of infectious pool of cases early from the community and health care facilities described above as well as the climatic conditions demanding specific infection control interventions that could be effective tailored to the country specific needs.

Observations:

- **Health system strengthening opportunities with PMDT service expansion are missed**
  - Expansion of PMDT services opens opportunities for health system strengthening as follows:
    - Xpert MTB/Rif promoted for TB and RR-TB diagnosis is a multi-disease platform for molecular diagnosis of a variety of diseases like HIV Viral load, Hepatitis B, HCV etc.
    - Pre-treatment evaluation and monitoring adverse events in MDR TB patients particularly with the recommendation of shorter MDR regimen and newer anti-TB drugs require further investment in strengthening the laboratories at TB sanatorium as well as specific equipment’s like ECG, audiometer, ophthalmoscope for ADR monitoring
- Complex management and the range of adverse effects or drug drug interactions make MDR-TB a multi-systemic venture and require specialist’s consultations at regular interval for almost every patient.
- Infection control interventions for TB are common to and can protect from many airborne infections at various settings

Recommendations:

- **Harness the health system strengthening opportunities with PMDT service expansion**
  
  i. Invest in procurement of Xpert-MTB/Rif assay considering it’s potential to serve in future as a multi-disease platform particularly with high prevalence of Viral Hepatitis in Korea
  
  ii. Strengthen laboratories at PTH and TB Sanatoria to conduct the complete set of investigations required for pre-treatment evaluation and ADR monitoring
  
  iii. Equip the DR-TB centers at PTH and TB Sanatoria to monitor ECG, audiometry and ophthalmoscopy for specific ADRs that occur with newer anti-TB drugs
  
  iv. Establish strong referral network with general hospitals at county and provincial levels for specialist consultation, emergency managements and surgical interventions
  
  v. Update the infection control guidelines and integrate the same with the public health systems to become standard operating procedures and integral part of building designs of health facilities.

  **Responsibility:** NTP, PMU, WHO
  
  **Timelines:** Nov 17 & ongoing

N. Human resource, Training and Technical support strategy

Sufficient human resources and training for NTP implementation, management and monitoring are provided as well as trained mainly by GoDPRK. This includes functionaries of the various people’s committees and TB preventive institutes are central, provincial, county and Ri/Dong clinic levels. External technical support is provided by WHO Country Office for DPR Korea, CFK for laboratories, UNICEF through TFG for PMU under NTP and EBF external teams.

The recommendations for human resource capacity building are covered in the above relevant sections. The technical assistance need for laboratories is covered in the relevant section above.
The role WHO Country Office DPR Korea could play in supporting PMDT expansion to universal DST and appropriate treatment by 2020 is proposed below:

- Play a convening role to steer the country dialogue and major initiatives to advance the country towards geographical coverage and phase advancement to universal DST and appropriate treatment with shorter MDR-TB regimen or longer conventional MDR-TB regimen with newer anti-TB drugs.
- Provided Technical Assistance to NTP in the following potential areas:
  1. Epi analysis - National DRS Survey – Protocol Finalization, capacity building, monitoring, data analysis and publication
  3. Organization of Joint Monitoring Mission in Feb 2017
  4. NSP 2018-2020 and GF NFM Phase II concept note development with budgets for universal access to quality TB care
  5. Capacity building for PMDT expansion and system up-gradation to implement bold policies and strategies enshrined in new guidelines and NSP.
  6. Re-programming current available grants and advocating for above allocation funding if necessary

O. Supervision and monitoring of the programme

It was informed that the supervision and monitoring functions are aligned to the NTP technical arm hierarchy of CTPI, PTPI, County People’s hospital and Ri/Dong Poly clinics. Supervisory visits are regularly conducted from each level to the immediate lower level of services by designated supervisory staff. The corresponding laboratory hierarchy from NRL, to regional, provincial, county level microscopy centers for external quality assurance is also functional. At the community level, the TB doctors at the Ri/Dong level supervise the household doctors for their functions of active case finding and direct observation of treatment at clinic level followed by home visits of patients who do not show up for their daily FDC for first line treatment. DOT for DR-TB patients are currently done at the TBS/PTH level while patients are managed in the hospital throughout treatment. The treatment support/supervision systems existing for drug sensitive treatment could be capitalized upon for ambulatory DR-TB systems in future with capacity building.

It was informed that the performance review are also conducted in alignment with the NTP technical arm hierarchy of CTPI, PTPI, Country People’s hospital and Ri/Dong Poly clinics with the following methodology and frequency:

- At TB Sanatorium/County level – a meeting to review the progress of all indoor patients on treatment with first or second line drugs is conducted on fortnightly basis
• At County Health Committee level – a meeting to review the progress of all ambulatory patients on first line treatment with Ri/Dong Clinics TB doctors and household doctors is conducted on fortnightly basis and a monthly meeting with TBS staff is also conducted to review the case notification and case holding status including reasons for LTFU, ADR management, DOTS implementation.

• At Provincial Health Committee level – a meeting with Chief of County health committee and heads of TBS/PTH to review the progress in PMDT services, programme management, case notification and case holding status including reasons for LTFU, ADR management, DOTS implementation and administrative issues etc. is conducted on a monthly and quarterly basis

• At Central level – a bi-annual review meeting with Directors of PTPIs and Chief of Provincial People’s committee is conducted by MoPH/NTP/CTPI to review the progress in PMDT services, programme management, case notification and case holding status and administrative issues etc.

A standard set of supervisory checklists and monitoring indicators exists in the national PMDT guideline that need to be updated in line with the End TB Strategy while revising the national PMDT guidelines recommended earlier.

There was no opportunity to verify these processes that need to be sustained and strengthened as DPRK heads towards universal access to PMDT services across the country.

**P. PMDT plan including funding source (Part of national TB plan or separate)**

The MoPH has developed a PMDT expansion plan 2018, however; it is based on the old STOP TB Strategy as well as old PMDT guidelines and most of it is not yet completely budgeted under the GF NFM or the domestic sources and need to be revisited particularly in light of the fact that the next NSP 2019-21 as well as the NFM GF Grant phase II are also due for development in 2017.

**Observations:**

• **Existing PMDT expansion plan - 2018 needs to be updated**
  i. The expansion plan suggests geographical coverage of services by 2018 with only 1 LPA lab, 5 Xpert machines and 28 DR-TB centers (10 PTH, 18 Sanatorium)
ii. The broad provisions under the PMDT expansion plan 2018 are enclosed at annexure 5.

iii. The expansion plan is restricted by the following:
   - By year 2018 only 2000 (25% of estimated ~8000) MDR TB patients proposed for treatment
   - LPA for SL-DST not proposed
   - Pre-XDR / XDR TB patients not proposed for treatment
   - Up-gradation of all TB Sanatoria to serve as DR-TB treatment sites not proposed
   - Xpert MTB-Rif Cartridges not proposed
   - Shorter MDR-TB Regimen and newer drugs expansion not proposed

iv. The expansion plan would have a total SLD gap of ~483 patients by 2018 as below:

<table>
<thead>
<tr>
<th>Patient courses of SLD</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expansion plan</td>
<td>500</td>
<td>1000</td>
<td>2000</td>
<td>3500</td>
</tr>
<tr>
<td>GF NFM (savings adjusted)</td>
<td>325</td>
<td>705</td>
<td>425</td>
<td>1455</td>
</tr>
<tr>
<td>EBF</td>
<td>662</td>
<td>600</td>
<td>300</td>
<td>1562</td>
</tr>
<tr>
<td>Total Surplus/Deficit</td>
<td>487</td>
<td>305</td>
<td>-1275</td>
<td>-483</td>
</tr>
</tbody>
</table>

- The next one year is critical for planning the new NSP 2018-20, the NFM Phase II proposal and greater political commitment for investment to End TB
  i. Revision of TB and PMDT Guidelines, bold policy decisions and new epidemiological realities with national TB prevalence survey and the planned National DRS survey would need a defined multi-fold investment to reach out to the missing TB and MDR-TB cases as per End TB Strategy.
  ii. The current NSP 2015-18 has to be updated in line with End TB Strategy along with the PMDT expansion Plan would need reprogramming for last year in line with policy and guidelines revision proposed
  iii. The new budgeted NSP duly approved by MoPH has to be ready by end of June 2017.
  iv. GF may issue allocation letters by sometime in December 2016 with ‘Catalytic funding’ as additional investments and countries are prioritized for specific investments in consultations with partners. The concept note submission is planned by DPR Korea in the May 2017 window following a joint programme review in Feb 2017

Recommendations:

- Update the PMDT Expansion plan – 2018 and re-programme the available resources to fill gaps

Suggested Steps:
  i. In collaboration with all partners, update the expansion plan to cover at least 1 PTH and selected Sanatorium in all remaining provinces in 2017, 3 LPA labs with SL-LPA by 2018 and 1 Xpert machine per province by 2018
ii. Augment the expansion plan with Shorter MDR-TB Regimen that would result in cost saving from reduction in the SL drug cost.

iii. Reprogramme with savings from Shorter regimen that could be allocated to procure SLD gap of ~483 patients in 2018, Xpert MTB-Rif Cartridges (quantification driven by estimates of amount saved)

iv. Advocate with GF for above allocation funding or with CFK / EBF for investment in laboratory capacity enhancements for FL SL DST
   a. either a high throughput GT Blot machine for NRL or 2 set of LPA with twincubator for RRLs and
   b. a MGIT and consumables for NRL Pyongyang

Responsibility: NTP, PMU, UNICEF, EBF and WHO
Timelines: Feb 17

- Develop NSP 2018-20 and GF NFM Phase II proposal with budgets to aim for universal access to quality TB care in DPR Korea

  Suggested Steps:
  i. After revision of the policy and guidelines for TB and MDR/TB, conduct a detailed work plan, forecast and budget development including funding gap analysis for phased scale up over 3 years of all the new policies and guidelines to cover universal access to rapid molecular diagnosis for TB and DR-TB, SL-LPA, shorter regimen, newer drugs, aDSM, social protection, digitization and research.
  ii. Develop the NSP 2018-20 as a joint collaborative country dialogue lead by NTP with technical support and commitment from partners before submission to MoPH for approval.

  Responsibility: NTP, PMU, UNICEF, EBF, CFK and WHO
  Timelines: May 17

The mission also covered a technical training of NTP staff in PMDT at Pyongyang with special focus on the updated WHO PMDT Guidelines – 2016. This training covered updates, and deliberations on:

1. Case finding and Diagnostics including Second Line – Line Probe Assay (SL-LPA),
2. Updates on treatment including Shorter MDR-TB Regimen (SMTR),
3. Introduction of newer drugs (ND) like Bedaquiline (BDQ), Delamanid (DLM) and
4. Effective management of adverse drug reactions (ADR) including concepts of active drug safety monitoring (aDSM).

The queries and questions on technical and operational aspects of these newer technical topics were addressed by the author.
The recommendations were gracefully accepted by the top brass as the author exercised transparency and openness to suggestions from them to enable refinement, improvisation and ownership for enactment.
III. Annexes:

Annexure 1 – Terms of Reference (TORS) for technical assistances on MDR-TB management

1. To assess the country progress in the scale up of PMDT activities especially since the last rGLC mission conducted in September 2015 using the available SEA PMDT monitoring template;
2. To review country MDR-TB treatment enrolment plan including capacity of the country programme to adequately manage the proposed patient cohort and the related second line drugs highlighting on the Global Fund supported MDR-TB activities;
3. To review status of partners’ support in PMDT implementation in the country and discuss harmonization of technical support in line with “End TB Strategy” on PMDT and in-country context
4. Assess the current capacity of MDR TB clinical management in the country and review the technical documents related to MDR-TB management for further improvement in line with international recommendations in relation to
   i) Case finding and diagnosis
   ii) Treatment protocol being followed and regimen being used
   iii) Management of adverse events
   iv) Declaration of treatment outcome
   v) Follow-up of patient during and after treatment
5. Provide recommendations including the priority recommendations (not more than 10) with timeframes in the executive summary of the report for implementation and further expansion of PMDT services for next one year.
6. Provide the technical trainings to improve the knowledge of participants on
   i) Case finding and diagnosis
   ii) Treatment protocol being followed and regimen being used
   iii) Promoting treatment adherence using patient support including
      (a) Patient and family counselling
      (b) Socio-economic support
      (c) Nutrition support
   iv) Early and effective management of adverse events
   v) Declaration of treatment outcome and following up of patient during and after treatment
   vi) Reporting and Recording system for PMDT
7. Provide technical consultation on current WHO recommended shorter regimen to in-country PMDT team for adaptation and assess the possibility to introduce and roll-out shorter MDR-TB regimen in the country.
Annexure 2 - Summary of activities (table)

The figure below summarizes the places visited and specific activities undertaken during the mission:

**rGLC PMDT Monitoring Mission Schedule**

7th – 18th November 2016

<table>
<thead>
<tr>
<th>Date</th>
<th>Location</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>8th Nov ‘16</td>
<td>(Pyongyang)</td>
<td>Briefing – WHO CO Team</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Visit to NRL at CTPI</td>
</tr>
<tr>
<td>9th Nov ‘16</td>
<td>(Pyongyang)</td>
<td>Visit to Sadong TB Sanatorium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Visit to Sasong TB Sanatorium</td>
</tr>
<tr>
<td>10th Nov ’16</td>
<td>(North Pyongan)</td>
<td>Provincial Specialized TB Hospital</td>
</tr>
<tr>
<td>14th Nov ’16</td>
<td>(Pyongyang)</td>
<td>Work at WHO CO</td>
</tr>
<tr>
<td>15th &amp; 17th</td>
<td>Nov ’16 (Pyongyang)</td>
<td>Technical Training on PMDT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discussion with NTP Manager, NTP Focal Point for Eugene Bell Foundation &amp; PMU team</td>
</tr>
<tr>
<td>18th Nov ‘16</td>
<td>(Pyongyang)</td>
<td>Debriefing NTP, PMDT Members, MoPH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meeting with WR DRP Korea</td>
</tr>
</tbody>
</table>

The following stakeholders were met during the mission and technical training on MDR-TB:

**At CTPI, NRL, TB PMU MoPH, Pyongyang:**

- Dr Ri Chan Hyok, Global Fund Coordinator, Vice-Director of Department of External Affairs, MoPH, GoDPRK
- Dr Choe Tong Chol, NTP manager, Director of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK
- Dr Choe Kum Song, Senior Officer of Department of Communicable Disease, Hepatitis and Tuberculosis, MoPH, GoDPRK
- Dr Kim Myong Chol, Vice-Director of Central TB Preventive Institute (CTPI), MoPH, GoDPRK
- Dr Jong Chol, Head of Clinical Research Center, CTPI (Member of central PMDT committee), MoPH, GoDPRK
• Dr Ri Chol Nam, Researcher of Clinical Research Center, CTPI (Member of central PMDT committee), MoPH, GoDPRK
• Dr O Yong IL, Head of National TB Reference Laboratory(NRL), CTPI, MoPH, GoDPRK
• Dr Ri Chang Son, Lab Doctor, NRL, CTPI, MoPH, GoDPRK
• Dr Jo Myong Chol, Senior Staff of Health Department, Pyongyang City People’s Committee, MoPH, GoDPRK
• Dr Kim Pok Nam, Vice-Director of Pyongyang city TB Preventive Institute, MoPH, GoDPRK
• Dr Kim Yong Ae, Member of Pyongyang city PMDT committee, Pyongyang city TB Preventive Institute, MoPH, GoDPRK
• Dr Jo Son Hak, Member of Pyongyang city PMDT committee, Pyongyang city TB Preventive Institute, MoPH, GoDPRK
• Dr Choe Tal Bom, Chief of TB Department, Pyongyang Medical College under Kim IL Sung University(Member of central PMDT committee), MoPH, GoDPRK
• Dr Jo Song Nam, Teacher of TB department, Pyongyang Medical College under Kim IL Sung University, MoPH, GoDPRK
• Dr Im Jong Song, Teacher of TB department, Pyongyang Medical College under Kim IL Sung University, MoPH, GoDPRK
• Dr Kim Hyon, TB PMU, Pyongyang, MoPH, GoDPRK
• Dr Pyon Gyong Ho, TB PMU, Pyongyang, MoPH, GoDPRK
• Dr Choe Song Hwan, TB PMU, Pyongyang, MoPH, GoDPRK
• Dr Yun Yong Hwa, TB PMU, Pyongyang, MoPH, GoDPRK
• Dr Sin Ji Song, TB PMU, Pyongyang, MoPH, GoDPRK
• Dr Ri Jun Hyok, TB PMU, Pyongyang, MoPH, GoDPRK
• Dr Ko Jin Hyok, TB PMU, Pyongyang, MoPH, GoDPRK

At WHO Country Office for DPR Korea, Pyongyang:
• Dr Thushara Fernando - WHO Representative to DPR Korea
• Mr Thinlay – Administrative Officer,
• Dr Gagan Singh Sonal - Technical Officer, Malaria
• Dr O Hyang Song – National Professional Officer -TB
• Meeting with Team of Christian Friends of Korea
  – Dr Heidi S. Linton, Executive Director, CFK
  – Dr Sissel Topple, Board Member, CFK
  – Dr Kathlene England, International Consultant, CFK
At Sadong district TB Sanatorium:
- Dr Ri Yong Sam, Director of Sadong district TB sanatorium, Pyongyang city, MoPH, GoDPRK
- Dr Kim Song Hyok, Vice-director of Sadong district TB sanatorium, Pyongyang city, MoPH, GoDPRK
- Mr Yun In Jun, Pharmacist of Sadong district TB sanatorium, Pyongyang city, MoPH, GoDPRK
- 2 XDR-TB patients on BDQ containing regimen interviewed

At Sosong district TB Sanatorium:
- Dr Kim Un Ryong, Director of Sosong district TB sanatorium, Pyongyang city, MoPH, GoDPRK
- Dr Kim Gi Taek, PMDT doctor of Sosong district TB sanatorium, Pyongyang city, MoPH, GoDPRK
- Mr Myong Ju Bong, Pharmacist of Sosong district TB sanatorium, Pyongyang city, MoPH, GoDPRK
- 2 patients on standard MDR-TB regimen interviewed

At North Pyongan Provincial TB Specialized Hospital, Kwaksan:
- Dr Kim Kwang Nam, Member of Provincial PMDT committee, North Pyongan Provincial TB Preventive Institute(PTPI), MoPH, GoDPRK
- Dr Kim In Sok, Member of Provincial PMDT committee, North Pyongan Provincial TB Preventive Institute(PTPI), MoPH, GoDPRK
- Dr Kim Chun Do, Director of North Pyongan Provincial TB Specialized Hospital(PTH), MoPH, GoDPRK
- Dr Paek Rak Gun, Vice- Director of North Pyongan Provincial TB Specialized Hospital(PTH), MoPH, GoDPRK
- Dr Kim Hyon Chol, Head of Lab Department of North Pyongan Provincial TB Specialized Hospital(PTH), MoPH, GoDPRK
Annexure 3 – TB Profile 2016 - DPR Korea

Democratic People's Republic of Korea

Estimates of TB burden, 2015

<table>
<thead>
<tr>
<th>Number (thousands)</th>
<th>Rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (excludes HIV-TB)</td>
<td>15 (10-22)</td>
</tr>
<tr>
<td>Mortality (HIV-TB only)</td>
<td>0.037 (0.016-0.065)</td>
</tr>
<tr>
<td>Incidence (excludes HIV-TB)</td>
<td>141 (109-178)</td>
</tr>
<tr>
<td>Incidence (HIV-TB only)</td>
<td>0.48 (0.32-0.6)</td>
</tr>
<tr>
<td>Incidence (MDR/RR-TB)</td>
<td>0.1 (0.07-0.14)</td>
</tr>
</tbody>
</table>

Estimated TB incidence by age and sex (thousands), 2015

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td>4.9</td>
</tr>
<tr>
<td>Boys</td>
<td>6.3</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
</tr>
</tbody>
</table>

TB case notifications, 2015

- Total cases notified: 120,722
- Total new and relapses: 112,542
  - % tested with rapid diagnostics at time of diagnosis
  - % with known HIV status
  - % pulmonary
  - % bacteriologically confirmed among pulmonary

Universal health coverage and social protection

- TB treatment coverage (notified/estimated incidence), 2015: 80% (64-100)
- TB patients facing catastrophic total costs: 5%
- TB case fatality ratio (estimated mortality/estimated incidence), 2016: 0.11 (0.07-0.17)

TB/HIV care in new and relapse TB patients, 2015

- Patients with known HIV status who are HIV-positive: 0%
  - on antiretroviral therapy: 0%

Drug-resistant TB care, 2015

- Estimated MDR/RR-TB cases: 4,969
- % tested for resistance to second-line drugs: 0%
- Laboratory-confirmed cases: MDR/RR-TB: 209, XDR-TB: 0
- Patients started on treatment: MDR/RR-TB: 115, XDR-TB: 0

Treatment success rate and cohort size

- New and relapse cases registered in 2014: 99%, 103,645
- Previously treated cases, excluding relapse, registered in 2014: 82%, 7,245
- HIV-positive TB cases, all types, registered in 2014: 0
- MDR/RR-TB cases started on second-line treatment in 2015: 84%, 170
- XDR-TB cases started on second-line treatment in 2015: 0

TB preventive treatment, 2015

- % of HIV-positive people newly enrolled in care: 92%
- % of children aged ≤ 5 household contacts of bacteriologically confirmed TB cases on preventive treatment: 0%

TB financing, 2016

- National TB budget (US$ millions): 50
- Funding sources: 19% domestic, 27% international, 54% unfunded

Data are as reported to WHO. Estimates of TB and MDR/RR-TB burden are produced by WHO in consultation with countries. Estimates are revised and totals are computed prior to rounding.

Data for all years can be downloaded from www.who.int/tb/data
Annexure 4 - Proposed Testing Algorithm for DR-TB diagnosis using WHO endorsed rapid diagnostics for DPR Korea:
Annexure 5 – Summary of PMDT Expansion Plan 2018 for complete geographical coverage in DPR Korea:

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of provinces covered by PMDT</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Name of provinces covered by PMDT</td>
<td>Pyongyang</td>
<td>Pyongyang</td>
<td>N. Hwanghae</td>
<td>S. Pyongan, N. Pyongan</td>
<td>S. Hamgyong, N. Hamgyong, Nampho Kangwon</td>
<td>N. Hamgyong, Rason, Ryanggang, Jagang</td>
<td></td>
</tr>
<tr>
<td>Culture and DST centers</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>2 (NRL+1 RRL)</td>
<td>2 (NRL+1 RRL)</td>
<td>3 (NRL+2 RRL)</td>
<td>3 (NRL+2 RRL)</td>
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<tr>
<td>Number of Sanatorium covered by PMDT</td>
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<td>8</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Number of PTH covered by PMDT</td>
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<td>6</td>
<td>8</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of MDR-TB patients enrolled in 2nd-line treatment</td>
<td>50</td>
<td>120</td>
<td>130</td>
<td>250</td>
<td>500</td>
<td>1000</td>
<td>2000</td>
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<tr>
<td>Functioning LPA</td>
<td>NA</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
</tr>
<tr>
<td>Functioning Xpert MTB/RIF</td>
<td>NA</td>
<td>1 (NRL)</td>
<td>1 (NRL)</td>
<td>2 (NRL+1 RRL)</td>
<td>2 (NRL+1 RRL)</td>
<td>3 (NRL+2 RRL)</td>
<td>5 (NRL+2 RRL+2 PTPI)</td>
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