DR-TB Scale-up Treatment Action Team (STAT)

A GDI TASK FORCE

1. Introduction

Only about 20% of people with multi-drug resistant TB (MDR-TB) have access to treatment and the chance of a cure is only around 50%. The cure rate for extensively -drug resistant TB (XDR-TB) is even lower, ranging from as low as 11% to as high as 34%, and studies have shown that in most settings, cases of XDR-TB come from primary transmission. **New and repurposed DR-TB drugs**[i], which could potentially improve cure rates and decrease ongoing transmission, are not reaching patients with DR-TB that could benefit.

Delamanid (DLM) and **bedaquiline** (BDQ) have been granted accelerated or conditional approval by stringent drug regulatory authorities. However, at the end of 2014, a little more than 600 people have received BDQ through expanded access programmes, and approximately 100 have received DLM outside clinical trial settings. Similarly, access to repurposed Group 5 drugs such as **linezolid** and **clofazimine** remains poor.

In order to make substantial progress, action is required from multiple actors:

- **National governments** need to develop implementation plans, ensure access to second line DST, build regulatory capacity and collaborate with regional regulatory counterparts to rigorously and rapidly review new drug applications, set up fast-track registration or import waiver processes as interim strategies, set up PV, update guidelines, train health care workers, procure the drugs, and render services;
- **Drug companies** need to allow early access through compassionate use (CU) or similar mechanisms, register products, make pricing/registration/licensing info transparent and fair for low and middle-income countries (LMICs), and make data available for others to submit initial dossiers thereby allowing generic equivalents to enter the market. Proprietary companies also need to conduct rigorous clinical trials and make their products available for consortium and investigator-initiated research for study in drug combinations;
- **Global health actors** need to provide and coordinate support (see below).

These terms of reference are for an 'action team' comprised of actors (see Annex 1) committed to meet time-bound goals for increasing access to new and repurposed DR-TB drugs in 50 top high-burden countries (see Annex 2) through greater collaboration, coordination and accelerated activities.[ii]

2. Goals

Given the momentum and activities of actors to date, there is an opportunity to strengthen, coordinate, and formalize the work around some time-based goals, including:

1. **Quickstart**: Ensure a minimum of 1000 patients are started on routine regimens, which include BDQ by Jan 2016 , and a minimum of 500 patients started on routine regimens, which include DLM by January 2016
2. **Optimal DR-TB treatment**: Key repurposed drugs (especially linezolid and clofazimine) should be included on the national Essential Medicines List (EML) in all 50 countries and national TB programmes (NTPs) should be using these drugs as part of the DR-TB regimens. Technical assistance provided for the 27 high DR-TB burden countries[iii] by 2016 and 50 countries by 2017 for drafting implementation plans for treatment with new and repurposed DR-TB drugs; implementation plans for DR-TB treatment containing new and repurposed drugs are adopted by 27 countries by 2016 and 50 countries by 2018; and BDQ and DLM are routinely used by 27 countries by end of 2016 and 50 countries by end of 2019. By September 2015 all regional Green Light Committees (rGLCs) are trained and able to provide advice on the use of new and re-

purposed drugs for the treatment of DR-TB so that these experts can facilitate optimal use in programs.

3. **Regulatory status**: BDQ and DLM dossiers are submitted by the originator manufacturers for registration in 27 countries by beginning of 2016 and 50 countries by 2017; import waivers are in place in 27 countries by January 2016 while BDQ and DLM are being registered.
4. **Pharmacovigilance (PV):** Supports a flexible approach for countries implementing BDQ and DLM (such as sentinel PV), proposes a set of standardised data for monitoring and reporting on adverse events, and works towards a supranational body to collect, analyse and disseminate data.
5. **Procurement**: Forecasting of drugs is completed; procurement strategies are developed for 50 countries by 2018; and, the turnaround time between ordering and drug delivery is reduced.

3. Functions of DR-TB STAT

1. Reviews progress (on a rolling basis) of scaling-up DR-TB treatment with new and Group 5 drugs in priority countries (data to come from main actors).
2. Generates "action lists" with time lines and responsible leads to ensure progress towards the goals.
3. Convenes biannual meetings of DR-TB STAT to review progress towards the goals above in the 50 countries, and develops a joint action plan with responsible leads.
4. Fosters coordination and collaboration between the different stakeholders and governments in scaling up DR-TB treatment with new and Group 5 drugs
5. Analyses global and national barriers to access and takes action, as needed, to support countries actors to address issues
6. Recommends concerted actions to be taken to achieve global goals

4. Set up, coordination, and communication

The DR-TB STAT is a Task Force of the Global Drug-Resistant TB Initiative (GDI), which is a working group of the Stop TB Partnership (TBP). The Task Force calls are to be convened by MSF/PIH/TBP, and follow up calls will have a rotating chair among the core members.

Resource requirements:

- A person playing the role of a secretariat would coordinate and facilitate meetings, ensure smooth functioning and communication, including the flow of information between meetings follow up with individual DR STAT actors regarding action plan items and responsibilities. To be arranged and funded by members of the task force.
- The operating costs of DR-TB STAT, to be covered partially by GDI and partially by the other organizations in the Task Force, includes monthly conference calls, meeting space and support for in-person meetings, travel and accommodation for actors who aren't able to pay their own way to attend in-person meetings.

Annex 1: DR-TB STAT members

1A. Core members – for the monthly conference calls:

- Dr. Charles Daley, Chair, and Agnes Gebhard, Vice Chair, Global Drug-Resistant TB Initiative (GDI)
- Dr. Lucica Ditiu, Executive Secretary, Stop TB Partnership
- To be decided, GDF Representative
- Dr. Mario Raviglione, Director, Global TB Programme, WHO, and GTB colleagues
- TB Situation Room Representative
- Mr. Mark Edington, Head, Grant Management Division, The GF
- Dr. Yogan Pillay, Deputy Director General, National Department of Health, South Africa
- Ms. Cheri Vincent, Chief, Infectious Diseases Division, USAID
- Dr. Ya Diul Mukadi, Senior Tuberculosis Technical Advisor, USAID
- Ms. Neha Agarwal, Clinton Health Access Initiative (CHAI)
- Dr. Susan van den Hof, KNCV
- Dr. Grania Brigden, Ms. Sharonann Lynch and Dr Francis Varaine MSF
- Dr. Michael Rich, PIH
- Dr. Jennifer Furin, Society Working on Implementation to Fight TB (SWIFT)
- Dr CY Chiang, Dr Pepe Caminero, The UNION
- Ms. Khairunisa Suleiman, independent activist, Kenya
- Representative from NGO and Communities affected by TB delegations (rotating), TBP Coordinating Board[iv] (starting with Mr. Aaron Oxley, Developed Country NGO representative, Executive Director, RESULTS UK, United Kingdom)
- Ms. Erica Lessem, Treatment Action Group (TAG)

1B. Others to attend conference calls as requested, including country representatives of countries being discussed on the call.

1) Implementing governments
   - Dr. Alena Skrahina, Deputy Director, Scientific Director, Republican Scientific & Practical Center for Pulmonology & Tuberculosis, Belarus
   - Dr. Zhou Lin, Director of Patients Care Division, National Center for Disease Control, China
   - Dr. Soumya Swaminathan, Director, National Institute for Research on Tuberculosis, India
   - Dr. KS Sachdeva, Additional Director General, Central TB Division, Ministry of Health and Family Welfare, India
   - Dr. Norbert Ndjeka, Director, DR-TB, TB and HIV, Department of Health, South Africa
   - Dr. Viet Nhung, Director of the National Lung Hospital and the National Tuberculosis Program, Vietnam

2) Technical agencies and supporters
   - Members of the 6 regional Green Light Committees (rGLC)

3) Donors and bilateral agencies
   - Dr. Peter Small, Deputy Director, Tuberculosis Program, Bill and Melinda Gates Foundation (replacement to be identified by Dr Small)
   - Dr. Susan Maloney, Global TB Coordinator, U.S. CDC
   - Mr. Hiroyuki Yamaya, Director, Global Health Policy Division, International Cooperation Bureau, Ministry of Foreign Affairs, Government of Japan
   - Amb. Deborah Birx, Office of U.S. Global AIDS Coordinator (OGAC)
   - Mr. Lelio Marmora, Executive Director, UNITAID

4) NGOs and community representatives
   - Mr. Albert Makone, Zimbabwe
   - Ms. Blessina Kumar, Global Coalition of TB Activists (GCTA)
   - Ms. Oxana Rucsineanu, Vice-Director, Moldova Society Against Tuberculosis (SMIT)
   - Mr. Marcus Low, Treatment Action Campaign (TAC)
   - Phumeza Tisile, South Africa
   - Dr Dalene von Delft, TB Proof, South Africa

5) Drug companies
   - Dr. Denis Broun, Global Access and Public Affairs Director, Cipla
   - Ms. Namrata Vyas, Assistant Manager, International Marketing, Hetero
   - Dr. Adrian Thomas, VP of Global Market Access & Commercial Strategy Operations and Head of Global Public Health, Janssen
   - Mr. Vijay Agarwal, Head of Institutional Business, Macleods
   - Mr. Nand Kishore Kothari, President International Business, Microlabs
   - Mr. David Hughes, Head of Global Public Policy, Novartis
   - Dr. Charles Wells, Senior Medical Director, Otsuka

Annex 2: Countries

Countries broken out by disease burden:

1) **Group 1**- The top 10 countries with the highest estimated MDR burden and the highest number of undetected cases representing 80% of the global cases (in order): India, China, Russia, Pakistan, Ukraine, Myanmar, Philippines, Uzbekistan, South Africa, Indonesia
2) **Group 2** – The remaining high DR-TB burden countries representing 15% of global cases (in order): Kazakhstan, Viet Nam, Bangladesh, Democratic People's Republic of Korea, Nigeria, Democratic Republic of the Congo, Kenya, Angola, Mozambique, Peru, Republic of Korea, Thailand, Belarus, Brazil, Kyrgyzstan, Republic of Moldova, Azerbaijan
3) **Group 3** - The remaining of the 50 countries representing 5% of global cases (in order): Ethiopia, Afghanistan, Nepal, Papua New Guinea, Tajikistan, Uganda, Zimbabwe, Somalia, Cameroon, Iran (Islamic Republic of), Georgia, Romania, Zambia, Cote d'Ivoire, Swaziland, Namibia, United Republic of Tanzania, Sudan, Cambodia, Mexico, Ghana, Haiti, Senegal

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[i] Including bedaquiline, delamanid, linezolid, clofazimine

[ii] The Global Fund TB Situation Room and the Paediatric ARV Procurement Working Group (PAPWG) and its Procurement Consortium are just two examples of successful collaborations

[iii] WHO identifies 27 countries as high MDR-TB burden: Armenia, Azerbaijan, Bangladesh, Belarus, Bulgaria, China, DR Congo, Estonia, Ethiopia, Georgia, India, Indonesia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Myanmar, Nigeria, Pakistan, Philippines, Republic of Moldova, Russian Federation, South Africa, Tajikistan, Ukraine, Uzbekistan, Viet Nam, (Stop TB Report 2014, Table 5.1: http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf?ua=1

[iv] Representatives of communities affected by TB: Mr. Timur Abdullaev, Uzbekistan, and Mrs. Thokozile Beatrex Nkhoma, Malawi; NGO representatives: Mr. Austin Obiefuna, Developing Country NGO, Executive Director, Afro Global Alliance, Ghana and Mr. Aaron Oxley, Developed Country NGO representative, Executive Director, RESULTS UK, United Kingdom