TUBERCULOSIS PROCUREMENT AND MARKET-SHAPING ACTION TEAM (TPMAT)

SUMMARY MEETING REPORT OF THE SEVENTH GENERAL MEETING

1 March 2022
Meeting Held Virtually

Background and Introduction

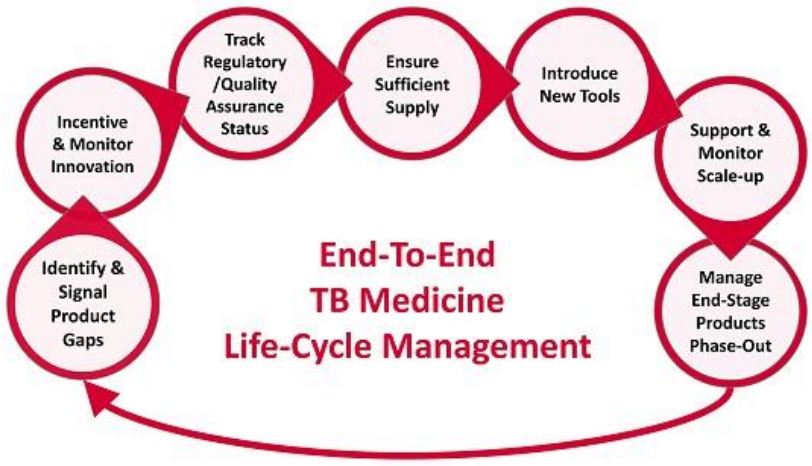
1. *TPMAT Overview and Progress Update* - Presenter: Brenda Waning (GDF)

TPMAT Overview

The Global Drug Facility (GDF) opened the meeting by providing an overview of the TB Procurement and Market–Shaping Action Team (TPMAT) and summarizing recent TPMAT progress. TPMAT—established in July 2016—is the key global forum bringing together stakeholders to address common market shaping and procurement challenges related to ultra-fragile TB commodity markets. TPMAT is comprised of procurers, donors, implementers, international organizations, regulators, WHO, civil society organizations (CSOs), and National TB Programmes (NTPs). A list of its current members can be found in **Annex 1**.

TPMAT serves as an umbrella for all stakeholders to align on issues and coordinate activities, irrespective of procurement modalities or funding sources, and works end-to-end across the TB product cycle (Figure 1). TPMAT's goal is to create fast, expansive access to the highest quality TB products for people living with TB and the NTPs that serve them.

Figure 1: TPMAT's End-to-End Product Life-Cycle Approach



TPMAT Progress Update

TPMAT progress updates focused on upstream harmonization and alignment efforts, downstream product availability and partner coordination.

TPMAT's key tool for harmonization is the TB Medicines Dashboard, bringing together information on TB medicines from 15 different sources within a single site to ensure that stakeholders are aligned on current recommendations and guidelines. TPMAT also supports coordination of the Global Fund Expert Review Panel (ERP) Expression of Interest (EOI), revisions to the WHO Essential Medicines List (EML) in relation to TB products, and the WHO Prequalification (PQ) Expression of Interest alignment

to both the Global Fund List of Health Products and the GDF catalog. TPMAT plays an essential role in ensuring the TB medicines space represents the only disease area to systematically coordinate, review, align, and ensure feedback across stakeholder groups.

Key upstream progress by TPMAT include:

- Supporting Global Fund to develop the Ad Hoc Priority Review process for the ERP in 2017-2018, allowing TPMAT and partners to signal to suppliers the most urgent products to develop (based on gaps in formulation development or supply security concerns) and ensuring these products could be quality assessed as soon as they were ready.
- Coordinating six ERP EOI revisions between 2018 and 2021, leading to more than 30 changes to prioritize, deprioritize, add or remove formulations to reflect current WHO recommendations and identified gaps in product development.
- Coordinating review of the TB sections of the WHO EML and EML for children, aligning partners on needed changes, additions and deletion and developing a plan for partners to submit applications and letters of support as needed – leading to more than 70 changes to the TB section of the EML across two update periods since 2018.

Key downstream progress by TPMAT include:

- Launching and procuring 12 products that were "priorities" before the formal prioritization process was implemented in 2018.
- Since the formal prioritization process was implemented, 15 formulations have been identified as key products, 13 of these have been developed and seven of these have been launched and procured – greatly expediting access to TB medicines although many products do not have a large market.

Key partner coordination progress by TPMAT include:

- Engaging the Vatican High Level Dialogue on Paediatric HIV to include paediatric HIV-TB coinfection and organizing over 200 commitments from partners.
- Supported the WHO Global Accelerator for Paediatric Formulations (GAP-f) Secretariat to develop its new strategic plan (launched after this TPMAT meeting), bringing lessons learned from the paediatric TB medicines space that could be used as a model for other diseases.

TPMAT now has a new website which will improve visibility and transparency with respect to TPMAT recommendations and how these are made. Partners can source key documents from the website.

Objectives and Overview of this Meeting

TPMAT's March 1st meeting was attended by 38 people and the agenda and list of participants can be found in **Annexes 2** and **3.** The meeting had two areas of focus:

1. Perspectives from NTPs and CSOs on the opportunities and tradeoffs (e.g., price vs. shelf life) as delamanid 50mg and other new TB medicines move from being single-source to being available as generics.
2. How to expand access to new child-friendly formulations for DR-TB which now are available but not procured at the volumes expected?

Session 1: Perspectives from NTPs and CSOs on New Medicine Introduction Opportunities and Tradeoffs

1. *Setting the Scene: Background* - Presenter: Christophe Perrin (MSF)

There have been single-source manufacturers for many new DR-TB drugs (e.g., Johnson and Johnson for bedaquiline, Otsuka for delamanid, and Viatris/Mylan for pretomanid). In the next 12-to-18 months, it is expected that new DR-TB medicines will begin to see generic competition or licensed generic development. For example, a Viatris/Mylan generic version of delamanid 50mg was recommended for procurement by the Global Fund's ERP in December 2021. Introduction of new generic versions of medicines can have tradeoffs. A generic supplier generally has lower production costs and contributes to price competition between suppliers, lowering costs to NTPs. However, generics generally also have lower shelf lives (e.g., 24 months) compared to the originator product (e.g., 36-60 months) at launch. These tradeoffs have implications for procurers, NTPs and their partners, and CSOs. The delamanid 50mg from Otsuka has a price per treatment course of $1700 and a total shelf life of 60 months. The Viatris/Mylan licensed generic version has a price per treatment course of $1125, and an initial total shelf life of 24 months. How NTPs and CSOs value these tradeoffs between price and shelf life can inform how to approach introduction of generic bedaquiline and pretomanid.

2. *Delamanid 50mg Tradeoff: Price vs. Shelf Life: NTP Perspectives from Georgia* - Presenter: Irma Khonelidze (National Centre for Disease Control and Public Health, Georgia)

Many countries in Eastern Europe and Central Asia are undergoing transition to domestic financing. In 2016, Georgia began transitioning from Global Fund to government resources for TB medicines procurement. Presently, all first-line and 75% to 80% of second-line drugs are procured through domestic financing. Georgia is now strengthening its public sector procurement and supply management (PSM) mechanisms and using GDF as a procurement mechanism. Relying increasingly on domestic financing means that Georgia is interested in having access to generic, quality-assured, lower-priced alternatives. The shorter shelf life of these medicines is challenging but can be managed via Georgia's current practice of frequent, twice annual orders, improved monitoring and planning of supply, demand, and utilization, and PSM capacity building.

3. *Delamanid 50mg Tradeoff: Price vs. Shelf Life: CSO Perspectives from Moldova* - Presenter: Oxana Rucsineanu (TB /CAB and Society of Moldova against Tuberculosis (SMIT))

Moldova is currently transitioning from donor to domestic financing and increasing the amount of its domestic budget for new TB drugs. Recent research comparing prices of TB drugs procured and funded via centralized mechanisms versus drugs procured and funded by external mechanisms showed that drugs procured centrally from Moldova's domestic budget had a price 4-times higher than drugs procured via GDF with Global Fund financing; hence, volume price and available exemptions (e.g., VAT, customs tax) are often dependent on funding source and procurement mechanism. Moldova is therefore keenly interested in generics. At the same time, shelf life is an important consideration and dependent on different country contexts (e.g., budget cycles, volume of drugs required, TB trends, presence of patent monopolies, and in what context TB drugs are generally delivered in the country). While NTPs will often prioritize lower prices, shorter shelf life may be more feasible for countries with stable economies and strong procurement and distribution strategies.

Key Points Discussed: Opportunities and Tradeoffs for Delamanid 50mg – Price vs. Shelf Life (Facilitator: Christophe Perrin, MSF)

Importance of context

- Tradeoffs depend on the country context.

- In the context of countries transitioning to domestic financing, generic competition and lower prices may be preferable (or even necessary, depending on local regulations).
- Short shelf life may be less of an issue in higher burden countries with greater turnover.
- In countries which have less capacity for PSM or difficulties with demand generation/case-finding, short shelf life may be a problem, as indicated by some representatives from NTPs.
- COVID-19 has played a role in slowing medicine turnover in some countries, which also influences shelf-life preferences.

Shorter shelf life can be overcome with several strategies

- Shorter shelf life may be managed by smaller, more frequent ordering, close monitoring of consumption, and strengthened PSM

Action Points: Opportunities and Tradeoffs for Delamanid 50mg – Price vs. Shelf Life

- GDF to share with suppliers how country programmes assess trade-offs between price and shelf-life and incorporate these perspectives as it plans for introduction of new products.

Session 2: Expanding Access to New, Child-Friendly Formulations for Paediatric DR-TB

1. *Lessons-Learned from the Paediatric DR-TB Initiative* – Presenter: Brian Kaiser (GDF)

Since 2018, there has been expansion of child-friendly formulations for DR-TB, as well as improved competition, with many new formulations now having 2+ suppliers. The latest developments include:

- A more child-friendly formation of clofazimine replacing liquid gel capsules (2019)
- FDA-approved child-friendly bedaquiline (2020)
- EMA-approved child-friendly delamanid (2021)
- Two linezolid 150mg dispersible tablet formulations currently in the PQ pipeline

All WHO-recommended medicines for DR-TB have now been developed in child-friendly formulations despite a market of less than 1,000 children < 5 years of age being treated per year (with 65% of countries treating less than 20 children per year). Additionally, there have been price reductions for these new formulations, with estimated prices for all-oral regimens for children nearly the same as 2016 prices for DR-TB regimens for adults. Thus, price is now not a primary barrier to uptake.

GDF has been able to catalyze introduction and scale-up of these child-friendly formulations, supporting programmes to rapidly procure these products:

- After 8 new paediatric DR-TB medicines were launched in 2018, the number of countries procuring increased from 16 in 2018, to 70 in 2020, to 74 in 2022.
- Paediatric bedaquiline was launched in 2020 Q3 and, by 2022, 41 countries were procuring.
- Paediatric delamanid was launched in 2021 Q4 following approval in September and 26 countries are now procuring.

However, overall volumes of child-friendly formulations have remained flat. Procurement has remained at 500 – 550 treatment courses a year in 2018, 2019, and 2021.[1] This trend disincentivizes investment in developing new formulations as manufacturers see little medium or long-term growth.

[1] Although there was a notable increase in procurement of child-friendly formulations in 2020, this was likely due to both the improvement in shelf life of moxifloxacin and levofloxacin (from 24 to 36 months) and the end of the Global Fund grant cycle requiring funding to be used up as new grants were developed.

Small volumes also make it difficult to align procurement with the batch sizes expected by regulators, as well as to keep two suppliers in the market. There is now a risk of suppliers exiting.

One of the main bottlenecks to access is paediatric case finding. It is estimated that 25,000 children aged <15 years develop DR-TB each year, but only 12,000 have been reported as having been treated since 2018. Collectively, NTPs are estimated to be treating only 500 – 1000 of the youngest children per year, which corresponds with GDF procurement numbers. How can case-finding of children with DR-TB be improved to both support NTPs and to support suppliers?

2. ***Expanding Access to New, Child-Friendly Formulations for Paediatric DR-TB: Perspectives of CSOs - South Africa's Experience with Increased Screening and Case Finding*** **-** Presenter: Shriya Misra Ramdin (The Health Ninja)

The Health Ninja is a CSO focused on training youth in Kwa Zulu Natal to be leaders in the community. The Health Ninja follows the WHO Engage TB approach, which spans prevention, detection, referral, treatment adherence, and stigma reduction. One of its key activities involves awareness raising and advocacy in support of case finding. Awareness raising involves a range of successful youth-friendly activities at schools, creches, and in the community, including games, art sessions, breakaway sessions, drama and theater productions, murals, focus-group discussions, utilization of champions, and the #KnowTBtoFindTBtoEndTB social media campaign. The Health Ninja has also carried out special activities focused on availability of child-friendly formulations, including the utilization of a medicine information board with visual demonstrations of child-friendly formulations to raise awareness among providers and caregivers. From October 2021 – February 2022, Health Ninja events at schools and creches reached more than 2,200 children, screened more than 1,339 of these children for symptoms, and linked the 70 of those who reported symptoms to care, resulting in 3 children identified as TB-positive and started on treatment (a rate of 4% of children screened). The Health Ninja also developed child-friendly tools. Community engagement and youth-friendly initiatives can increase case finding and such tools and engagement modalities can easily be taken to scale.

3. ***Expanding Access to New, Child-Friendly Formulations for Paediatric DR-TB: Perspectives from NTPs - Tanzania*** - Presenter: Dr Isack Lekule (PMDT Coordinator, NTP, Tanzania)

Since 2015, Tanzania has been greatly improving DS-TB notification, including among children aged <15 years. Tanzania has also improved MDR-TB notification among adults. Among children aged <15 years, however, MDR-TB notification has long been an issue. There are challenges to case-finding in children. DR-TB diagnosis requires laboratory confirmation, which in turn requires a sputum sample, the collection of which is difficult in children. Health workers do not have the skills for sputum induction and aspiration and there have been numerous stock outs of equipment (e.g., sputum cups), along with problems accessing GeneXpert (e.g., stock out of cartridges). Tanzania has embarked on a strategy to improve paediatric case finding including: a) establishing Centers for Excellence for Paediatric TB Management, scaling these Centers up to 50 around the country; b) putting in place plans to increase the number of hospitals which can both perform sputum induction and gastric aspiration by 75% by 2025; c) improvement in contact investigation of all bacteriological-confirmed DR-TB cases; d) scale up of distance learning-based Integrated Management of Childhood Illness (d-IMCI), targeting all facility departments in order to pick up cases in children who go to facilities for other conditions; e) improved availability of child-friendly medicines.

4. ***Expanding Access to New, Child-Friendly Formulations for Paediatric DR-TB: Perspectives from NTPs - Zambia*** - Presenter: Dr Patrick Lungu (Manager, NTP, Zambia)

Diagnosing DR-TB in children is challenging, especially bacteriological confirmation. Zambia has started to use stool samples for bacteriological confirmation in all ages. Using stool has contributed greatly to bacteriological confirmation and case identification. From January to September 2021, use of stool led to 54 out of 3,324 paediatric specimens tested detected as positive, a 1.6% positivity rate. In adults, the positivity rate from stool was 5%. Other modalities Zambia is using for case identification

in children include LAM and gastric lavage for both DS- and DR-TB, improved contact tracing, as well as a high index of suspicion for children who are close contacts of cases of LAM-positive DR-TB. Using all these modalities, Zambia has scaled up childhood TB case notification and prevented loss of life.

Key Points Discussed: Access to Child-Friendly Formulations for Paediatric TB (Facilitator: Lindsay McKenna, TAG)

There should be a high index of suspicion for child contacts of DR-TB cases

- The index of suspicion should be high, especially in children not responding to treatment or with a history of having a household contact who either has DR-TB or has had a poor treatment outcome. If any of the above conditions are true, the child should be started on DR-TB treatment, a clinical decision made easier by the availability of new child-friendly formulations.

Strengthening country capacity to diagnose is also important

- Finding children with DR-TB requires a number of complex steps; therefore, it is essential to support NTPs' and providers' ability to clinically diagnose paediatric DR-TB cases (e.g., establishing Paediatric Centers of Excellence to build health worker capacity). The utilization of stool to facilitate easier diagnosis is of interest to NTPs and should be further explored.

Dedicated contact tracing activities are essential

- MSF/Khayelitsha worked with stakeholders to household contact trace children aged < 18 years in households of newly-diagnosed people with DR-TB, leading to a threefold increase in case-finding of children, with results to be published in Lancet Respiratory Medicine.

There is an important role for community organizations in outreach and case-finding

- Community engagement activities—especially those that are child- and youth-friendly—can support case-finding in the community.

The new WHO guidelines and operational handbook on child and adolescent TB will support these efforts

- WHO will launch new consolidated guidelines, along with an operational handbook on World TB Day in March 2022. These will include new guidance on the use of additional specimens for diagnosis and models of care. TPMAT meeting participants are eager to support programmes to quickly incorporate these new recommendations into national policies.

Action Points: Access to Child-Friendly Formulations for Paediatric TB

- GDF should continue to balance supply and demand, including tools like the Strategic Rotating Stockpile (SRS) to maintain access to child-friendly formulations.

Wrap-Up

Brenda Waning thanked participants for attending and noted that presentations and a meeting report would be shared with participants.

Annex 1: Current Members of TPMAT

Elizabeth Glaser Paediatric AIDS Foundation (EGPAF)
Global Drug Facility (Stop TB Partnership)
Global Fund
KNCV Tuberculosis Foundation
Médecins sans Frontières, Access Campaign
Medicines Patent Pool
Pan American Health Organization (PAHO)
Representatives of Country TB Programmes
TB Civil Society Organizations
TB Clinical Experts and Researchers
The International Union Against TB and Lung Diseases (The Union)
The Sentinel Project
Treatment Action Group (TAG)
UNICEF
UNITAID
United Nations Development Programme (UNDP)
United States Agency for International Development (USAID)
WHO Essential Medicines Programme (EMP)
WHO Global TB Programme (GTBP)
WHO Prequalification Team (PQT)

Annex 2: Final Meeting Agenda

TB Procurement and Market-Shaping Action Team (TPMAT) Meeting

1 March 2022, 8:00-9:30am New York/ 2:00–3:30pm Geneva

Background

The TB Procurement and Market-Shaping Action Team (TPMAT) brings together national, regional, and global TB stakeholders to identify and address procurement and market-based challenges towards expedited and equitable access to TB commodities. TPMAT works end-to-end across the entire TB product life cycle – from identifying and signaling product priorities, formulation development, introduction and scale-up through to management of product phase-out. Established in 2016, TPMAT stakeholders include representatives from procurement entities, donors, implementers, researchers, civil society organizations, national TB programmes and others.

Objectives

The objectives of this TPMAT meeting are to:

- Review progress and status of TPMAT priority products, including harmonization activities across GDF, WHO Global TB Programme, Global Fund Expert Review Panel, WHO Prequalification Programme, WHO Model Essential Medicines Lists, and GAP-f
- Gain perspectives on new product trade-off considerations to inform new product launch and introduction strategies
- Identify key action steps to expand access to newly developed, child-friendly DR-TB formulations

Chair: Brenda Waning

14:00–14:15	Opening; TPMAT Progress on Priority Products	Brenda Waning, GDF
Session 1. New Medicine Introduction: Opportunities & Tradeoffs: Perspectives from National TB Programs (NTPs) and Civil Society. **Facilitator:** Christophe Perrin, MSF		
14:15-14:20	Setting the Scene, Background	Christophe Perrin, MSF
14:20-14:30	NTP Perspective 1	Irma Khonelidze, National Centre for Disease Control and Public Health, Georgia
	CSO Perspective 2	Oxana Rucsineanu, TB CAB, Moldova
14:30-14:45	Brief Discussion, Wrap-up, Action Steps	Christophe Perrin, MSF
Session 2. Paediatric DR-TB: Child-Friendly Formulations Now Available, but How to Expand Access to More Kids? **Facilitator:** Lindsay McKenna, TAG		
14:45-14:55	GDF Lessons Learned from Paediatric DR-TB Initiative	Brian Kaiser, GDF, Switzerland
14:55-15:05	South Africa Experience: Increased Screening and Case Finding	Shriya Misra Ramdin, The Health Ninja, South Africa

15:05-15:15	NTP Perspective 1	Dr Isack Lekule, PMDT Coordinator, NTP, Tanzania
	NTP Perspective 2	Dr Patrick Lungu, NTP Manager Zambia
15:15-15:25	Brief Discussion, Wrap-up, Action Steps Meeting Closure	Lindsay McKenna, TAG
15:25-15:30	Meeting Closure	Brenda Waning, GDF

Annex 3: List of Participants

1. **Brenda Waning (Chair)**
   GDF Chief – Stop TB Partnership
   Geneva, Switzerland

2. **Cheri Vincent**
   Chief Infectious Diseases Division - USAID
   Washington DC, USA

3. **Thomas Chiang**
   Senior TB Technical Advisor - USAID
   Washington DC, USA

4. **Mukadi YaDiul**
   Medical Officer - USAID
   Washington DC, USA

5. **Charlotte Colvin**
   Senior TB Technical Advisor – USAID
   Washington DC, USA

6. **Sarah Cook-Scalise**
   TB Diagnostics Technical Advisor – USAID
   New York, USA

7. **Brian Kaiser**
   Technical Officer, GDF – Stop TB Partnership
   Geneva, Switzerland

8. **Elena Mochinova**
   Country Supply Team Leader, GDF – Stop TB Partnership
   Geneva, Switzerland

9. **Ramon Crespo**
   Knowledge and Project Management Officer, GDF – Stop TB Partnership
   Geneva, Switzerland

10. **Lindsay McKenna**
    TB Project Co-Director – Treatment Action Group
    New York, USA

11. **David Branigan**
    TB Project Officer – Treatment Action Group
    New York, USA

12. **Sharonann Lynch**
    Senior Scholar, Global Health Policy & Politics Initiative, O'Neill Institute, Georgetown University || Senior Visiting Fellow, Yale Global Health Justice Partnership
    New York, USA

13. **Christophe Perrin**
    TB Advocacy Pharmacist – MSF Access Campaign
    Paris, France

14. **Stijn Deborggraeve**
    Diagnostics Advisor Infectious Diseases – MSF
    Amsterdam, Netherlands

15. **Martina Casenghi**
    Technical Director, CaP TB Project
    Elizabeth Glaser Pediatric AIDS Foundation
    Geneva, Switzerland

16. **Jennifer Furin**
    Director of Clinical Capacity Building at Sentinel Project on Pediatric Drug-Resistant TB
    Boston, USA

17. **Tiziana Masini**
    Technical Officer – WHO
    Geneva, Switzerland

18. **Annemieke Brands**
    Technical Officer, Global TB Programme – WHO
    Geneva, Switzerland

19. **Ademola Osigbesan**
    Programme Manager, Procurement and Supply Chain Management – UNITAID
    Geneva, Switzerland

20. **Grania Brigden**
    Senior TB Advisor – The Global Fund
    Geneva, Switzerland

21. **Anneke Hesseling**
    Director, Paediatric TB Research,
    Desmond Tutu TB Centre
    Stellenbosch University
    Stellenbosch, South Africa

22. **Dr Mansa Mbenga**
    PMDT Consultant – KNCV Tuberculosis Foundation
    The Hague, Netherlands

23. **Shriya Misra**
    Director – The Health Ninja Pty Ltd
    Durban, South Africa

24. **Oxana Rucsineanu**
    Director of Programs – Society of Moldova against Tuberculosis (SMIT)
    Balti, Moldova

25. **Patrick Migambi**
    Division Manager, Tuberculosis and Other Respiratory Diseases Division – Rwanda Biomedical Centre
    Kigali, Rwanda

26. **Karataev Madamin Musaevich**
    Director – National Center for Phthisiology
    Bishkek, Kyrgyzstan

27. **Atyrkul Toktogonova**
    Deputy Director – National Center for Phthisiology
    Bishkek, Kyrgyzstan

28. **Aimgul Duishekeeva**
    Medical doctor – KNCV BG
    Bishkek, Kyrgyzstan

29. **Parpieva Nargiz Nusratovna**
    Director – RSSPMC of phthisology and pulmonology
    Tashkent, Uzbekistan

30. **Sharaf Yuldashev**
    Global Fund Principal Recipient Transition Coordinator, USAID STAR consultant – NTP Uzbekistan
    Tashkent, Uzbekistan

31. **Naira Khachatryan**
    Head of National TB Office, National Center of Pulmonology – MoH Republic of Armenia
    Yerevan, Armenia

32. **Irma Khonelidze**
    Deputy Director General – National Center for Disease Control and Public Health
    Tbilisi, Georgia

33. **Dr. Isack Lekule**
    PMDT Coordinator - National TB and Leprosy Program, Tanzania
    Dar Es Salaam, Tanzania

34. **Mr Jumanne Mkumbo**
    Pharmacist – National TB and Leprosy Program, Tanzania
    Dar Es Salaam, Tanzania

35. **Dr Lungu Saili Patrick**
    National TB and Leprosy Programme Manager – MOH Zambia
    Lusaka, Zambia

36. **Lim Sheng Teng**
    Programme Assistant, GDF – Stop TB Partnership
    Geneva, Switzerland

37. **Katherine Ireri**
    Programme Assistant, GDF – Stop TB Partnership
    Geneva, Switzerland

38. **Beth Ann Pratt**
    Senior Technical Writer for GDF – Stop TB Partnership
    Nairobi, Kenya