Guidance to develop Global Fund Round 11 proposal for tuberculosis control

Document intended for country and other stakeholder applicants, writing committees and consultants supporting TB proposal development for Global Fund Round 11

TB TEchnical Assistance Mechanism

World Health Organization

Stop TB Partnership

Contents

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Abbreviations

AIDS	acquired immunodeficiency syndrome
CCM	country coordinating mechanism
HIV	human immunodeficiency virus
MDG	Millennium Development Goal
MDR-TB	multidrug-resistant tuberculosis
NGO	nongovernmental organization
SDA	service delivery area
SMART	specific, measurable, attainable, relevant and time-bound
TB	tuberculosis
XDR-TB	extensively drug-resistant tuberculosis
WHO	World Health Organization

1. Purpose and target audience

This document targets the writing committees of the applicant countries, and the consultants, involved in the development of tuberculosis (TB) proposals to be submitted to Round 11 of the Global Fund to Fight AIDS, Tuberculosis and Malaria (hereafter, Global Fund). It aims to provide guidance on key aspects of the process of proposal development.

In particular, the document provides guidance on:

- the preparatory aspects specific to submission of TB proposals, particularly indicating how to address the weaknesses identified by the Technical Review Panel of the Global Fund in TB proposals submitted to previous Global Fund rounds;
- the identification of the key components that should be carefully considered and clarified to enhance the development of a successful proposal;
- the key requirements that must be respected in the proposal submission;
- the analysis determining an appropriate basis on which to develop a proposal to the Global Fund.

Moreover, the document aims to help applicants develop a sound framework justifying the objectives to be reached and the interventions to be implemented through the Global Fund grant.

It is expected that applicants will avoid including in their proposals all the interventions specified in the Stop TB Strategy without any appropriate justification. This has been often observed in TB applications for previous Global Fund rounds and has resulted in the Technical Review Panel failing to approve many applications for funding.

2. Issues observed in TB proposals submitted to the Global Fund

On average, 48% of the proposals submitted to the Global Fund for funding to implement TB control activities were approved by the Technical Review Panel from Round 1 to Round 10.

At the end of each round of the Global Fund, the Technical Review Panel highlights the overall issues encountered across the three categories of proposals targeting human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS), TB and malaria, and the issues specific to proposals for each disease. The Technical Review Panel usually makes recommendations to address these issues.

Some proposals were screened out at the preliminary stage by the Secretariat of the Global Fund because of administrative issues and therefore were not eligible to be reviewed by the Technical Review Panel. Examples of such weaknesses are:

- establishment of a country coordinating mechanism (CCM) that did not respect the requirements defined by the Global Fund;
- absence of documented evidence regarding the public announcement for the submission of an application to the Global Fund;
- omission of the description of the process used to select the principal recipients.

For TB proposals, various insufficiencies and inconsistencies were commonly reported by the Technical Review Panel.

Many TB applications were not approved for funding after review by the Technical Review Panel because of issues associated with the technical content of the proposal. The following deficiencies were often identified:

- indiscriminate inclusion of all the components of the Stop TB Strategy in the proposal, without clear linkages and appropriate description of the realities of TB control in the country to justify the need for implementing all these components;
- inappropriate or absent analysis of the TB situation –for instance, some proposals did not provide any information on the TB burden in the country or show any findings of a basic analysis of the routine data on TB suggesting how TB is distributed among population groups, across the regions and over time;
- unclear description of TB control measures that have already been undertaken, including those funded by previous Global Fund grants;
- lack of clarity in the gap analysis – for instance, in some proposals there was confusion between the gap analysis and the objectives or interventions planned to be implemented through the Global Fund grant;
- confusion between the identified gap and absence of the appropriate intervention to address the gap;
- inconsistencies between the identified gaps and constraints and the proposal objectives;
- vague proposal objectives;
- confusion between objectives and interventions;

- unjustified interventions to be implemented – for instance, the implementation of the advocacy, communication and social mobilization component was considered irrelevant by the Technical Review Panel members in a significant number of proposals and resulted in their rejection for funding;
- omission of appropriate interventions that would contribute to achieving the operational objectives defined in the proposal;
- weak specificity of the activities proposed for implementation;
- weak or no clarification on the additionality inherent to the proposal with respect to the previous or existing funding mechanisms, including those of previous Global Fund grants;
- inconsistency between the relevant components, such as objectives, strategic interventions and activities, specified in the proposal and those identified in the budget and workplan;
- oversized budget;
- inflated costs in some budget components;
- monitoring and evaluation indicators inconsistent with the proposal targets and objectives.

These weaknesses have been reported in many TB proposals and contributed to a failure for funding by the Global Fund.

A summary of selected Technical Review Panel reports, including typical observations made in Rounds 6 and 10 on TB proposals, is given in Annex 1.

3. Country eligibility and prioritization criteria

Before embarking on any application process, the country must check whether it is eligible to apply for funding from Global Fund Round 11. The Global Fund has established a comprehensive list of eligible countries using criteria such as national income, disease burden level and history of recent funding by the Global Fund. Detailed information on country eligibility is provided at http://www.theglobalfund.org/en/application .

The list also specifies whether eligible countries can apply for grants targeting the general population (general funding pool) or specific population groups (targeted funding pool), or both. Grants targeting the implementation of interventions that will potentially have a high impact on TB control (highest-impact interventions) can be considered in the context of a targeted funding pool. Countries that need to focus on specific targeted population groups or highest-impact interventions cannot apply for more than US$ 12.5 million within a 5-year grant, with a maximum of US$ 5 million for the first 2 years of the grant. Upper-middle-income countries with a moderate or low TB burden are not eligible to apply. The information note available at http://www.theglobalfund.org/en/application provides valuable clarifications on eligibility, counterpart financing and prioritization.

4. Global Fund Guidelines for Round 11

The Global Fund has issued guidelines entitled *Guidelines for proposals: Round 11 – Single country applicants* (hereafter, the Global Fund Guidelines) available at http://www.theglobalfund.org/en/application/materials .Applicants are highly encouraged to read these guidelines thoroughly. The guidelines not only specify the requirements needed to submit a proposal to the Global Fund Secretariat but also describe the steps that need to be taken to develop a proposal.

It is expected that the Global Fund Guidelines will help applicants meet the administrative requirements established by the Global Fund. It is important to recall that many TB proposals have been screened out in previous rounds by the Secretariat of the Global Fund because some of the administrative requirements were not fulfilled by applicants.

The Global Fund Guidelines provide clarifications on the various sections that need to be completed in the proposal template and explain how to develop key components of the application, such as the logical framework and the budget plan.

5. Key principles of Global Fund policy

The development of a TB proposal should reflect as much as possible key principles to promote equity, human rights, aid effectiveness, a multisectoral approach with a special angle on civil society and community involvement, efficiency, additionality and sustainability, as well as to save lives and preserve health through the activities supported by the Global Fund grant. The TB control issues associated with maternal and child health must be considered and highlighted clearly in the proposal for Round 11. These elements are in line with the Global Fund policy and are likely to contribute to making the proposal technically sound. These principles, and the approach to include them in the proposal, are explained and detailed in the Global Fund Guidelines (pages 6–12). Issues related to ethics, equity and human rights that should be considered in TB control services are described in Annex 2.

6. Grant consolidation

The main characteristic inherent to the development of the grant application to Global Fund Round 11 is consolidation with previous Global Fund grants. Grant consolidation is mandatory in Round 11. The proposal should present a consolidated request incorporating financial information and programmatic interventions specified in any ongoing Global Fund grants for TB control in the country. The aim of the consolidated proposal is to ensure that the present funding request to the Global Fund is programme-based rather than project-based and holistic. The process of developing a consolidated proposal is explained fully in the Global Fund Guidelines (pages 12–15) and at http://www.theglobalfund.org/en/application/infonotes/ in the section entitled "Consolidated proposals".

7. Key steps in applying to Global Fund Round 11

After checking the eligibility and prioritization status of the country, applicants can initiate the process of proposal development if the eligibility and prioritization criteria are met.

The key steps that need to be considered in submitting an application for TB control to Global Fund Round 11 are listed in Table1.

Table 1

Key steps in applying to Global Fund Round 11

Step	Action	Time
1	Establishment of CCM	*t*0
2	Public announcement by CCM of the submission of a TB proposal to the Global Fund Round 11 to invite stakeholders to participate in the proposal development	*t*0 +4 weeks
3	If necessary, review and updating of national strategic plan	*t*0 +4 weeks
4	Identification of gaps and priorities to be addressed through the Global Fund Round 11 grant[a]	*t*0 +5 weeks
5	Establishment of writing committee to develop proposal	*t*0 +5 weeks
6	Identification and definition of goals and objectives to be achieved through grant[a]	*t*0 +6 weeks
7	Identification of interventions and activities to be implemented to achieve goals and objectives[a]	*t*0 +6 weeks
8	Identification of principal recipients and subrecipients	*t*0 +6 weeks
9	Establishment of workplan to develop proposal	*t*0 +7 weeks
10	Identification of need for technical assistance for proposal development	*t*0 +7 weeks
11	Establishment of budget needed for proposal development (national, regional and international meetings, technical assistance and other costs)	*t*0 +7 weeks
12	Development and writing of core proposal[a]	*t*0 +9 weeks
13	Development of logical framework[a]	*t*0 +9 weeks
14	Review and revision of first draft, including core proposal and logical framework[a]	*t*0 +10 weeks
15	Development of budget and workplan[a]	*t*0 +11

		weeks
16	Establishment of monitoring and evaluation framework[a]	*t*0 +11 weeks
17	Second review[b] and revision of various components of application[a]	*t*0 +13 weeks
18	Finalization of application[a]	*t*0 +15 weeks
19	Final check of various components of the application, including initial parts on country and CCM information	*t*0 +16 weeks
20	Endorsement of application by CCM members	*t*0 +18 weeks
21	Submission of application to Global Fund Secretariat[c]	

*t*0, time zero.

[a]Area of work for which technical assistance may be needed.

[b]The proposal may be reviewed in one of the "mock reviews" that are usually organized by the World Health Organization (WHO) at the regional or global level.

[c]The TB proposal may be included with other disease components in a single application and submitted to the Global Fund Secretariat.

Table 1 suggests that the development of the Global Fund application is characterized by two broad aspects related to administrative and technical issues that must be considered carefully by applicants. The following sections in this document identify and describe the main components of these issues.

8. Administrative issues

8.1 Establishment of CCM

A CCM must be established in line with the six requirements defined by the Global Fund. These requirements are well described in the Global Fund Guidelines (pages 16–20) and in the CCM guidelines recently issued by the Global Fund (available at http://www.theglobalfund.org/en/ccm/).

CCM members should meet and make a decision to apply for Global Fund Round 11 funding.The note of record for this meeting must be included in the application.

8.2 Public announcement by CCM of submission

A public announcement must be made using appropriate communication channels to invite partners, nongovernmental organizations (NGOs) operating at national, regional or community levels, and any relevant stakeholders to participate in the development of the application to Global Fund Round 11. This process should be documented in the application.

8.3 Identification of principal recipients and subrecipients

The principal recipients must be selected upfront during the proposal development process. To this end, a public call must be undertaken to the potential principal recipients. A Global Fund grant can be implemented by one or more principal recipients. The selection of each principal recipient must be transparent and documented as required by the Global Fund. The CCM should assess the ability of each principal recipient to (i) take the leadership of the grant implementation and (ii) interact, under the established legal agreement, with the Global Fund on issues associated with finances and the grant implementation progress.

A principal recipient could be from the government sector, such as a ministry of health or a national TB programme; from a nongovernmental network, such as a civil society entity; or from an international organization. A report documenting how the principal recipients were selected must be attached to the application.

The selected principal recipients must sign off on the proposal, confirming that they endorse the various components of the application to the Global Fund.

The selected principal recipients must then select subrecipients, usually from among the stakeholders that responded positively to the public announcement made by the CCM. The principal recipients are fully responsible for the involvement of the selected subrecipients in the implementation of the Global Fund grant.

Further details on principal recipients are provided in the Global Fund Guidelines (pages 17–18 and 37–38).

8.4 Multisectoral approach to proposal development and implementation

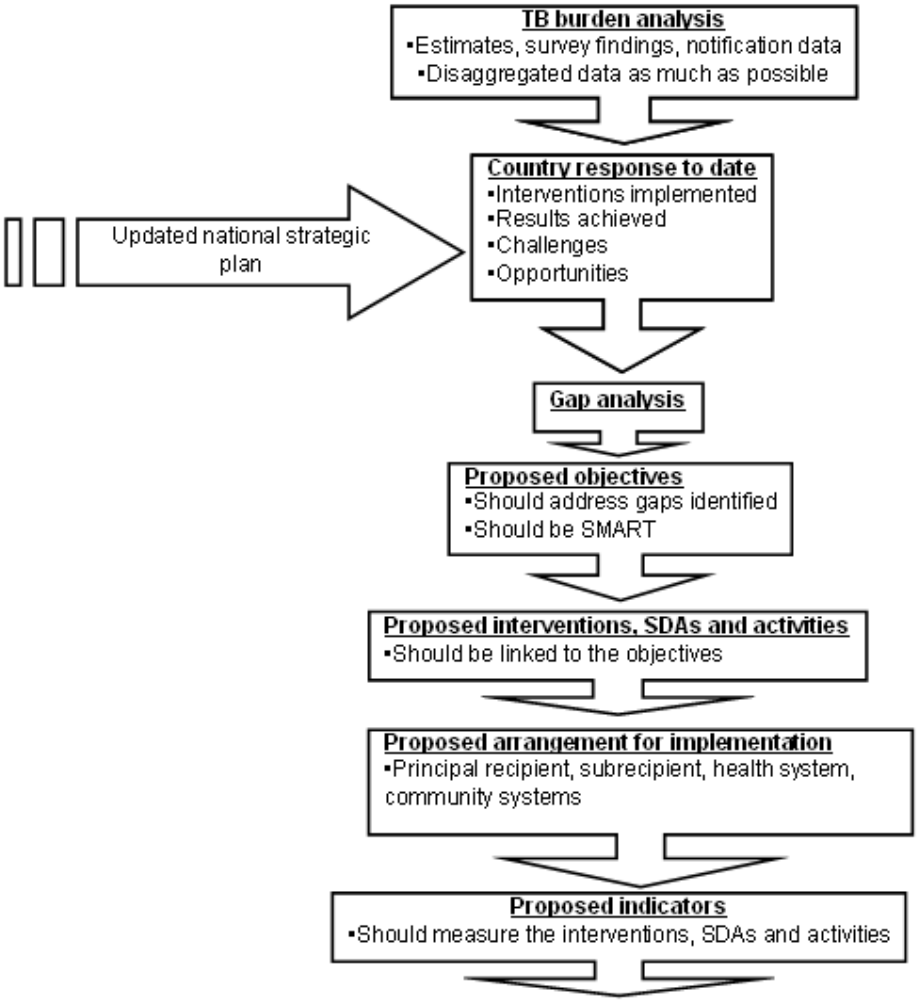
The proposal development process should involve multisectoral stakeholders. To this end, government and nongovernment entities should jointly identify the relevant gaps and agree on the priorities that need to be addressed through the Global Fund grant

proposal. Input from the various entities will contribute to establishing a basis for the development of the application. The process of proposal development involving stakeholders is described in the Global Fund Guidelines (pages 4–5). In this context, a country may consider including in its proposal activities related to the partnering process that would foster the sound involvement of multisectoral stakeholders. Such a proposal would also include funding for partners' activities that will contribute to the achievement of the country's goal and objectives.

9. Technical issues

All sections of the proposal template must be developed properly in order to apply to the Global Fund, but some of the narrative sections constitute the backbone of the application, in particular Sections 3.1, 3.2, 3.4 and 4.3. These sections should reflect the thinking process on which the application was built (see Figure 1). When appropriately developed and written, these sections should convince the Technical Review Panel that the proposal is sound and should reflect the practical reasons why the grant is needed.

Figure 1: Proposal development



Before defining any goals or strategic interventions, however, it is paramount to describe the status of TB burden and TB control policy implemented in the country to date. Specifically, the results achieved and not achieved and the identified gaps and constraints must be described. This section constitutes the situational analysis of TB control and allows the strategic orientations of the application to the Global Fund to be defined. In addition, the contribution of national and international partners (technical and financial) to the TB control programme must be clearly identified before the process of proposal development is initiated. The contribution of any previous Global Fund grants must be included in this exercise.

The proposal must define clear goals that will contribute significantly to reaching the overall goal specified in the national strategy to control TB in the country. Operational objectives should also be defined clearly; their definitions should be formulated in such a way that if the operational objectives are achieved, then the goals of the proposal will be attained. The linkage between the operational objectives and the goals needs to be described properly. The operational objectives should be linked appropriately to the gaps that will be addressed through the Global Fund grant. In order to achieve the operational objectives, appropriate strategic interventions and their inherent activities must be identified and specified in the proposal. If there is a significant incompatibility between the selected strategic interventions and the operational objectives, then the application is likely to be rejected by the Technical Review Panel.

9.1 Identification of gaps, constraints and priorities to be addressed through the Global Fund Round 11 grant

9.1.1 Situational analysis of TB and TB control

9.1.1.1 TB burden analysis

The proposal should include the most relevant and recent epidemiological data on TB in the country. All the available sources of information on TB should be considered in this exercise, namely WHO estimates, vital statistics and the information system established by the national TB Programme, and surveys and operational research studies.

Data from surveys on the annual risk of TB infection, from TB prevalence surveys and based on WHO estimates must be reported. TB mortality estimates must also be highlighted. The analysis of data collected through the routine information system on TB in the country should provide the annual number and incidence of notified TB cases. These figures should be distributed by age group, gender and area (district, state, region, province or oblast, depending on the country). The trend over time of the notified number and incidence of TB cases must be described.

The distribution study of the data will provide information on:

- who is more affected by TB – this will result in the identification of:
    - the age groups with the highest numbers and notification rates of TB;
    - the gender group with the highest number and notification rate of TB;
- the place where TB is more frequently observed – this will:
    - identify geographical areas with the highest TB burden;

        - compare TB occurrence between rural and urban settings;
        - determine the urban areas with the highest numbers and notification rates of TB;
    - trends of notified TB cases to describe any increase or decrease over time of their rate and specify the annual rate of increase or decrease;
    - trends over time of the average age of notified TB patients. For instance, an increase in the average age suggests that TB is probably affecting older individuals; such information along with data showing a significant decline in the TB notification rate among young people also suggests that TB transmission is probably decreasing in the general population.

For all proposals, the TB/HIV component should be described through:

- the estimated number of people living with HIV and the HIV prevalence in the general population;
- the cumulative number of people living with AIDS identified to date;
- the estimated prevalence of HIV infection among people with TB;
- data on notified TB among people living with HIV.

Any particular distribution of the HIV/AIDS burden should be highlighted, such as the prevalence of HIV infection in pregnant women, in people who inject drugs and in sex workers.

In addition, the analysis should provide key data on population groups with a significantly higher TB notification rate compared with the general population, such as:

- people living in slums;
- TB contacts;
- incarcerated people;
- people from indigenous populations;
- miners;
- suburban residents;
- migrants;
- refugees;
- asylum seekers.

The number of previously treated people with TB should be reported, along with, if possible, any relevant aspects of their distribution, such as retreatment category and geographical distribution.

Any information on drug-resistant TB, particularly multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), should be specified, such as:

- the estimated total number (measured or modelled) of people with MDR-TB;
- the prevalence of MDR-TB:
    - among people with TB without previous TB treatment;
    - among people previously treated, if possible stratified by the following categories: relapse, treatment after interruption (default) and treatment after failure.

Such information may be available from previous drug resistance surveys, ongoing surveillance systems for drug-resistant TB, and existing MDR-TB/XDR-TB case management programmes.

It would be appropriate to:

- report the number of cases of MDR-TB and XDR-TB identified through national TB programme services or any other health services;
- describe, if possible, the distribution of these cases by:
    - area (state, region, province, oblast, district or other; urban versus rural areas or any spatial distribution);
    - gender;
    - age groups;
    - any other characteristic.

This narrative part of the application will contribute to understanding the reasons why certain population groups or regions are specifically selected to be targeted by the interventions proposed to be funded by Global Fund grant. In addition, for each of the target groups or regions, available information on knowledge gaps, cultural beliefs and behavioural patterns that affect health-seeking behaviour must be provided.

9.1.1.2 Organization of TB control in the country

This narrative section helps the Technical Review Panel understand the overall context in which TB control has been organized to date and how it has evolved over time.

The entity or entities organizing TB control should be clearly specified. In most low- and middle-income countries, TB control is usually organized in the framework of a national TB programme hosted by the ministry of health.

Brief descriptions should be provided on:

- the structure of the national TB programme, namely:
    - the central unit and its role;
    - the role of the intermediate health level (e.g. state, region, province, oblast, district) in the organization of TB control activities and in the management of the resources of the TB control programme at this level;
    - the integration of national TB programme services in health facilities and in general health services;
    - the TB laboratory network, including information on the national reference laboratory, and the number and role of TB laboratories at the intermediate level and at other peripheral levels;
- the national policy adopted by the national TB programme to control TB and, if needed, its evolution over time, and the aims of this national policy;
- the most recent multiyear strategic plan, including:
    - a core plan, where the goals and the operational objectives of the national policy to control TB should be specified, along with the strategic interventions and the activities to reach these goals and objectives. In addition, any data on the number of deaths that would be avoided by implementing the strategic plan would be appropriate;
    - a budget plan with a clearly identified financial gap;
    - a monitoring and evaluation plan;
    - an operational plan;
    - a technical assistance plan;
- the sources of funding for TB control, with information on the financial contribution of the government. National and international funding partners

should also be identified. The components of the strategic plan that are financially supported by the partners should, wherever possible, be specified. Information on previous Global Fund grants, including their level of implementation, should be provided. The financial gap that still needs to be addressed, both now and in the coming years, according to the TB control activities, should be highlighted;

- the present level of implementation of the strategic interventions and activities – information should be provided on:
    - the provision of TB care and control services in general health services, particularly in primary health-care settings, first referral health facilities and hospitals;
    - the involvement of health networks outside the national TB programme, such as the private health sector, health services run by NGOs and faith-based organizations, university hospitals, and the health services of the army, police, social security and penitentiary systems;
    - the level of implementation of some components of the Stop TB Strategy, such as TB/HIV collaborative activities, MDR-TB case management, practical approaches to lung health, and community involvement;
    - wherever possible, TB care and control services targeting people in high-risk groups, such as TB contacts and disadvantaged populations such as people living in slums;
- the level of implementation of previous Global Fund grants that have been approved by the Technical Review Panel.

9.1.1.3 Results of TB control policy implemented

This narrative section should present the results that have been achieved and not achieved with the implementation of the national TB control policy. These results need to be reflected through the indicators defined by the national TB control programme to evaluate whether the targets and operational objectives have been reached. Some examples of what the indicators can measure are:

- the impact of the national TB control policy adopted, such as a significant decrease over time of the TB notification rate;
- the outcomes of the strategic interventions implemented, such as an increase or decrease of the TB treatment success rate;
- an increase or decrease in TB treatment failure among new TB cases;
- the outputs of the activities, such as:
    - an increase in the number of people suspected to have TB and appropriately identified and screened for TB;
    - an increase in the number of people with TB detected through TB contact investigation activities;
    - an increase in the number of people with MDR-TB who have access to second-line TB drugs and are properly managed and followed up;
    - an increase in the number of people with TB who have been tested for HIV.

Furthermore, the findings and conclusions of the most recent external or international review of the national TB programme, and those of external monitoring and

evaluation missions, must be considered in the analysis of the results of the TB control policy in the country.

The results achieved or not achieved under previous Global Fund grants should be highlighted in the application. The contribution of Global Fund grants still being implemented must be clarified where necessary.

The key assets that have contributed to achieving significant results and strengthening the implementation of TB control activities in the country should be described in the proposal.

The reasons why some areas have failed to achieve the expected results must be carefully identified, critically analysed and discussed within the writing committee and with the relevant stakeholders. This will help to clarify the extent to which there are linkages between the identified causes and the poor achievement or non-achievement of the expected results.

In addition, it is important to describe the possible opportunities existing in the country, such as changes in the overall national policy, in the national health policy or in the rules of the ministry of finance to allocate budgets. The possibility of taking advantage of these changes to improve and enhance TB control should be considered seriously. For instance, many countries have mobilized resources to alleviate poverty through national initiatives; the inclusion of TB as a disease of poverty is an adequate opportunity to promote TB in the national health priorities and therefore to strengthen TB care and control services.

It would also be useful to provide information on the possible threats that may jeopardize the implementation of TB control activities. These threats may be related to changes in the overall national policy or in the national health policy. For instance, a national policy resulting in decentralization of public services, including health services, at the regional, provincial or district level may make TB control services inefficient if the managerial capacities of health resources are weak at these levels. Clear and appropriate identification of the potential threats will contribute to adequately specifying the possible approaches to be considered to avoid additional weaknesses in TB control.

9.1.1.4 Gap analysis

Normally, a gap analysis should be well described and included in the national strategic plan of the country.

A gap analysis is not a description of the Stop TB Strategy components that have not yet been implemented; nor is it a list of TB control activities to be implemented. Many TB proposals submitted to previous rounds of the Global Fund highlighted that certain activities had not been initiated or that certain interventions should be implemented, but without providing any reason, but interventions that may need to be implemented through the Global Fund grant should not be discussed in the gap analysis. The formulation of gaps such as “Activities to involve all care providers have not been yet implemented” or “The practical approach to lung health must be implemented” have been observed in TB proposals; such formulations are not compatible with the gap analysis. The gap analysis should describe the constraints and insufficiencies that have been identified and that can explain the current and expected weaknesses in TB control strategy. The gap analysis should describe what has been lacking, missed or not achieved through implementation of the ongoing TB control services.

The Global Fund Guidelines (pages 20–21) provide guidance on what can appropriately be considered in this analysis.

A gap analysis cannot be appropriately carried out and fully understood by the Technical Review Panel if the four elements discussed in the previous paragraph are not well described, namely:

- the strong assets that contributed to achieving appropriate results;
- clear identification and full understanding of the reasons for non-achievement of certain expected results;
- the possible opportunities that have not been considered yet in the national policy to improve TB control;
- the potential or actual threats for TB care and control services already implemented and for which no measures have been defined yet.

Based on these four points, any identified constraints and gaps should be highlighted. It is appropriate to establish an order of priority for any issues identified in the gap analysis that need to be addressed.

Box 1 shows an example of formulations that can be made in a gap analysis.

Box 1 : Example of formulations in a gap analysis

In Tubercoland (population 40 million), the TB burden is high. Approximately 40 000 people with TB (all forms) are identified every year, with an annual notification rate of 100 per 100 000 population. The analysis of TB data collected on a routine basis through the national TB programme network shows that in general 55% of notified people with TB are male and 70% of notified people with TB are aged 15–55 years. The notification rate of smear-positive pulmonary TB is nearly 80% higher in males than in females. Further analysis suggests that the detection of TB is stagnating at the national level but increasing slightly (by less than 1% per year) in the heavily populated districts. On average 62% of cases of TB notified each year are identified in the 46 most urbanized districts, where the 9 major cities are located. The data suggest that these 9 cities account for nearly 40% of the national TB burden. Moreover, in some poor neighbourhoods of Teebeegrad, the capital city (population 6 million), the notification rate reached 851 cases of TB per 100 000 people in 2009.

Tubercoland includes 125 districts and is in a process of administrative decentralization. To this end, 20 administrative regions will be created, each including 4–8 districts.

The national TB programme in collaboration with partners has developed a national strategic plan for 2006–2015 to meet the MDGs. In order to financially support this plan for the period 2011–2015, a proposal was submitted to Global Fund Round 10. In this proposal, the following weaknesses were highlighted in the gap analysis:

- The managerial capacity of the national TB programme is insufficient:
  - The national TB programme central unit includes the programme manager, one medical officer, one statistician and two clerks. Given their small number, the staff cannot cope with the requirements needed for strategic planning, management of national TB programme resources, development of guidelines, development of surveillance capacities, monitoring and evaluation, and other tasks. As a result, the managerial and technical support capacities of the central unit are insufficient.
  - There are 125 health districts; all are assumed to be supervised and technically assisted by the small team of the national TB programme central unit, which cannot play this role fully.There is no intermediate administrative level between the Ministry of Health and health districts.

- The TB laboratory network is also insufficient: There are only 168 TB microscopy laboratories for a population of 40 million, resulting in a ratio of 1 TB microscopy laboratory for 238 000 people, when the minimum required is 1 laboratory for 100 000 people. Moreover, in the 46 most urbanized districts with the highest TB notification rates (200–350 TB cases per 100 000 population), there is an average of 1 TB microscopy laboratory per 500 000 people; in the urban district of Respirovich, the ratio is 1 TB microscopy laboratory per 850 000 people.

9.1.2 Identification and definition of goals and objectives to be achieved through the Global Fund Round 11 grant

9.1.2.1 Proposal goals and prioritization of gaps to be closed

Each proposal must have specific goals. The goals should be established in such a way that their achievement will contribute significantly to reaching and maintaining the overall goals defined in the national TB control policy (see Box 2 for an example). This is in line with the key principle of "value for money" of the Global Fund. The goals must be defined in line with "SMART" criteria – that is, they must be specific, measurable, attainable, relevant and time-bound. The definition of the proposal goals will prioritize the gaps and constraints that need to be addressed through the Global Fund grant. The process of identifying and defining goals and prioritizing the gaps to be addressed needs thorough discussion and must involve all the stakeholders contributing to the development of the proposal. All the identified gaps and constraints may be considered in the grant proposal, but addressing specific gaps or particular constraints may have a much greater impact on the improvement of TB control compared with other gaps or constraints. If the prioritization process selects only some of the gaps, the applicant should explain how the gaps and constraints not targeted by the grant proposal would be addressed.

Box 2: Example of a proposal goal formulation

Based on the situation analysis described in Box 1, the national TB programme of Tubercoland and the other stakeholders defined the following goal of the TB proposal submitted to Round 10 of the Global Fund: "To reduce TB burden in the 46 most urbanized districts by decreasing the notified TB incidence by at least 6% per year from 2016 onwards."

Given the contribution of the 46 most urbanized districts to fuelling TB burden in Tubercoland, the national TB programme and the stakeholders believed that a significant impact on TB burden in these 46 districts would significantly improve the TB situation at the national level and would contribute to meeting the MDGs.

9.1.2.2 Formulation of operational objectives

Identification of the gaps and constraints will help to define the operational objectives of the Global Fund grant proposal. Each operational objective must be rationally linked to one or more gaps or constraints described in the proposal that are to be addressed through the grant. Also, each operational objective should be established on the basis of SMART criteria. A formulation specifying that the objective is to implement only a particular component of the Stop TB Strategy is not relevant. For instance, the phrase "the objective is to implement TB/HIV collaborative activities" is

not an appropriate formulation; in this example, there is confusion between an objective and an intervention (see Box 3 for an example).

The formulation of the operational objectives should also take into account the objectives defined in the previous or ongoing Global Fund grants in order to ensure adequate consolidation. If these objectives are still maintained for the coming grant, then this should be highlighted.

Box 3 : Examples of an operational objective

Box 1 highlighted that the managerial capacities of the national TB programme of Tubercoland were weak. One of the objectives formulated in the proposal submitted to the Global Fund Round 10 was:

"Objective 1: To improve the managerial and technical capacities of the national TB programme through the presence of appropriate and competent staff in the central unit by 2012 and to ensure functional and effective managerial links within the national TB programme network by 2013."

Box 1 reported that TB detection in Tubercoland is stagnating at the national level and increasing slightly in the most urbanized districts, where the TB notification rate is very high and the capacity of the TB diagnostic network is insufficient. To this end, the following operational objective was also specified in the proposal submitted for the Global Fund Round 10:

"Objective 2: To intensify TB case finding and to ensure adequate TB care and control services within the health system of the 46 most urbanized districts by increasing the following in these 46 districts: (i) TB notification, in comparison with 2010, by at least 1% in 2011, 3% in 2012 and 5% in 2013–2015; and (ii) the current 80% treatment success rate to at least 85% by 2011 and then at least 90% by 2015."

9.1.3 Identification of strategic interventions and activities to be implemented

Meaningful guidance is provided for this section in the Global Fund Guidelines (pages 23–26).

Each operational objective will be reached through the implementation of a set of strategic interventions called service delivery areas (SDAs). Therefore, it is important to carefully identify the appropriate SDAs that are likely to help achieve a specific operational objective. The operational objectives and their inherent SDAs must be logical, understandable and compatible. The aim of each SDA needs to be established and linked to the relevant operational objective (see Box 4 for an example).The SDAs specified in the Global Fund proposal should be consistent with the interventions with no available funding as highlighted in the multiyear strategic plan.

Countries eligible for Global Fund Round 11 funding but needing to focus on the targeted funding pool may wish to consider specific interventions ("highest-impact interventions") in their application that would have a major impact on the TB control situation. The implementation of such interventions, however, should be clearly compatible with the weaknesses identified in the gap analysis and the operational objectives targeted in the proposal.

The introduction of new TB diagnosis tools such as Xpert MTB/RIF (see http://whqlibdoc.who.int/hq/2011/WHO_HTM_TB_2011.12_eng.pdf, http://whqlibdoc.who.int/publications/2011/9789241501569_eng.pdf and Annex 3), and the implementation of a particular intervention such as community involvement in TB control (see Annex 4) or advocacy and communication (see Annex 5), must be clearly justified with regard to the defined objectives and the gaps or constraints to be addressed. Unjustified interventions may result in failure of the proposal for funding by the Global Fund.

The activities implemented under each SDA must be specified clearly. The proposal should highlight who will implement the SDA or activities (principal recipient, subrecipient or other implementer). An SDA can be implemented by more than one implementer. Outcome and output indicators must be identified for each SDA and when needed for the key activities.

Valuable and detailed information on the SDAs and their inherent activities are described in the WHO Stop TB Planning Tools. These were initially developed for the Global Fund Round 5 TB proposals and have been improved and updated for each subsequent Global Fund round. The latest version of the Tools was prepared for the Global Fund Round 10 TB proposals and is available at http://www.who.int/tb/dots/planningframeworks/en/index.html. This document specifies the inherent activities of each SDA as a function of the components of the Stop TB Strategy (pages 8–91).

Many applicants have misused the WHO Stop TB Planning Tools in the development of their proposals. Some applicants have simply copied the full components of the Stop TB Strategy, including SDAs or entire sets of SDAs with their inherent activities, and included them in their proposals without any justification or linkages with the described gap analysis. The Technical Review Panel made strong criticisms in previous rounds regarding such use of the Tools.

The Tools, updated for Round 10, can be used in the development of TB proposals for the Global Fund Round 11. The Tools can facilitate the identification of SDAs and activities that may need to be implemented through the Global Fund grant. The identification and selection of the SDAs and activities through the Tools, however, must be justified and compatible with the findings of the gap analysis and the operational objectives described in the application. Crude incorporation into the proposal of SDAs and activities from the Tools, without stating any reason for their inclusion, may result in rejection of the proposal by the Technical Review Panel.

In addition, the WHO TB Planning and Budgeting Tool provides valuable and detailed information on the SDAs and their inherent activities (see http://www.who.int/tb/dots/planning_budgeting_tool/download/en/index.html).

Similarly to the formulation of the operational objectives, the identification of the SDAs and their inherent activities must take into account the SDAs and activities of ongoing Global Fund grants to ensure proper consolidation.

Box 4: Examples of service delivery areas and activities

The Tubercoland applicants specified the following service delivery areas and activities to meet the objectives identified in Box 3:

Objective 1:

- SDA 1.1 Improving and strengthening the capacities of the national TB programme central unit
  1.1.1 Clear definition of the mission of the national TB programme central unit
  1.1.2 Recruitment or reassignment of the appropriate staff according to the post descriptions in the central unit
  1.1.3 Procurement of computers, printers and didactic material
  1.1.4 Appropriate training of staff
  1.1.5 External technical support
  1.1.6 Exchange visits and study tours
  1.1.7 Etc.
- SDA 1.2 Implementation of managerial units for TB control in each of the 9 administrative regions where the 46 most urbanized districts are located
  1.2.1 Recruitment/reassignment for each regional unit of one manager, one TB laboratory technician and one statistician
  1.2.2 Appropriate training of regional unitstaff
  1.2.3 Computer and printer for each regional unit
  1.2.4 Didactic material to ensure training at regional level
  1.2.5 Availability of car and fuel for each regional unit for supervision
  1.2.6 Supervision missions
  1.2.7 Organization of training and refreshing courses in each administrative region
  1.2.8 Organization of quarterly meetings in each administrative region
  1.2.9 Etc.

Objective 2:

- SDA 2.1 Improving and strengthening of TB laboratory capacity in the 46 most urbanized districts
  2.1.1 Revision of national guidelines on TB microscopy, culture and drug sensitivity testing
  2.1.2 Printing revised guidelines
  2.1.3 Procurement of 70 fluorescent microscopes with light-emitting diode
  2.1.4 Training of microscopist
  2.1.5 Implementation of five culture laboratories
  2.1.6 Etc.
- SDA 2.2 Improvement and strengthening of TB care and control services in public health services
  2.2.1 Training of primary health-care workers
  2.2.2 Training of staff practising at first referral health level
  2.2.3 Training of hospital staff
  2.2.4 Etc.
- SDA 2.3 Strengthening TB/HIV collaborative activities
  2.3.1 Preparation of national guidelines on TB/HIV management
  2.3.2 Implementation of an Xpert MTB/RIF machine in an antiretroviral clinic
  2.3.3 Procurement of cartridges for Xpert MTB/RIF machines
  2.3.4 Training on TB/HIV case management
  2.3.5 Design and development of adapted didactic material to inform and encourage people with TB to be tested for HIV infection and to promote systematic screening for TB among people living with HIV
  2.3.6 Etc.

- SDA 2.4 Involvement of private health workers practising in poor neighbourhoods
  2.4.1 Training in TB care and control for private nurses
  2.4.2 Training of general practitioners
  2.4.3 Provision of microscopes to private laboratories in these neighbourhoods
  2.4.4 Training in TB microscopy for staff of these laboratories
  2.4.5 Development and printing of guidelines, stationery, and information, education and communication material to be used by private health workers to ensure TB care and control services in line with national TB programme policy
  2.4.6 Etc.

9.2 Establishment of a logical framework

The narrative parts of the application explain in detail the purpose of the proposal and the interventions that will be implemented through the grant. The logical framework intends to provide an overview of the key elements of the proposal, namely goals, operational objectives, SDAs and their inherent activities. The activities should be mentioned in the logical framework as exactly specified in the narrative parts and identified using a specific number for every element. This will result in a numbering system that should be used and repeated throughout the proposal and in the budget and workplan (see Box 5 for an example). Such an approach will contribute to ensuring consistency among the narrative component of the proposal, the logical framework, the budget and workplan, and the performance framework. Implementers and outcome or output indicators should be highlighted according to the objectives and SDAs and in line with the narrative part of the proposal. The development of the logical framework is explained in the Global Fund Guidelines (pages 23–24).

Box 5: Example of numbering system to identify key elements specified in the proposal

Goal 1: (to specify)

Objective 1.1: ...

SDA 1.1.1: ...

1.1.1.1 Specify first activity

1.1.1.2 Specify second activity

1.1.1.3 Specify third activity

1.1.1.4 ...

...

SDA 1.1.2: ...

1.1.2.1 Specify first activity

1.1.2.2 Specify second activity

1.1.2.3 Specify third activity

1.1.2.4 ...

…

SDA 1.1.3: ...

1.1.3.1 Specify first activity

1.1.3.2 Specify second activity

1.1.3.3 Specify third activity

1.1.3.4 ...

Objective 1.2: ...

SDA 1.2.1: ...

1.2.1.3 Specify third activity

1.2.1.4 ...

...

SDA 1.2.2: ...

1.2.2.1 Specify first activity

1.2.2.2 Specify second activity

1.2.2.3 Specify third activity

1.2.2.4 ...

...

Goal 2: (to specify)

Objective 2.1: ...

SDA 2.1.1: ...

2.1.1.1 Specify first activity

2.1.1.2 Specify second activity

...

9.3 Performance framework

The performance framework must identify the impact and outcome indicators and the most relevant output indicators. These indicators aim to provide an overview of the key results of the interventions that will be implemented through the grant. In general, the aim of the impact indicators is to assess the goals and outcome indicators of the operational objectives, and the output indicators of the strategic interventions or SDAs. The aim of the process indicators is to evaluate the progress made in the implementation of activities and, in principle, cannot assess the results associated with the implementation of activities; process indicators may have to be specified in the performance framework for some key activities, however.

It is paramount that the indicators are formulated in such a manner that they are appropriate for assessing the objectives, interventions and key activities. The indicators should be consistent with those specified in the narrative part of the proposal and the logical framework.

A well-established TB information system will significantly contribute to obtaining sound data on TB in the country. The sources of data and the data-collection process must be clearly specified. This will help to determine whether a selected indicator would be easy to assess. An indicator that cannot be evaluated because of a lack or absence of data should not be selected. An impact indicator may be difficult to evaluate. For instance, the phrase "the decline of mortality from TB" implies robust and reliable vital statistics, but such data are often nonexistent or unreliable in many countries; therefore, selecting mortality from TB as an impact indicator must be discussed thoroughly before proposing it. Data for other important impact indicators can be collected with the funding support of the Global Fund; for instance, the population-based prevalence of TB or the prevalence of MDR-TB among people with TB can be estimated in surveys carried out in the framework of a Global Fund Round 11 grant. Therefore, the writing committee should fully discuss and select appropriate indicators that can be measured through data that can be collected from a reliable routine information system, surveys or studies. The Global Fund Monitoring and Evaluation Toolkit is helpful in identifying appropriate indicators (see http://www.theglobalfund.org/en/me/documents/toolkit/).

Further explanations are provided in the Global Fund Guidelines (pages 26–29) on monitoring and evaluation, including the performance framework.

9.4 Development of budget and workplan for the proposal

The Global Fund Guidelines (pages 31–36) describe the preparation of a funding request and the development of the various sections of the proposal template inherent to this request. Inappropriate development of the funding request is a common reason for TB proposals not receiving approval for funding by the Global Fund. The funding request should be in line with the financial gap identified in the multiyear strategic plan and must never exceed this gap.

The budget and workplan is a key section of the request and must include full details of the budget. To this end, applicants are advised to use the Global Fund Budget and Work Plan template. Instructions are provided on how to complete the budget template step by step. All the activities identified in the proposal should have a corresponding budget, which is the amount requested for funding from the Global Fund. The objectives, SDAs and activities should be reported in the budget spreadsheet of the template using the same numbering system described in the logical framework, in order to ensure consistency with the other components of the application.

To calculate the budget for a given activity, work through the following steps:

1. Establish the unit cost of the activity. For instance, if the activity is training, the unit cost of training to be established is the cost of one training session.
2. Establish the quantity of units required to implement the activity for each year of the proposal. For the example of training, the number of training sessions needed for each year of funding should be specified.
3. Establish the quantities of units by quarter for the first 2 (or 3) years of the proposal. For the remaining 3 (or 2) years, establish the annual quantities.
4. Calculate the amount requested for funding for each year for each activity, by multiplying the quantities by the unit cost of the activity.

To calculate and present the unit cost of each activity in line with the expectation of the Technical Review Panel, bear in mind the following:

- *Keep order:* In the spreadsheet template, each activity must be numbered as it is in the proposal and the logical framework. The activity must be indicated under the SDA and the operational objective to which it is linked. The implementer (principal recipient or subrecipient), the budget cost category (see the list described in the Global Fund Guidelines, pages 32–34) and the measurement unit must be specified for every activity. For instance, for training, the measurement unit is the training session.
- *Be precise:* The unit cost for each activity should be well demonstrated (see the examples in Table 2). Many proposals have been rejected in previous Global Fund rounds because of the lack of clarity in the calculation of unit costs.
- *Use an adequate price:* The price attached to an element should be acceptable. Do not overprice the elements. Proposals have been rejected by the Technical Review Panel because some specific activities were overpriced.
- *Be consistent:* Use the national standards to establish the per diem, salaries and other local prices. The same standards should be used for all activities, wherever needed.

Given the process of consolidation in Round 11, the funding remaining from the previous Global Fund grant should be separated from the new required funding. Both will constitute the total funding request for Global Fund Round 11.

The WHO Planning and Budgeting Tool can help, under certain circumstances, in developing a budget for the Global Fund application. Further clarifications on this tool are given in Box 6.

Table 2

Example of presenting and calculating unit cost for an activity in the spreadsheet template of the Global Fund[a,b]

Ref. N°	Objective	SDA	Activity	Assumptions (of the unit cost)	Measurement unit	Unit cost year 1	Quarter 1[c] quantity	Quarter 1[c] total amount	Total quantity year 1	**Total year 1**
1.2	1	1.2 Improving diagnosis	1.2.1.2. Procurement of Binocular microscope	$1,000 for each microscope x 5 microscopes	Number of microscopes	$ 1,000	5	$5,000	5	$5,000
1.5.3.3	1	1.5.3. Human Resource Development	1.5.3.3. Training on drug management	$2,970 ={[(Per diem $8*30particpants) +(Perdiem$10*5 Facilitators) + (Refreshment$2*35 persons) + (Hotel $10*30person) + (Room rental $30/day+Stationary $20/day)]*2days +(Travel cost$30* 30participants) + (Travel cost$30*5 facilitators) + (Training material$10*30 participants) + Opening ceremony $200} X 17 courses	Number of training sessions	$ 2,970	3	$ 8,910	3	$8,910

[a] These rates are fictional examples. Applicants should not use the rates shown here but should use the rates in line with their national standards.

[b] For the purpose of this example, the table excludes the columns “responsible for implementation”, “implementing entity type” and “cost category”.

[c] Quarters 2-4 are not shown and their quantities are assumed to be zero.

Box 6: Using the WHO TB Planning and Budgeting Tool

The WHO TB Planning and Budgeting Tool is used to develop the budget required for implementing the national TB plan in a certain time period. The national strategic plan for TB control includes all the activities envisaged by the national TB programme and partners to control TB in the country, most often in line with the Stop TB Strategy. Usually, the national strategic plan also includes the information available on the planned sources of funding from the different donors (e.g. Department for International Development, Global Fund, United States Agency for International Development). This tool allows countries to budget for all activities and to identify the different potential sources of funding, including the Global Fund. The tool and the accompanying information can be downloaded from http://www.who.int/tb/dots/planning_budgeting_tool/en/index.html .

Countries can use the information this tool generates to develop a Global Fund proposal. In theory, the activities identified with a funding gap in this tool are those to be presented in the Global Fund application. However, applicants are advised to copy the relevant information (those activities that require funding) into the tools recommended by the Global Fund for presenting the budget.

Annexes

Annex 1

Comparison of the Stop TB Planning Frameworks and selected Technical Review Panel comments from failed proposals in Rounds 6 and 10

		Round 6 (success rate 35/56 = 62%)	Round 10 (success rate 26/48 = 54%)
Practical tools for proposal development		WHO/STB provide Stop TB Planning Frameworks, with proposed objectives/SDAs/activities, with 12 SDAs and 77 pages	WHO/STB provide Stop TB Planning Tools, with proposed objectives/SDAs/activities, with 21 SDAs and 98 pages
Major weaknesses of failed proposals raised by TRP	Selected TRP comments on situational/gap analysis	"Situational analysis is deficient and the gap analysis is incomprehensible" (Cameroon) "The link with overall context is not described" (Guinea-Bissau) "Discrepancy between detailed problem analysis and lack of detail in the description of the strategy and activities to achieve the goal" (Madagascar) "Gap analysis shows the need to explore new initiatives such as private–public mix (PPM), Practical Approach to Lung Health and community-based care, but only PPM is considered. This contradicts the statement in proposal on equity between urban and rural areas, where the latter	"There are insufficient linkages between the gap analysis and the proposed interventions" (Nicaragua) "Access to health system appears to be a major barrier to increasing case detection, but there is no clear response which addresses this" (Burundi) "The programmatic gap analysis is not explicit, making it difficult to assess the identified gaps. There is no coherence between gaps, activities and budget" (Kyrgyzstan)

	strategies have clear added value" (northern Sudan)	
Selected TRP comments on budget	"There are important and unexplained budget inconsistencies" (Cambodia) "The budget is grossly inflated" (Cameroon) "The amount budgeted for the procurement of anti-TB drugs by far exceeds the number of TB patients expected to be identified and treated" (Sierra Leone)	"Activities mentioned in the budget do not align with activities described under the interventions" (Zimbabwe) "Planning, administration costs and overheads which account for 44% of the budget is too high" (East, Central and Southern Africa Health Community) "Many unit costs for pharmaceuticals and equipment are set substantially higher than international standards" (United Republic of Tanzania)
Selected TRP comments on additionality of previous grants/other funding sources	"There is no description/evaluation of additionality between the two TB grants" (Honduras) "Additionalities between Rounds 3 and 6 not demonstrated" (Swaziland) "Relationship with and additionality to prior Global Fund grant and other support/sources of funding not detailed enough" (Zambia) "Difficult to analyse additionality between the two previous Global Fund grants and this proposal as the gap analysis doesn't include Round 3 and the only area mentioned for Round 2 is advocacy, communication and	"The links with other Global Fund grants are poorly explained. This makes it difficult to evaluate any overlap, complementarity and additionality" (Kyrgyzstan) "Linkages with other funding sources haven't been made or explained" (Sierra Leone) "Major constraints in gaps in disease, health and community systems lack in-depth analysis and do not reflect the achievements from Rounds 5 and 8 nor additionality" (Zimbabwe)

		social mobilization”(Pakistan)	
	Selected TRP comments on feasibility	“The proposal is very ambitious and there are concerns about the feasibility of implementation. The link between the activities and objectives is not clear” (Niger) “Proposal is significantly too ambitious, considering the complex environment in which it is to be implemented” (Afghanistan) “Objective 1 covers too many components with a large scope of activities and the budget is concentrated in the first 2 years. This raises the question of feasibility and impact” (Senegal)	“The proposal suggests 100%antiretroviral therapy provision in the first year. It is not clear how this is feasible” (Sierra Leone) “Given the very poor performance of the national TB programme, the proposed programme of decentralization and scale-up is unrealistic” (Chad) “The proposal appears to be a mechanical consolidation of subrecipient plans without clear indication on how strategic coherence will be assured” (Cambodia)

STB, Stop TB; TRP, Technical Review Panel.

Annex 2

Information note on Tuberculosis and human rights

Introduction

Tuberculosis is a disease of poverty and inequality that particularly affects key vulnerable populations[1] with little or no access to basic services. Many of the factors that increase people's vulnerability to tuberculosis (TB) or reduce their access to diagnostic, prevention and treatment services are associated with people's ability to realize their human rights.

Access to TB prevention, treatment, support and care services, as well as to basic necessities such as food, housing and social services, are fundamental human rights embedded in the right to health. A human rights-based approach to TB prevention, treatment and care can help overcome the legal, structural and social barriers to quality TB prevention, diagnosis, treatment and care services.

WHO Stop TB Strategy and Human Rights

An important objective of the WHO Stop TB Strategy[2] is to protect and promote human rights in TB prevention and care. Addressing HIV related TB (TB/HIV), multidrug resistant (MDR)-TB and the needs of poor and vulnerable populations[1]; and empowering communities and people with TB have been identified as core components in the *Stop TB Partnerships Global Plan to Stop TB (2011-2015[3]).*

These components emphasize patients rights and responsibilities and the obligations

of programs, policy-makers and donors to foster community participation in TB care, prevention and health promotion. The Patients' Charter for TB Care[4] is also referenced in the strategy.

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[1] Key TB vulnerable and at risk groups include: women, children, people working in settings that facilitate TB transmission (e.g. health care workers, miners, and prison officers), prisoners, migrants (including undocumented migrants), refugees and internally displaced people, indigenous peoples, people living with HIV and people who use drugs.

[2] WHO Stop TB Strategy http://www.who.int/tb/strategy/en/

[3] Global Plan to Stop TB, 2011-2015: http://www.stoptb.org/assets/documents/global/plan/TB_GlobalPlanToStopTB2011-2015.pdf

[4] Patients' Charter for TB Care,2010: http://www.worldcarecouncil.org/content/patients-charter-tuberculosis-care

The Global Fund supports the integration of human rights into health programming in order to maximize health outcomes.

Health and human rights

Human rights are a set of entitlements which apply to all human beings. They are interdependent and indivisible as all are necessary to ensure a person's dignity. The *right to health* is dependent on and contributes to the realization of many other human rights. It extends not only to adequate and appropriate care but includes also a wide range of factors, the underlying "*determinants of health"* such as safe drinking water, food, adequate nutrition, housing, non discrimination, healthy occupational and environmental conditions and education.

The right to health and other human rights are legally recognized and guaranteed through numerous national constitutions as well as international and regional treaties that the majority of countries have ratified. Under human rights law, States have the duty to respect, protect and fulfill human rights. These obligations require that States must refrain and prevent others from interfering with the enjoyment of the right and adopt appropriate measures towards the full realization of the rights.

The *right to health* further requires immediate and targeted steps to be taken to progressively ensure that health services, goods and facilities are *available, accessible, acceptable and of quality.* The right to non-discrimination, including on the grounds of social and health status, is an immediately enforceable obligation.

Why are human rights important in the TB response?

The integration of a human rights- based approach into TB programmes, policies and interventions can help achieve universal access to TB prevention, care and treatment through:

Contributing to TB prevention. Economic, social and cultural rights are strongly interlinked. For example vulnerability to TB infection and disease increases with a lack of access to: education; appropriate nutrition; quality housing and sanitation; health services and facilities; employment and social security. Being ill with TB also increases vulnerability to poverty. A human rights-based approach addresses the socio-economic determinants of health that impact TB by ensuring that the rights to food, education, housing and social security of vulnerable and marginalized groups are promoted and protected.

Facilitating access to care. Effective diagnosis is often hindered by costs, lack of social security or health services and other barriers associated with seeking care, such as stigma and discrimination, or lack of information and specific public policies. Accessing care can lead to catastrophic expenditures which may contribute to impoverishment for the individual and his or her entire family. These barriers can be removed if human rights implications of TB policy, legislation and programming are addressed within an integrated and multisectoral response to TB.

Empowering patients and communities. Patients and communities play an integral role in TB treatment literacy, social support, advocacy, communication and social

mobilization. TB cannot be adequately addressed without meaningfully involving representatives of the most affected communities in the planning and implementation of polices and programs that impact on them. A human rights based approach to TB places affected persons and communities at the centre, as equal partners, driving health policy, providing them with the tools to participate and claim specific rights

Reaching key vulnerable groups[1]. A rights-based approach to TB requires particular attention to ensuring that the specific needs and rights of vulnerable groups are recognized and adequately addressed. Stigma and discrimination against people with TB and those vulnerable to TB can prevent those most in need from accessing TB prevention, treatment and care services.

Improving quality of services. Poor quality of care hampers global TB control efforts. Inadequate training and supervision of health workers, inconsistent drug supplies, inadequate diagnostic tests and limited resources inhibit early detection and proper treatment resulting in increased transmission and poor health outcomes. By tailoring services to meet the needs of patients and communities, a human rights based approach will improve service delivery, ensure that resource use matches community priorities and provide evidence that can be used to mobilize additional resources.

Addressing co-morbidities, including HIV. Early diagnosis among people living with HIV is challenging but vital. Prevention, diagnosis and treatment of TB should be integrated or coordinated to meet the needs of patients with HIV, Hepatitis C, diabetes, those on opiate substitution therapy and other common co-morbidities. Integrating and coordinating services facilitate adherence and ensures patients are not forced to choose between the therapies they need.

Preventing drug resistant TB and promote rights-respecting treatment. Drug-resistant TB, including multi-drug resistant and extensively drug resistant TB, is associated with poor prescribing, irregular drug supply, inadequate access to quality care, mandatory treatment or confinement and inability to complete treatment. Human rights approaches emphasize appropriate treatments that meet patients' needs to prevent the development of drug resistance, patients' right to be free from discrimination (including in health care settings) and to be free from forced or coerced treatment.

When drug resistant TB does develop, community-based treatment options that respect patients' rights, have excellent treatment completion rates, are cost effective and protect public health should be considered. Community based palliative care for some patients with drug resistant TB is also needed, including access to both effective opiate pain relief and social support. Treatment for drug resistant TB should be non-restrictive and avoid long in-patient hospitalization and detention of TB patients. It should be 'patient-centered', as outlined by the International Standards for Tuberculosis Care[5], the Patient's Charter for Tuberculosis Care[6] and the Guidelines

[5] International Standards for Tuberculosis care, 2006: http://www.who.int/tb/publications/2006/istc_report.pdf

[6] Patients' Charter for TB Care,2010: http://www.worldcarecouncil.org/content/patients-charter-tuberculosis-care

for the Programmatic Management of drug resistant-TB[7], among other guidance documents.

How a human rights-based approach to TB can be integrated into Global Fund proposals

The Global Fund encourages applicants to include rights-promoting activities in proposals in order to improve access to TB prevention, treatment, care and support and increase the effectiveness of TB programmes. Human rights interventions to stop TB must be appropriately targeted to address the needs of key vulnerable and most at risk populations as well as the social and structural barriers to universal access to TB prevention, treatment, care and support.

Key activities to consider include:

Monitoring and analysis of vulnerabilities and rights issues related to TB:

- Development of disaggregated data - for example by sex and/or risk group; and development of indicators and research to identify and analyze TB socio-economic determinants, risk factors and vulnerable groups.
- Support to public monitoring bodies for monitoring human rights issues focusing on key vulnerable groups as noted above
- Patient support (peer) groups and local civil society organizations can also contribute to documentation of rights violations and identifying gaps in the implementation of laws and policies related to TB.

Programmes to ensure continuity of care for key vulnerable groups[1]:

- Economic and social support such as travel vouchers
- Food packages
- Conditional cash transfers
- Microcredit schemes
- Vocational training
- Health education

Policies and programs to integrate and/or coordinate services are key elements for ensuring continued access to quality care[8]. Such approaches need careful design, monitoring and documentation of best practice, and operational research can be encouraged in this and other areas. Applicants are also encouraged to plan for continuity of care beyond the lifetime of the Global Fund grant.

Increase accessibility, availability, acceptability and quality of TB prevention and care:

- Community-based TB and MDR-TB case-finding and treatment programs that

[7] WHO Guidelines for the Programmatic Management of drug resistant-TB, 2006: http://whqlibdoc.who.int/publications/2006/9241546956_eng.pdf

[8] The GFATM Board resolution , November 2008, reiterates that all TB proposal should explain how they will address HIV in TB patients and all HIV proposals should explain how they will address TB in PLHIV.

reduce the economic and social costs of seeking and staying in care
- Expansion of peer educators and community health workers role in TB
- Preventive therapy programs for people living with HIV

Programmes to reduce stigma and discrimination:
- Health education and information targeting key vulnerable groups[1]
- Training of health workers on non-discrimination, informed consent, confidentiality and duty to treat
- Human rights and TB treatment literacy such as 'know your rights' campaigns
- Law and policy reform
- Community -based treatment
- Patient support initiatives
- Advocacy and social mobilization campaigns
- Capacity building of affected communities to lead and manage interventions
- Use of new technology such as mobile phone messages for patient and adherence support.

Legal services for TB patients and vulnerable groups:
- Advice and support – including strategic litigation where appropriate - on legal issues, such as discrimination and problems in accessing care, privacy, confidentiality and informed consent issues
- Support for TB patients made redundant and/or facing deportation in relation to the completion of TB treatment

Support to empower communities:
- Social mobilization and campaigns to improve awareness of rights relevant to TB and capacity building of affected communities and vulnerable groups to claim their rights
- Meaningful and accountable involvement of patients and their community based organizations in the development of policies and programs that impact on them.

Law and policy review and reform:
- Review and reform of laws and policies that hamper effective TB responses (i.e. access to TB prevention services for key vulnerable groups) or those which encourage rather than discourage involuntary detention for patients. Policies should promote access to community based care models, patient economic and social support for TB and MDR-patients.
- Support to legal service providers (referred to above), Ombudsmen offices, and National Human Rights Institutions to engage in community outreach, campaigns, and advocacy with government for changes in law and policy.

Monitor and evaluate proposed interventions using human rights principles:
- The use of participatory research approaches that involve patients and communities in monitoring and evaluating interventions
- Establish evaluation indicators based on human rights criteria for example measuring levels of service access and involvement for marginalized groups
- Develop redress mechanisms for use when human rights are violated
- Share best practices and ensure lessons learned are transferred across programs

Key References

Human rights documents

- *Briefing Note on Tuberculosis and Human Rights, Stop TB Human Rights Taskforce (2011)* *http://www.stoptb.org/assets/documents/global/hrtf/Briefing%20note%20on%20TB%20and%20Human%20Rights.pdf*
- *Declaration of Human Rights (1948)* http://www.un.org/en/documents/udhr/
- *International Covenant on Economic, Social and Cultural Rights (1966)* http://www2.ohchr.org/english/law/cescr.htm
- *International Covenant of Civil and Political Rights (1966).* *http://www2.ohchr.org/english/law/ccpr.htm*
- *Committee on Economic, Social and Cultural Rights, General Comment No. 14* http://www.unhchr.ch/tbs/doc.nsf/(symbol)/E.C.12.2000.4.En
- *Committee on Economic, Social and Cultural Rights, General comment No. 20 on non discrimination in economic, social and cultural rights,* http://www2.ohchr.org/english/bodies/cescr/comments.htm
- *Convention on the Rights of the Child (1989)* http://www2.ohchr.org/english/law/crc.htm
- *Convention on the Elimination of All Forms of Discrimination Against Women (1979)* http://www.un.org/womenwatch/daw/cedaw/
- *International Convention on the Elimination of All Forms of Racial Discrimination (1963)* http://www2.ohchr.org/english/law/cerd.htm
- *Convention on the Rights of Migrant Workers (1990)* http://www2.ohchr.org/english/law/cmw.htm
- *Declaration of Alma Ata (1978)* http://www.who.int/hpr/NPH/docs/declaration_almaata.pdf
- *Siracusa principles:* http://www1.umn.edu/humanrts/instree/siracusaprinciples.html
- *Special Rapporteur on the Right to Health (2002):* http://www2.ohchr.org/english/issues/health/right/

TB-related documents

- *WHO Stop TB Strategy:* http://www.who.int/tb/strategy/en/index.html
- *Updated Global Plan to Stop TB, 2011-2015:* http://www.stoptb.org/assets/documents/global/plan/TB_GlobalPlanToStopTB2011-2015.pdf
- *Global Plan to Stop TB, 2006-2015:* http://www.who.int/tb/features_archive/global_plan_to_stop_tb/en/index.html
- UNAIDS Strategy (including TB/HIV): http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2010/JC2034_UNAIDS_Strategy_en.pdf
- *Patients' Charter for TB Care:* http://www.who.int/tb/publications/2006/patients_charter.pdf
- *Social determinants and TB:*

http://whqlibdoc.who.int/publications/2010/9789241563970_eng.pdf

- *Poverty and TB:* http://www.who.int/tb/challenges/poverty/en/index.html
- *TB in Prisons:* http://www.who.int/tb/challenges/prisons/en/index.html
- *TB care and control in refugees and displaced populations:* http://www.who.int/tb/challenges/refugees/en/index.html
- *Women and TB:* http://www.who.int/tb/womenandtb.pdf
- *Union statement on TB among undocumented migrants:* http://www.theunion.org/images/stories/download/guide/Undocumented-migrants-Statement_2008.pdf
- *Guidelines for social mobilization. A human rights approach to TB:* http://www.who.int/hhr/information/A%20Human%20Rights%20Approach%20to%20Tuberculosis.pdf
- *Community involvement in TB:* http://www.who.int/tb/people_and_communities/involvement/resources/en/index.html
- *Active engagement of civil society organizations* http://whqlibdoc.who.int/hq/2010/WHO_HTM_TB_2010.15_eng.pdf
- *Policy guidelines for collaborative TB and HIV services for injecting and other drug users* *http://www.who.int/hiv/pub/idu/tb_hiv/en/index.html*
- *WHO guidance on human rights and involuntary detention for xdr-tb control* *http://www.who.int/tb/features_archive/involuntary_treatment/en/index.html*
- *Principles for the Greater Involvement of People with TB (GIPT)* *http://www.worldcarecouncil.org/content/greater-involvement-people-tb-gipt*
- *Guidance on ethics of tuberculosis prevention, care and control* *http://whqlibdoc.who.int/publications/2010/9789241500531_eng.pdf*

Health and Human Rights documents

- *WHO Health and Human Rights/Department of Ethics, Equity, Trade and Human Rights*: www.who.int/hhr/
- *HIV and human Rights:* http://data.unaids.org/Publications/IRC-pub07/jc1252-internguidelines_en.pdf http://www.unaids.org/en/PolicyAndPractice/HumanRights/20070601_reference_group_
- *TB/HIV and human Rights*: http://data.unaids.org/pub/ExternalDocument/2010/20100324_unaidsrghrtsissuepapertbhrts_en.pdf

Annex 3

Information note on Tuberculosis diagnostics and laboratory services

Introduction

Care of patients with tuberculosis (TB) starts with a quality assured diagnosis. Successful DOTS expansion, as well as programmatic management of drug-resistant and HIV-associated TB therefore require - at its core - a robust network of TB laboratories with adequate biosafety, modern methods for diagnosis, standard operating procedures and appropriate quality assurance.

Arguably the weakest component of health systems, laboratory services have historically been grossly neglected, under-staffed and underfunded. Diagnostic capacity is therefore a major bottleneck for scaling up management and control of drug-resistant and HIV-associated TB, largely as a result of:

- Slow policy change and technology transfer, especially in low-and middle-income countries;
- Insufficient and underfunded laboratory strengthening plans;
- Inadequate laboratory infrastructure and biosafety;
- Vastly inadequate numbers of skilled staff;
- Insufficient technical assistance.

Strengthening TB laboratory services offers one of the best avenues for overall laboratory improvement as an essential health systems activity. Fundamental to this activity is collaboration between TB control programmes and public health laboratory services at country level, as adequate laboratory capacity consists of several essential elements which need to be addressed simultaneously, within comprehensive strategies and national laboratory strengthening plans.

An unprecedented effort to improve and expand TB laboratory capacity is currently under-way, spearheaded by the WHO and Stop TB Partnership Global Laboratory Initiative (GLI) and its network of international collaborators (http://www.stoptb.org/wg/gli). At the same time research on new TB diagnostic tools has been accelerated and the diagnostic pipeline is now rapidly growing.[9]

Genotypic (molecular) methods have considerable advantages for scaling up programmatic management and surveillance of drug-resistant TB, offering speed of diagnosis, standardized testing, potential for high throughput, and fewer requirements for laboratory bio-safety. The development of the Xpert MTB/RIF assay for the GeneXpert platform was completed in 2009 and is considered an important breakthrough in the fight against TB. For the first time, a molecular test is simple and robust enough to be introduced outside conventional laboratory settings. The assay provides results directly from sputum in less than 2 hours.

[9] *World Health Organization, Stop TB Partnership Retooling Task Force, Stop TB Partnership New Diagnostics Working Group. New Laboratory Diagnostic Tools for Tuberculosis Control*. 2009. Available at: http://www.stoptb.org/retooling.

The WHO evidence synthesis process confirmed a solid evidence base to support widespread use of Xpert MTB-RIF for detection of TB and rifampicin resistance. It is therefore recommended that 1) Xpert MTB/RIF should be used as the initial diagnostic test rather than conventional microscopy, culture and DST in individuals suspected of MDR-TB or HIV-associated TB (strong recommendation); and that 2) Xpert MTB/RIF may be used as a follow-on test to microscopy in settings where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (conditional recommendation, recognising major resource implications). Xpert MTB/RIF technology does, however, not eliminate the need for conventional microscopy culture and DST, which are required to monitor treatment progress and to detect resistance to drugs other than rifampicin.

Robust, point-of-care diagnostic tests for TB are not expected before 2015; therefore, uptake of existing WHO-recommended technologies must be accelerated, which requires adequate laboratory infrastructure and clear policies at country level on their use in TB screening and diagnostic algorithms. Because of the complexity of laboratory strengthening, the involvement of an expert laboratory consultant is recommended to guide the implementation process at country level.

Technologies must be used in appropriate laboratory services

Establishing, equipping and maintaining laboratory networks are challenging, complex and expensive. Introducing new technologies is bound to fail if all core elements of laboratory services are not addressed at the same time. These include:

- Laboratory infrastructure, appropriate biosafety measures and maintenance;
- Equipment validation and maintenance;
- Specimen transport and referral mechanisms;
- Management of laboratory commodities and supplies;
- Laboratory information and data management systems;
- Laboratory quality management systems;
- Appropriate, adequate strategies and funding for laboratory human resource development.

The GLI has developed a Roadmap for TB laboratory strengthening aimed at ensuring quality TB diagnostics in appropriately laboratory services within the context of national laboratory strategic plans,[10] available at http://www.who.int/tb/dots/laboratory/policy/en.

Laboratory biosafety

M. tuberculosis is classified as a Risk Group 3 pathogen but handling of specimens poses different risks based on the methods employed. Using a risk-based assessment of different technical procedures performed in a TB laboratory permits the development of a set of minimum requirements for laboratory facilities. The risk assessment approach considers the bacillary load of materials (specimens, cultures), the viability of bacilli, whether the material handled is prone to generate aerosols, the number of manoeuvres generating infectious aerosols with each technique, the

[10] *World Health Organization, Global Laboratory Initiative. Roadmap for TB Laboratory Strengthening, 2010.* Available at: http://www.stoptb.org/wg/gli.

workload of the laboratory, the epidemiological characteristics of patients, and the medical fitness of the laboratory workers. A summary of relative risks follows below:

Preparing direct smears for AFB microscopy and processing samples for Xpert MTB/RIF

Minimum requirements

- Adequate ventilation*;
- Laboratory separated from other areas;
- Access to the laboratory restricted to authorized persons;
- The bench for smear-preparation separated from other work benches in the laboratory.

Adequate ventilation can be ensured by opening windows if local climatic conditions allow. An exhaust fan can be used to ensure adequate room air changes. When climatic conditions prevent window opening, consideration should be given to mechanical ventilation systems that provide an inward flow of air without recirculation in the room.

Processing sputum specimens for primary culture inoculation, direct nitrate reductase assays (NRA), direct MODS or direct line-probe assays (LPA)

Minimum requirements

- Laboratory separated from other areas;
- Access to the laboratory restricted to authorized persons;
- Floors, walls, ceilings, benches and furniture have impervious surfaces;
- Windows permanently closed. Air supply either passive or mechanical without recirculation;
- Centrifuge with aerosol tight buckets;
- Handling of specimens in appropriate biological safety cabinets (BSC), class I (EN12469/NSF49) or Class IIA2 (NSF49) or Class II (EN12469) equipped with HEPA filters H14;
- BSCs designed by certified manufacturers, properly installed, regularly maintained and re-certified at least annually on site;
- Controlled ventilation system that maintains a directional airflow into the laboratory from functionally clean to dirty areas, with a minimum of 6 up to 12 air changes per hour*.

**Installation of a controlled ventilation system should be planned with engineering specialists.*

Manipulating cultures for identification and drug-susceptibility testing (DST) with phenotypic methods and/or line probe assays

Minimum requirements:

- Meeting ALL requirements for abovementioned tests, and in addition:
- Containment laboratory with double door entry;
- Autoclave available on site and in close vicinity of the laboratory, for safe waste disposal.

Technologies are suitable for different laboratory service levels

The specialised nature of technical procedures, laboratory management and administration, and ensuring laboratory quality require different levels of laboratory testing, with clear specimen referral mechanisms.

Conventional tiered laboratory services for TB diagnosis are described in many resource documents.[11] Three main laboratory service levels are common to the majority of countries:

- Peripheral (typically district) level: Performing sputum smear microscopy; TB and rifampicin resistance testing using Xpert MTB/RIF; referring specimens or patients in need of further tests to higher level laboratories.
- Intermediate (typically regional) level: Performing smear microscopy; TB and rifampicin resistance testing using Xpert MTB/RIF; and conventional culture, with or without species identification and first-line drug susceptibility testing (DST); referring cultures in need of further tests (eg. second-line DST) to higher level laboratories.
- Central (typically national or reference) level: Performing sputum smear microscopy, TB and rifampicin resistance testing using Xpert MTB/RIF, conventional and rapid culture and phenotypic DST, and molecular tests; referring isolates in need of further tests (eg. second-line DST or molecular sequencing) to Supranational Reference Laboratories in other countries or regions.

WHO-recommended technologies

MICROSCOPY

Mycobacteria are distinguished from other micro-organisms by thick lipid-containing cell-walls that retain biochemical stains despite decolourisation by acid-containing reagents (so-called 'acid-fastness').

Advantages: Microscopy of sputum smears is simple and inexpensive, quickly detecting infectious cases of pulmonary TB; Sputum specimens from patients with pulmonary TB - especially those with cavitary disease - often contain sufficiently large numbers of acid-fast bacilli to be readily detected by microscopy.

Disadvantages: Direct smear microscopy is relatively insensitive as at least 5,000 bacilli per millilitre of sputum are required for direct microscopy to be positive. Smear sensitivity is further reduced in patients with extra-pulmonary TB, those with HIV-co-infection, and those with disease due to nontuberculous mycobacteria (NTM).

Limitations: Microscopy for acid-fast bacilli (AFB) cannot distinguish *Mycobacterium tuberculosis* from NTM, nor viable from non-viable organisms, or drug-susceptible from drug-resistant strains.

Conventional light microscopy

Ziehl-Neelsen (ZN) light microscopy performed directly on sputum specimens is suitable for all laboratory service levels, including peripheral laboratories at primary health care centres or districts hospitals.

[11] *World Health Organization. Laboratory services in TB control, Part I: Organization and management. Geneva, WHO, 1998 (WHO/TB/98.258)*. Available at: http://www.who.int/tb/dots/laboratory/resources)

There is not sufficient evidence that processed (eg. concentrated or chemically treated) sputum specimens provide superior results to direct smear microscopy. Implementation of such methods in programmatic settings is therefore not recommended.
The number of ZN smears examined per microscopist per day should not exceed 20 as visual fatigue leads to a deterioration of reading quality; on the other hand, proficiency in reading ZN smears can only be maintained by examining at least 10-15 ZN smears per week.[12]
In general, one ZN microscopy centre per 100,000 population is sufficient; however, expansion of ZN microscopy services should also take into account the location and utilisation of existing services, urban/rural population distribution, and specimen transport mechanisms.

Conventional fluorescent microscopy

Conventional fluorescence microscopy typically uses quartz-halogen or high-pressure mercury vapour lamps as light sources. A lower magnification objective is used to scan smears, allowing a much larger area of the smear to be seen and therefore taking less time than ZN microscopy.
Conventional fluorescence microscopy is on average 10% more sensitive than ZN microscopy, but requires considerable technical expertise. Capital and running costs are also considerably higher. Conventional fluorescent microscopy has therefore been recommended by WHO at intermediate laboratory level where more than 100 smears are examined per day.[13]

Light-emitting diode (LED) fluorescent microscopy

LED technology allows the use of fluorescent microscopy with a much less expensive light source. LED microscopes or -attachments require less power, are able to run on batteries, the bulbs have a very long half-life and do not release potentially toxic products if broken.

Recent WHO evaluation confirmed the diagnostic accuracy of LED microscopy compared to conventional fluorescent microscopy, and superior efficiency of LED over conventional ZN microscopy. It is therefore recommended that conventional fluorescence microscopy be replaced by LED microscopy and that LED microscopy be phased in as an alternative for conventional ZN light microscopy in both high- and low-volume laboratories.[14]

CULTURE AND SPECIES IDENTIFICATION

Advantages: Mycobacterial culture and identification of *M. tuberculosis* provide a definitive diagnosis of TB, significantly increases the number of cases found (often by 30-50%), and can detect cases earlier (often before they become infectious). Culture also provides the necessary isolates for conventional DST.
Disadvantages: Culture is much more complex and expensive than microscopy to perform, requiring facilities for media preparation, specimen processing, and growth

[12] *World Health Organization. Laboratory services in TB control, Part II: Microscopy. Geneva, WHO, 1998 (WHO/TB/98.258).* Available at: http://www.who.int/tb/dots/laboratory/resources)
[13] *World Health Organization. Laboratory services in TB control, Part II: Microscopy. Geneva, WHO, 1998 (WHO/TB/98.258).* Available at: http://www.who.int/tb/dots/laboratory/resources)
[14] World Health Organization. *Policy Statement on Fluorescent Light Emitting Diode Microscopy for Diagnosis of Tuberculosis, 2010.* Available at: http://www.who.int/tb/dots/laboratory/policy/eng);

of organisms, specific laboratory equipment, skilled laboratory technicians, and appropriate biosafety conditions.

Limitations: Specimens have to be decontaminated prior to being cultured to prevent overgrowth by other micro-organisms. All decontamination methods are to some extent also harmful to mycobacteria, and culture is therefore not 100% sensitive. Good laboratory practices maintain a delicate balance between yield of mycobacteria and contamination by other micro-organisms.

Solid and liquid culture methods are suitable for central/national reference laboratories (or regional laboratories in large countries). Usually, one culture laboratory is adequate to cover 500,000 - 1 million population. Solid culture methods are less expensive than liquid culture systems, but results are invariably delayed due to the slow growth of mycobacteria. Liquid culture increases the case yield by 10% over solid media, and automated systems reduce the diagnostic delay to days rather than weeks. Liquid systems are, however, more prone to contamination and the manipulation of large volumes of infectious material mandates appropriate and adequate biosafety measures.

Positive cultures have to be identified to differentiate *M. tuberculosis* from NTM. NTM are more common in HIV-infected patients and the prevalence varies from country to country. Treatment of NTM is entirely different from treatment of TB and drug-resistant TB. As a minimum, laboratories performing DST must differentiate *M. tuberculosis* from other NTM (further speciation is not recommended at programmatic level).

Confirmation is usually done by a combination of biological characteristics of the culture growth and selected molecular or biochemical tests (which invariable delay the final result).[15] Rapid immunochromatographic assays (so-called strip speciation tests) for species identification on culture isolates provide a definitive identification of *M. tuberculosis* in 15 minutes and are recommended.[16] Molecular tests, biochemical methods and strip speciation assays are suitable for laboratories where culture and DST are performed.

DRUG SUSCEPTIBILITY TESTING

Advantages: DST provides a definitive diagnosis of drug-resistant TB. A number of different DST techniques are available:

- Phenotypic methods involve culturing of *M. tuberculosis* in the presence of anti-TB drugs to detect growth (indicating drug resistance) or inhibition of growth (indicating drug susceptibility)..
- Genotypic methods target specific molecular mutations associated with resistance against individual drugs.

Phenotypic DST methods are performed as direct or indirect tests on solid or liquid media. In direct testing, a set of drug-containing and drug-free media is inoculated

[15] World Health Organization. *Laboratory services in TB control. Part III: Culture. Geneva, WHO, 1998 (WHO/TB/98.258*. Available at: http://www.who.int/tb/dots/laboratory/resources).

[16] World Health Organization. Use *of Liquid TB Culture and Drug Susceptibility Testing in Low- and Medium-income Settings, 2007*. Available at: http://www.who.int/tb/dots/laboratory/policy/en/print.html).

directly with a concentrated specimen. Indirect testing involves inoculation of drug-containing media with a pure culture grown from the original specimen.

Indirect phenotypic tests have been extensively validated and are currently regarded as the gold standard. Three methods are commonly used: proportion, absolute concentration, and resistance ratio. DST results do not differ significantly between the three methods for first-line anti-TB drugs.
Disadvantages: DST methods are suitable for use at central/national reference laboratory level only, given the need for appropriate laboratory infrastructure (particularly biosafety) and the technical complexity of available technologies/methods.
Limitations: The accuracy of DST varies with the drug tested (see below).

For both first- and second-line DST, formal links with one of the laboratories in the Supranational Reference Laboratory (SRL) network is recommended to ensure adequate expert input on laboratory design, specimen and process flow, biosafety, standard operating procedures, maintenance of equipment and external quality assurance.

First-line DST

DST is most accurate for rifampicin and isoniazid and less reliable and reproducible for streptomycin, ethambutol and pyrazinamide.

As a minimum, national TB control programmes treating MDR-TB patients should establish laboratory capacity to detect MDR-TB. Rifampicin resistance is a valid and reliable indicator/proxy of MDR-TB in high burden settings.

Rapid DST is essential for identifying patients at risk of MDR-TB, as the first priority. Automated liquid systems and molecular line probe assays (see later) for first-line DST are recommended as the current gold standard. Xpert MTB/RIF is recommended as a stand-alone diagnostic test in individuals at risk of MDR-TB (see below).

Once MDR-TB has been confirmed, additional first- and second-line drug susceptibility results should be obtained following current WHO recommendations.[17]

Second-line DST

Second-line DST is complex and expensive. Commercial liquid methods and the proportion method on solid medium have been studied; methods for the absolute concentration or resistance ratio on solid medium have not been validated. Automated liquid systems for second-line DST are recommended as the current gold standard.

Routine second-line DST is not recommended unless the required laboratory infrastructure and capacity has been established, rigorous quality assurance is in place, and sustainable proficiency has been demonstrated. In order to retain proficiency and expertise, it is recommended that second-line DST only be performed if at least 200 specimens from high-risk patients are expected per year.

[17] World Health Organization. *Policy Guidance on Drug Susceptibility Testing (DST) of Second-line Anti-tuberculosis Drugs. Geneva, WHO, 2008 (WHO/HTM/TB/2008.392*. Available at: http://www.who.int/tb/dots/laboratory/policy/en/print.html).

Aminoglycosides, polypeptides, and fluoroquinolones have been shown to have relatively good reliability and reproducibility, allowing a quality-assured diagnosis of XDR-TB.

Routine DST for other second-line drugs (ethionamide, prothionamide, cycloserine, terizidone, *P*-aminosalicylic acid, clofazimine, amoxicillin-clavulanate, clarithromycin, linezolid) is not recommended as reliability and reproducibility of laboratory testing cannot be guaranteed.

DST using non-commercial methods

Non-commercial culture and DST methods are less expensive than commercial systems; however, non-commercial methods are prone to errors due to a lack of standardization and local variations in methodology. Performance of these methods is highly operator-dependent and good laboratory practice, good microbiological technique, and adequate quality assurance, supported by adequate training, are therefore imperative. As for commercial systems, stringent laboratory protocols, standard operating procedures, and internal quality control mechanisms must be implemented and enforced.

The evidence base for selected non-commercial culture and DST methods has been reviewed by WHO and the performance of these methods found to be acceptable under stringent laboratory protocols in reference/national laboratories in selected settings.[18] These methods include microscopic observation of drug susceptibility (MODS), colorimetric redox indicator (CRI) methods, and the nitrate reductase assay (NRA). Recommendations for their respective use are:

- MODS: A microcolony method in liquid culture, based on inoculation of specimens to drug-free and drug-containing media followed by microscopic examination of early growth;
  - Recommended as direct or indirect tests, for rapid screening of patients suspected of having MDR-TB;
- CRI methods: Indirect testing methods based on the reduction of a coloured indicator added to liquid culture medium in a microtitre plate after *in vitro* exposure of *M. tuberculosis* strains to anti-TB drugs;
  - Recommended as indirect tests on *M. tuberculosis* isolates from patients suspected of having MDR-TB, and acknowledging that time to detection of MDR-TB is not faster (but less expensive) than conventional DST methods using commercial liquid culture or molecular line probe assays (see below);
- NRA: A direct and/or indirect method on solid culture based on the ability of *M. tuberculosis* to reduce nitrate, which is detected by a coloured reaction;
  - Recommended as direct or indirect tests, for screening of patients suspected of having MDR-TB, and acknowledging that time to detection of MDR-TB in indirect application is not faster than conventional DST methods using solid culture (see below).

Both commercial and non-commercial culture and DST systems/methods are suitable for implementation at central/national reference laboratory level only.

[18] World Health Organization. *Policy Statement on Non-commercial Culture and DST Methods for rapid screening of Patients at Risk of Multidrug-resistant Tuberculosis. WHO, Geneva, 2010*. Available at: http://www.who.int/tb/dots/laboratory/policy/en/print.html).

MOLECULAR TESTING

The ultimate aim should be to implement molecular assays (such as the line-probe assay, Xpert MTB/RIF or other WHO-endorsed molecular platforms in the future) for rapid first-step identification of MDR-TB or HIV-associated TB.

Molecular line probe assays (LPAs) focused on rapid detection of rifampicin resistance (alone or in combination with isoniazid) have been endorsed by WHO in 2008 with detailed policy guidance on its introduction at country level.[19]

Xpert MTB/RIF assay was endorsed by WHO in December 2010[20] and supported by a document describing practical considerations for rapid implementation and operational how-to[21].

Advantages: Genotypic methods have considerable advantages for scaling-up programmatic management of drug-resistant and HIV-associated TB, in particular with regard to speed, standardised testing, potential for high throughput, and reduced biosafety needs.

Xpert MTB/RIF detects both TB and rifampicin resistance in a single test. Rifampicin resistance is a good and reliable proxy for MDR-TB in high burden settings. Xpert MTB/RIF is suitable for all levels of laboratories but capacity of one device is limited to 20 specimens per day. Higher-volume settings may require more than one device. Xpert MTB/RIF can be used as a stand-alone diagnostic test in individuals at risk of MDR-TB.

Disadvantages: **LPA**s do not eliminate the need for conventional culture and DST capability. Currently available LPAs are registered for use only on smear-positive sputum specimens *M. tuberculosis* isolates grown from smear-negative specimens by conventional culture methods.

Limitations: **LPA**s are suitable for implementation at central/national reference laboratory level, with potential for decentralisation to regional level if appropriate infrastructure can be ensured. Conventional culture (solid or liquid) is required to monitor treatment response (culture conversion) of DR-TB patients.

Xpert MTB/RIF requires uninterrupted and stable electrical power supply and yearly calibration of the cartridge modules. The positive predictive value of Xpert MTB/RIF is low in settings where rifampicin resistance is rare and results need to be confirmed by phenotypic DST or LPA.

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[19] World Health Organization. *Policy Statement. Molecular Line Probe Assay for Rapid Screening of Patients at Risk of Multidrug-resistant (MDR) TB. Geneva, WHO, 2008.* Available at: http://www.who.int/tb/dots/laboratory/policy/en/print.html).

[20] World Health Organization *Policy Statement Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system* Geneva WHO 2011 Available at: http://www.who.int/tb/dots/laboratory/policy/en/print.html

[21] World Health Organization. *Rapid Implementation of the Xpert MTB/RIF diagnostic test.* Available at: http://www.stoptb.org/wg/gli/assets/documents/

Annex 4

Information note on Community-based activities for improved TB prevention, diagnosis, treatment and care

Community-based TB activities represent a range of activities contributing to TB case notification, treatment adherence and improved outcomes. They also include activities for health promotion including generation of demand for TB prevention, diagnosis and treatment services. Community based TB activities are often implemented by the Ministry of Health or other line Ministries or Civil Society Organizations (CSOs). CSOs are operationally defined as non-profit organizations that do not belong to the state or the private for profit sectors. CSOs cover a spectrum of entities including nongovernmental, faith-, community-, and patient-based organizations, working on service delivery, advocacy, demand generation and technical support. This constitutes the framework of bringing together all stakeholders and patients in the form of social mobilization.

Integrating community-based activities for improved TB prevention, diagnosis, treatment and care in Global Fund applications

Community Systems Strengthening (CSS) Framework[22] of The Global Fund provides guidance on the goals, principles, strategies, roles, activities and indicators for community-based actors and networks, for HIV/AIDS, TB, and Malaria. This Framework provides guidance based on the Stop TB Strategy component: *Empower people with TB, and communities through partnership* and underlines the importance of placement of effective and sustainable systems to support these activities.

Therefore, all applicants are strongly encouraged to refer to the Framework when planning to adopt or scale up community-based TB approaches in Global Fund applications to ensure the core components community system strengthening are included in the applications.

Key characteristics of good-quality community-based TB activities in Global Fund applications and special considerations in Round 11

Mandatory linkage with programmatic gap analysis.

All community-based TB activities must be clearly linked to the country's programmatic gap analysis. This means that community interventions must be answering a clearly stated programmatic need, supported by data on target population(s). For example, if the justification for community-based interventions includes "improving geographic access to services", it is vital to provide data (*and* reference it) to support this. All proposed community-based interventions must also be accompanied by a clear implementation plan, with carefully prioritized activities which are visibly linked to the programmatic gap(s) identified in the proposal. Similarly, the community-based activities proposed for TB prevention, diagnosis,

[22] Link to the Community Systems Strengthening Framework of The Global Fund: http://www.theglobalfund.org/WorkArea/DownloadAsset.aspx?id=5485

treatment and care should be clearly specified in the proposal and included in the budget plan in a consistent manner as highlighted in the logical framework.

Documented linkage with past implementation experience.
Applicants who have been implementing community-based activities for improved TB prevention, diagnosis, treatment and care in previous Rounds should demonstrate lessons learned from previous implementation; namely, what approaches have or have not been working and why, and what concrete plans are there to integrate those learned lessons in Round 11. Requests for mere continued funding without such analysis will be perceived as weak.

Choice of indicators in the Performance Framework.
When reviewing proposals, the Technical Review Panel (TRP) will be paying increasing attention to the *quality* of Performance Framework indicators. Choosing indicators that seek to track contribution of communities to key TB outcomes, such as treatment outcome or case detection, will be perceived very positively. Proposing indicators that track processes, such as number of conducted trainings or number of CSOs involved, without a clear linkage to improved TB case notification, treatment adherence and outcomes should be avoided.

Clear presentation of linkage with outcome and advocacy and communication activities.
Several TRP comments of failed proposals noted absence of clear presentation of community-based activities for improved TB prevention, diagnosis, treatment and care and overlap with other related areas such as advocacy, communication and social mobilization. It is imperative to identify and clearly link community-based TB activities with improved TB case notification, treatment adherence and outcomes. Similarly, if the proposed community based TB activities include generation of demand for services through the engagement of communities and patients, it is important to clearly present the additional and complimentary link with proposed activities in advocacy and communication activities, which should be linked to every major component of the Stop TB Strategy

Value for Money.
Given the increasing scarcity of funds available at The Global Fund, the TRP will be scrutinizing this new cross-cutting theme in Round 11 proposals, in addition to all criteria discussed so far. This means that more attention will be given to cost-effectiveness and sustainability of the entire national response, and priority will be given to maximizing impact of available resources. For community-based interventions, it is vital to be able to demonstrate, *with data*, the added value or complementarity of such approaches. For example, if community-based care has helped reduce defaulting during previous implementation, showing data in support of further community care activities will help the TRP judge such activities as key. Furthermore, any stand-alone or vertical activities (including TB activities) conducted by CSOs are usually quite costly and difficult to sustain; therefore, identifying effective ways to integrate community-based activities for improved TB prevention, diagnosis, treatment and care in the work of existing CSOs and community health workers engaged in topics relevant for TB (eg. Maternal and Child Health, education, development, etc.) can be less costly, and more efficient and sustainable.

Further reading

Community Systems Strengthening Framework of the Global Fund; The Global Fund 2010.
http://www.theglobalfund.org/WorkArea/DownloadAsset.aspx?id=5485

Community involvement in tuberculosis care and prevention: Guiding principles and recommendations based on a WHO review; WHO 2008.
http://whqlibdoc.who.int/publications/2008/9789241596404_eng.pdf

Annex 5

Information note on Advocacy and Communication

Introduction

The Stop TB Strategy[23] emphasizes that advocacy, communication and social mobilization (ACSM) can improve case detection and treatment adherence by combating stigma and discrimination and empowering individuals and communities to mobilize political commitment and resources for TB. It is important to remember that ACSM includes a set of **cross-cutting activities** that are relevant to all aspects of the Stop TB Strategy. ACSM can support **specific objectives** for interventions for TB, TB/HIV, MDR-TB, Childhood TB, PPM or other programme components to address the social, cultural, financial, and psychological barriers to successful implementation.

Since the adoption of ACSM as a component, many countries have made progress in developing ACSM strategies. However, over the past few years, the Global Fund TRP has noted that ACSM activities in TB proposals remain weak. One reason is that ACSM has been understood as an independent Service Delivery Area (SDA) rather than a cross-cutting component, with proposed activities that are not evidence-based and have unclear or no TB-related justification for selection. In addition, the TRP has noted that ACSM proposals lack appropriate indicators to measure ACSM outcomes and activities are often seen as a generic "laundry list" without clear linkages to actual TB control challenges on the ground.

A complexity of developing strong and TB-oriented ACSM activities lies in the fact that it is specific to the country context and involves diverse strategies and approaches. In order to provide clearer guidance for countries, partners, and consultants in preparation for Round 11, ACSM will be discussed by each of its individual components (i.e. advocacy, communication, and social mobilization). This should help countries to develop activities that suit their needs rather than pick from a standard list of activities. This information note will focus on advocacy and communication. Social mobilization will be covered in the Information Note on "Community-based activities for improved TB prevention, diagnosis, treatment and care".

What are advocacy and communication?

Advocacy:

At the country-level, advocacy for TB can include a broad set of coordinated activities designed to prioritize TB on the national health agenda, generally accomplished by: a) building political will to increase and sustain financial and other resources for TB, and b) holding authorities accountable to ensure that pledges are fulfilled within an acceptable timeframe.

[23] http://www.who.int/tb/strategy/en/

In country contexts, advocacy efforts seek to ensure that national governments remain strongly committed to implementing national TB control/elimination policies. Advocacy goals at country level should be set by reviewing all objectives under a TB control plan and then determining which would benefit most from advocacy, or which area has the least political support. This would include activities such as stakeholder meetings, review of existing evidence, and situation analysis to identifying policy gaps, resource needs, and key roles of different actors. Advocacy goals should be linked to objectives and desired outcomes.

Increasing political commitment needs inputs from many stakeholders. NTP leaders can influence national leaders by using a mix of advocacy approaches themselves but by also supporting other people to take up TB advocacy such as journalists, researchers, HIV advocates, and celebrities. Although it is slow to achieve, policy change can be measured incrementally and is an important step for lasting change.

Communication

Within countries, and in the context of TB control, communication is principally concerned with informing and creating awareness in the general public or targeted populations about TB, and empowering people to take action. It is concerned with communicating a series of messages about the disease (e.g. "if you have a cough for more than two weeks, seek treatment", or "TB is curable"), or informing the public about what services exist (for diagnosis and treatment).

Communication is aimed at ultimately changing behaviors such as persuading people with symptoms to seek diagnosis and treatment. Knowledge alone will not be enough to get people to seek treatement, as in every specific context there are a number of different barriers to seeking diagnosis and treatment (for example, access to DOTS centres, stigma in the community, etc). Communication strategies should therefore focus on the specific issue and activities and messaging should be focused on addressing that main barrier to health-seeking behaviour.

IMPORTANT TIPS for advocacy and communication planning and proposal preparation

It is crucial to note that advocacy and communication are **not stand-alone activities.** Taken together with other technical interventions, they can enhance the speed and effectiveness of TB control improvements. Advocacy and communication activities should be designed to support overall progress in TB control and integrated within the national TB control plan. If this is not the case, the advocacy and communication strategy/plan must have objectives that are **directly linked** to TB control priorities and gaps as stated in the national TB strategy.

When writing a proposal, advocacy and communication activities should directly reflect the TB control problems identified and prioritized in the proposal itself and should clearly show how the proposed activities will address <u>those specific challenges.</u> Proposed activities should follow a logical progression from intervention to outcome, as described in the *attached table on the last page of this note,* using an example of case detection. Generic activities with no clear connection to the identified gaps should be avoided.

Advocacy and communication in Global Fund proposals - changes in Round 11
This information note aims to introduce changes that are being made in WHO's Stop TB Planning Matrix and Frameworks Tool to address the specific weaknesses in the area of advocacy and communication that have been noted over the years.

The key change for Round 11 is that *Service Delivery Area 5.1: Advocacy, Communication and Social Mobilization (ACSM)* will be removed from the Stop TB Planning Matrix and Framework as a stand-alone SDA. Instead, advocacy and communication activities will be integrated into every other SDA to reinforce the idea that advocacy and communication are not an end in themselves, but should be used as tools to reach a specific purpose in a specific SDA (examples provided in next section). It is encouraged that proposals for Round 11 follow this format. This means that proposals should avoid having a separate SDA on advocacy and communication. Instead relevant advocacy and/or communication objectives, strategies and activities, should be integrated into the other SDAs, such as TB/HIV, MDR-TB, patient support, human rights and high-risk groups, PPM, as determined by the situation analysis.

Furthermore, proposals for Round 11 should also strengthen the justification for chosen advocacy and communication activities. That is, all interventions should be based on quantitative and/or qualitative research to determine which advocacy and/or communication interventions are the most appropriate and likely to be effective for the proposed target population or geographic area. Proposals should always include a budget line for formative research and/or situation analysis, if it has not already been completed.

Indicators for advocacy and communication activities
Coming up with indicators for advocacy and communication activities has also been a weakness in proposals due to the fact that activities have been too generic and not linked to specific TB control challenges.

Advocacy and communication are tools used to reach targets that are supported by a number of interwoven interventions and so setting specific outcome indicators for advocacy and communication are less necessary. Some activities have clear objectives - such as advocacy for resource mobilization (the outcome one would measure would be level of funding before and after the advocacy intervention). However, other activities are much harder and more expensive to measure - such as the impact of mass media campaigns or distribution of IEC materials.

Process indicators for advocacy and communication are essential to monitor progress of implementation. But in terms of outcome and impact, it is advised that focus should be on measuring the **end-result** of what those activities were aimed at supporting, such as additional cases detected or additional cases cured.

ACSM activities should be planned with the help of experienced practitioners or by using existing ACSM resources, as listed below. Support for ACSM planning, implementation and evaluation can be requested from TBTEAM[24] (tbteam@who.int) or by emailing stoptbacsm@who.int.

[24] http://www.stoptb.org/countries/tbteam/

Resources and links to tools and guidance

References and web links:

Partnership Centre for Resource Mobilization:
http://www.stoptb.org/bi/resmob/index.asp

Advocacy partnership tool (UK)

ACSM for TB control: a handbook for country programmes:
http://www.stoptb.org/assets/documents/resources/publications/acsm/ACSM_Handbook.pdf

ACSM for TB control: a guide to developing knowledge, attitude and practice surveys:
http://www.stoptb.org/assets/documents/resources/publications/acsm/ACSM_KAP%20GUIDE.pdf

Working with the media: how to make your messages on tuberculosis count:
http://www.stoptb.org/assets/documents/resources/publications/acsm/Working%20with%20the%20Media%20Final%20Web.pdf

Advovcacy, commuication and social mobilization: collection of country-level good practices:
http://www.stoptb.org/assets/documents/resources/publications/acsm/ACSM_final_24%20Nov.pdf

Sample analysis framework for developing ACSM interventions. This is an example of how advocacy and communication activities would be planned for the challenge of low case detection.

National TB control objective	Challenge	Barriers (possible contributing factors)	Needed changes	Potential advocacy or communications interventions to address barriers and support changes	Expected results
Example: *Reach the target of 70% case detection by 2011.*	*Case detection is only 55%, below the target of 70%.*	*1. Lack of sufficient human resources to staff all microscopy centers.* *2. High level of stigma related to TB and HIV prevents people from seeking services.*	*1. Additional personnel hired to staff all existing microscopy facilities.* *2. Reduction of stigma around TB and HIV and behavior change among TB suspects to allow for greater access to services.*	*1. Advocacy for positions to be filled through presentation of current case detection data to key decision-makers.* *2. Survey of specific issues related to stigma and implementation of a communications strategy to address those issues.*	*1. Resources made available and microscopy positions filled by December 2012.* *2. Ten percent increase in number of suspects reporting to services for evaluation.*

Other Annexes

Information note on

Addressing and preventing childhood TB

Introduction

It is estimated that 1 million of the global total of 9 million tuberculosis (TB) cases each year occur in children (0-14 years). However, estimates of the burden of childhood TB are very uncertain. Children with TB are not usually given high priority by National TB control Programmes (NTP) because children are less likely to transmit disease. Basic and translational research on diagnostic tools has not focused on paediatric needs to date. Childhood TB has been largely absent from the global public health agenda despite being a major contributor to childhood morbidity and mortality particularly in high-burden TB settings. The expanded WHO Stop TB Strategy (2006) recognised that children are a vulnerable and important group. Recent evidence has shown that the prevention and control of childhood TB should be an integral part of NTP strategies. A recent call for action for childhood TB has highlighted the rationale for raising attention and scaling up TB control and prevention among children (See ''Call for Action for Childhood TB'' - annex)

Why is it important to address childhood TB?

There is an urgent need to recognize that prevention, diagnosis and treatment of TB in children are important for public health as well as for ensuring the individual right of the child to health. Children suffer severe TB related illness that contributes significantly to the overall burden of TB and to overall child mortality. The risk of progression from infection to disease is increased among children, particularly in the young (0-4 years), HIV-infected and malnourished. These are also the groups that pose the greatest diagnostic challenges. Young children are also at risk of developing severe and disseminated TB such as miliary TB and TB meningitis. Bacteriological confirmation of the diagnosis of TB is challenging because of difficulties with obtaining sputum samples, the paucibacillary nature of disease and a lack of culture facilities in most high-burden TB settings. For these reasons, the burden of disease and the extent of drug resistant TB in children are not well documented.

MDGs 4,5, and 6

The Global Fund recommends integrated approaches to achieve Millennium Development Goals (MDGs) 4 (reducing child mortality), 5 (improving maternal health) and 6 (combating HIV, malaria and other diseases) and improve health outcomes for women and children. The integration of child mortality reduction approaches and childhood TB control could play a pivotal role in achieving the mentioned MDGs.

To date, the focus on TB has been under the framework of Millennium Development Goal (MDG) 6. Children and mothers are particularly vulnerable within the context of

TB-associated poverty, and it is critical to ensure that their needs are not forgotten. Improving child and maternal health are the focus of MDG 4 and 5. The challenges for TB control in adults, mothers and children overlap and require integration between services that address TB, HIV, and maternal and child health.
The acceleration towards TB elimination called by the Stop TB Strategy requires the recognition that children with TB infection today represent the reservoir of TB disease tomorrow and therefore play a pivotal role in the progress in global TB control and elimination.

What tools are available for addressing and preventing childhood TB within National Tuberculosis Programmes?

The basis for establishment of effective childhood TB control is available and supported by evidence and best practices. Improved TB control in the community will reduce the burden of child TB. The diagnosis of TB in children is a clinical diagnosis, supported when possible by laboratory diagnostic techniques. Treatment of childhood TB is highly effective and has an excellent safety profile. Prevention of progression of latent TB infection to active disease by identification of at risk cases through contact screening and other active case finding approaches, and provision of preventive therapy are interventions with well documented effectiveness in all settings that can be scaled up within NTPs. These elements provide the basis for development of national, regional and global comprehensive childhood TB control approaches. Guidelines for NTPs that focus on management of TB in children have been developed in the last 5 years, and have provided a framework for many NTPs to adapt or update national guidelines to increase the attention to childhood TB. The challenge is broader implementation to address the policy-practice gap.

What should be specifically addressed within strategies to address and prevent childhood TB?

Five major areas of intervention can be indicated for planning and strategy purposes when NTP are faced with addressing childhood TB control. The Table below broadly indicates the objectives linked to implementation of activities within these areas.

Prevention

Approaches include prevention of infection through improved TB control and prevention from infection to disease. BCG is effective in protecting children from severe TB disease. Contact screening and management has enormous potential to prevent children exposed to and infected with TB from developing TB disease.

Activities in this area may include the following but could be extended and/or modified in line with the specific TB epidemiology and control situation:

- Implementation of child contact screening and management
- Development of setting-specific active case finding strategies to identify infected children and prevent progression of disease

Diagnosis & Management

Children with TB disease present to the health services in many contexts from peripheral primary care to tertiary referral level. Despite the known difficulties in confirming bacteriological diagnosis of TB in children, diagnosis can be made in most children in an outpatient setting based on careful clinical assessment and in line with international guidelines. Furthermore, standardized treatment is as effective in

children as in adults. The correct implementation of standardized and recommended approaches, through the proper capacity building of the TB service delivery system, can lead to an optimal identification and management of childhood TB. Health care workers at all levels need to be familiar with the approach to clinical diagnosis and indications for investigation and/or referral. NTP staff needs to be familiar with particular needs for children such as diagnostic and therapeutic options as well as the importance of registering and reporting child TB cases.

Activities in this area may include the following but could be extended and/or modified in line with the specific TB epidemiology and control situation:

- Training of health care workers and NTP staff on diagnosis and management of childhood TB in line with International Standards for TB Care, WHO or National Childhood TB Management Guidelines.

Monitoring and surveillance

Monitoring and surveillance of childhood TB cases has traditionally been overlooked because of the prior emphasis on sputum smear positive cases. However, the expanded Stop TB Strategy highlights the importance of improved case detection, recording and reporting of all forms of TB. NTPs need to be aware of established global policy changes in reporting childhood TB age groups and the importance of implementing this change.

Activities in this area may include the following but could be extended and/or modified in line with the specific TB epidemiology and control situation:

- Implementation of paediatric age specific grouping surveillance for both bacteriologically positive and negative childhood TB cases
- Development of routine monitoring of childhood TB data to assess diagnostic practices, epidemiological and forecast childhood TB drugs needs.

Operational Research

Operational research has a critical role to play in helping NTPs improve management of childhood TB. Many activities are now recommended for childhood TB control within NTPs but have often not been implemented by NTPs. There is a need for evidence to assess the impact and effectiveness of interventions such as training or child contact screening, and evidence to inform effective implementation of interventions.

Activities in this area may include the following but could be extended and/or modified in line with the specific TB epidemiology and control situation:

- Evaluate current national diagnostic guidelines and approaches for diagnosis, detecting and screening for childhood TB vis-à-vis the criteria defines in the International Standards for TB Care and the Guidance for Childhood TB control (refer to resources list).
- Evaluate adaptation/adoption of diagnostic approaches inclusive of rapid diagnostics and other new tools in support of childhood TB detection and management
- Determine and assess how many childhood TB contacts qualify for chemoprophylaxis defining highest risk groups to prioritize interventions.

- Document and assess at what level children enter NTPS, the availability of qualified staff and their effectiveness in performing diagnosis and delivering treatment.
- Assess and ensure private, non-public, NGO and other sectors contribution and/or potential contribution to childhood TB detection and management

Advocacy & Communication

Children with TB are a particularly vulnerable population. The main public health messages that address TB relate to reducing the infectiousness of TB and do not relate to the impact of TB disease on children. Advocacy on behalf of children such as the recent "Call to Action" (see Annex) is critical for improved management and increased attention by NTPs.

Activities in this area may include the following but could be extended and/or modified in line with the specific TB epidemiology and control situation:

- Development of communication and advocacy strategies and activities to involve private, non-public, NGO and other sectors in contributing to childhood TB detection and management
- To document success stories and local best practices in childhood TB prevention and control to increase local and international acceptability of the importance of ensuring sustainability of childhood TB control
- To develop communication strategies to reach out to local child health stakeholders and highlight the benefits and needs for inclusion of childhood TB in overall approaches for reduction of child mortality and morbidity

Table. Potential areas for interventions and related objectives

Areas of intervention	Objectives
Prevention	*To diminish progress to active TB in children exposed to infectious TB cases * To diminish the reservoir of latently infected children that might fuel the epidemics in the decades to come
Diagnosis & Management	*To improve capacity for best practice approaches for diagnosis and treatment of childhood TB cases * To increase the number of childhood TB cases promptly and correctly detected thus limiting severe morbidity and mortality
Monitoring & Surveillance	*To provide a reliable assessment of childhood TB epidemiology, diagnostic and control practices
Operational Research	* To provide evidence of effectiveness, feasibility and potential for scaling-up of prevention, diagnosis and management approaches (including the use of new tools for TB) in childhood TB.
Advocacy	*To increase awareness on the need to integrate childhood TB prevention and control in national tuberculosis programmes and in national childhood mortality reduction strategies

Annex - Call for Action for Childhood TB

We, participants gathered at the 'International Childhood Tuberculosis Meeting' held March 17-18, 2011 in Stockholm, Sweden recognize that:

o Worldwide, at least 1 million TB cases occur each year in children under 15 years of age.
o The true burden of TB in children is unknown because of the lack of child-friendly diagnostic tools and inadequate surveillance and reporting of childhood TB cases.
o Children with TB infection today represent the reservoir of TB disease tomorrow.
o Children are more likely to develop more serious forms of TB such as miliary TB and TB meningitis resulting in high morbidity and mortality.
o Despite policy guidelines, the implementation of contact tracing and delivery of isoniazid preventive therapy (IPT) to young and HIV-infected children is often neglected by public health programmes.
o Most public health programs have limited capacity to meet the demand for care and high-quality services for childhood TB.
o TB care for children is not consistently integrated into HIV and care and maternal and child health programs.
o BCG, the only licensed TB vaccine, has limited efficacy against the most common forms of childhood TB and its effect is of limited duration.
o Due to inadequate case detection it is estimated that a large number of children suffering from TB are not appropriately treated. This is further compounded by drug stock outs and the lack of child-friendly formulations of drugs for TB treatment and prevention.
o Children are rarely included in clinical trials to evaluate new TB drugs, diagnostics or preventive strategies.

To address this current situation, we, the undersigned, call for:

o National TB programmes to include and prioritize childhood TB in their national strategic plans in order to address millennium development goals for children and pregnant women.
o All health care providers to integrate childhood TB into their services.
o The scientific community to include children—of all ages—in clinical and operational studies.
o TB drug and diagnostic product developers to specifically include children in development plans and implementation of research at an early stage.
o Donors to encourage collaboration with researchers, local communities, TB control programmes and other stakeholders to address the growing problem of childhood TB concentrating on:
o Innovative research to develop child-friendly TB diagnostics, drugs, biomarkers and vaccines
o The strengthening of public health facilities and services so that mothers and children with and without HIV can receive appropriate TB care
o Providers of technical assistance to invest in building local technical and programmatic capacity to prevent, diagnose and treat TB in children in all age groups.
o The WHO to accelerate in-country adoption and use of childhood TB guidelines.

o Policy makers to adopt the existing and new WHO recommendations for childhood TB, evaluate implementation, scale-up and assess the impact of implementation strategies.
o Civil society to demand equitable prevention, diagnostics, treatment and care services for childhood TB and to monitor the scale- up of these services.

To ensure that all children exposed to TB or suffering from TB are correctly managed and receive the appropriate treatment, the individuals and institutions signing on to this call to action, pledge to advocate for universal access to prevention, diagnosis and treatment of TB for people of all ages.
We furthermore call on the international community to endorse this call for action to ensure that there is capacity to address the needs of children with TB.

Resources

Guidance for national tuberculosis programmes on the management of tuberculosis in children. WHO/HTM/TB/2006.371
http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.371_eng.pdf

Guidance for national tuberculosis and HIV programmes on the management of tuberculosis in HIV-infected children: recommendations for a public health approach. WHO and IUATLD. 2010

Rapid advice: treatment of tuberculosis in children. WHO/HTM/TB/2010.13
http://whqlibdoc.who.int/publications/2010/9789241500449_eng.pdf

International Standards for Tuberculosis Care, 2nd edition, 2009
http://www.tbcta.org//Uploaded_files/Zelf/ISTCReport2ndEdition1258118339.pdf

Desk-guide for diagnosis and management of TB in children
http://www.theunion.org/index.php/en/resources/scientific-publications/item/193-desk-guide-for-diagnosis-and-management-of-tb-in-children-

Information note on

Management of multidrug-resistant tuberculosis

Introduction

Major progress has been made towards achieving global control of tuberculosis (TB) over the past two decades. During 1995–2009, a total of 49 million patients were treated in DOTS programmes worldwide, of whom 41 million were successfully treated, and up to 6 million lives were saved. Incidence rates have been declining globally and in all sub-regions except in certain African countries since 2004. This progress is being threatened by multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), forms of TB that are more difficult and costly to diagnose, treat and cure than drug-susceptible TB. M/XDR-TB is particularly lethal in people living with the human immunodeficiency virus (HIV). In 2008, the World Health Organization (WHO) estimated that 440 000 cases of MDR-TB emerged globally; 85% of its global burden occurs in 27 countries.

The World Health Organization (WHO) has recognized M/XDR-TB as a major challenge to be addressed as part of the Stop TB Strategy, launched in 2006. In April 2009, WHO convened a ministerial meeting of countries with a high burden of MDR-TB in Beijing, China, at which countries committed to tackling the epidemic with innovation and urgency. The Beijing "Call for Action" paved the way for the 62nd World Health Assembly in May 2009 to adopt resolution WHA62.15 on prevention and control of MDR-TB and XDR-TB, urging Member States to take action on multiple fronts towards achieving universal access to diagnosis and treatment of M/XDR-TB by 2015.

What is MDR-TB?

Multidrug-resistant TB (MDR-TB) is caused by bacteria that are resistant to at least isoniazid and rifampicin, the two most effective anti-TB drugs. MDR-TB results from either primary infection with resistant bacteria or may develop during the course of treatment, often due to mismanagement. Extensively drug-resistant TB (XDR-TB) is a form of TB caused by bacteria that are resistant to isoniazid and rifampicin (i.e. MDR-TB) as well as any fluoroquinolone and any of the second-line anti-TB injectable agents (amikacin, kanamycin and/or capreomycin). These forms of TB do not respond to the standard six-month treatment with first-line anti-TB drugs and can take up to two years or more to treat with drugs that are less potent, more toxic and much more expensive.

Issues for consideration

Despite the important progress being made, severe bottlenecks are limiting the response to the
M/XDR-TB epidemic. Indeed, only 10% (24,511 / 250,000) of the estimated MDR-TB cases among notified TB cases in 2009 in the high MDR-TB burden countries, and 11% (30,475 / 280, 000) globally were enrolled on treatment. Some countries are making progress by implementing policy changes that rationalize the use of hospitals, such as South Africa, or treating patients through community-based models of care, such as the Philippines. However, diagnostic capacity

remains limited. Furthermore, the price of some quality-assured second-line drugs has not fallen, and shortages of drugs still occur. Overall, there is recognition that the response to MDR-TB must be built across health systems, and corresponding plans have been made. It is well accepted that weak health-care systems are often at the root of M/XDR-TB, hampering progress on two major fronts: prevention of the M/XDR-TB epidemic and treatment of those affected. In many countres, both the human and financial resources are grossly insufficient and frequently inadequate.

The Global Fund at it's Third Board Meeting (GF/B4/2 [January 2003]) recognized that the Green Light Committee (GLC) provides a package of services for MDR-TB control and determined that Principal Recipients of GF grants would be required to procure second-line anti-tuberculosis drugs through the GLC Initiative (via the Global TB Drug Facility [GDF]). At it's Thirteenth Board Meeting (GF/B13/8 (27-28 April 2006), the GF further determined that CCMs applying for funding of MDR-TB control activities in a proposal under Round 6 and subsequent rounds of funding or in a Request for Continued Funding, must include in such Proposal or Request for Continued Funding provision to share the cost of the GLC Initiative. Resultant to this decision a cost-sharing scheme was introduced in all grants with MDR-TB components to contribute to the efforts made by the GLC initiative in countries receiving Global Fund grants. This scheme represents a USD 50 000 flat fee for GLC services per grant, per year of implementation of the MDR-TB component.

During 2009, key stakeholders supporting the expansion of MDR-TB services and care concluded that a revision of the global framework that addresses MDR-TB diagnosis and management was necessary. At retreats of partners convened by WHO in October 2009 and February 2010, it was agreed that a new model of coordination and support to countries was needed. The model should **emphasize *support* to countries rather than control, and *advocacy* to ensure countries honour the commitments made at the 62nd WHA.** In addition, the new model aims **to increase access to quality assured second line drugs,** and **provide more, better, and more extensive technical assistance** over the short, medium and long term. Three Task Forces were set up to look into: i) the provision of technical assistance; ii) availability of quality assured second-line TB drugs (SLDs); and iii) monitoring and evaluation, and the governance structure for MDR-TB management scale-up. The three Task Forces worked over 14 months to develop the new framework and presented their recommendations to a meeting of key stakeholders on the "way forward to achieve universal access to diagnosis, treatment and care of MDR-TB" held in Geneva, Switzerland, 22-23 February 2011.

Following the stakeholders meeting, the transition plan was finalized and, with the new global framework to support scale-up of MDR-TB services and care, presented at the 20th Stop TB Partnership Coordinating Board meeting in Washington DC, USA, 31 March - 1 April 2011. The Board endorsed the plan and the new global support framework. The main points under the new global support framework to scale-up DR-TB services and care are:

- focus will be on building national capacity to scale-up MDR-TB services and care, via increased technical assistance
- no separate GLC application or approval process, but rather, review of national MDR-TB management expansion plans at time of grant negotiation

- programmes/projects can request directly to GDF for QA second-line drug procurement and supply
- MDR-TB related advocacy activities to be strengthened
- establishment of a strategic committee at the global level (gGLC) with dual role of advising WHO and Partners, with it's Secretariat to be hosted in WHO Geneva
- decentralised regional entities (rGLCs) to be established in a phased manner (Year 1 - AMRO, EURO and WPRO). The rGLC Secretariats are to be housed in a STP partner - in the first three regions this will be in the WHO Regional Offices.

The new framework, with the global and three regional GLCs, will be in place from 1 July 2011.

In light of the new framework for global support to the scale-up of MDR-TB services and care, applicants for Global Fund support for MDR-TB activities should therefore explain their plans for scaling up universal access to diagnosis and treatment of M/XDR-TB by 2015, including a detailed description of MDR-TB activities, the budget and indicators. Activities may include surveillance, prevention, diagnosis and treatment, and/or care and support interventions.

The submission of a National TB Strategic Plan incorporating a DR-TB component (preferable), and/or a specific MDR-TB management expansion implementation plan, is highly encouraged when submitting a proposal to the Global Fund Round 11 that includes DR-TB activities. If the proposal requests funding for MDR-TB, the applicant should click the "Yes" box in Section 6.3 of the application form indicating that USD $50,000 per year over the full proposal term is to be included in the detailed budget and the funds must be reserved for payment to the GLC Secretariat support services over the period of the proposal. These funds cannot be used for any implementation activities

In its report on Round 10 proposals, the TRP noted that ".. that in many proposals the approach to screening and follow-up of MDR-TB patients was not sufficiently described and recommends that in the future Technical Partners work with applicants to ensure that these issues are adequately addressed." Please contact the GLC secretariat at glc_secretariat@who.int in case you wish to receive technical assistance specifically to support the preparation of the DR-TB component of the National Strategic TB Plan and GF Round 11 application. In addition, it should be noted that applicants should include in the proposal budget any technical assistance that may be required to implement DR-TB related activities during the proposal timeframe.

Incorporating DR-TB activities in Global Fund proposals

The WHO *Guidelines for the programmatic management of drug-resistant tuberculosis* and its update from 2011 provide guidance on recommended interventions that countries should implement. [25] Interventions are required to cover the diagnosing, treating and caring for people affected by M/XDR-TB, and also those aimed at preventing M/XDR-TB through basic TB control.

[25] WHO. *Guidelines for the programmatic management of drug-resistant tuberculosis: Emergency Update 2008* (WHO/HTM/TB/2008.402). Geneva, Switzerland: WHO, 2008. and WHO. *Guidelines for the programmatic management of drug-resistant tuberculosis - 2011 update* (WHO/HTM/STB/2011.XX). Geneva, Switzerland: WHO, 2011.

The Global Fund encourages applicants to work with partners, including WHO, to determine which activities to prioritize to include in their DR TB proposals based on country context.

International guidelines promote integration of services for basic TB control and for MDR-TB within a framework approach, consisting of an essential core of five components based on fundamental principles of TB control and flexible options for country-specific implementation. The core components are comprehensive, ensuring that all essential elements of MDR-TB treatment are included. The design and implementation may vary from one country or region to another depending on the local situation. These core components are:

1. Sustained political commitment

2. Appropriate case-finding strategy including quality-assured culture and DST

3. Appropriate treatment strategies that use second-line drugs under proper case management conditions

4. Uninterrupted supply of quality-assured second-line anti-tuberculosis drugs

5. Recording and reporting system designed for DR-TB control programmes that enables monitoring of performance and evaluation of treatment outcomes

The following DR-TB related activities/interventions are strongly recommended that build on the existing WHO policy and which countries are encouraged to consider:

- Addressing the factors leading to the emergence of MDR-TB
    - Strengthening of National Drug Regulatory Authorities to ensure proper registration, availability, quality, safety and distribution of second-line drugs
    - Strengthening of basic TB control activities, in both public and private sectors
    - Development of appropriate infection control measures and their implementation across all levels of health facilities
- Setting up national level expert DR-TB committee/advisory body to guide DR-TB related policy development and provide oversight of implementation of DR-TB related services
- Establishment of DR-TB management expertise within the NTP structure to ensure proper organization and coordination of DR-TB services with local institutions, the general medical and social services, and other relevant partners
- Conducting appropriate surveillance of DR-TB prevalence among tuberculosis patients
- Appropriate case finding activities based on the local epidemiological situation and local capacity for diagnosis of DR-TB cases
- Establishment and/or strengthening of appropriate laboratory services for the diagnosis of DR-TB patients (drug susceptibility testing for first and second line anti-TB drugs), including the introduction of newer and rapid diagnostic technologies.

- Establishment and/or strengthening of appropriate transportation systems of sputa samples for diagnosis and follow-up of DR-TB patients
- Implementation of appropriate models of care for DR-TB cases, including use of in-patient, ambulatory and community based care as required
- Consistent supply of quality assured second-line anti-TB drugs for the treatment of MDR-TB patients at all levels of the health system, with establishment and/or strengthening of stocking and distribution systems
- Mechanisms for the monitoring and management of adverse drug effects
- Increasing human resource capacity through the provision of appropriate standardized DR-TB related trainings for staff at all levels of health systems, adequate pay, motivation of staff and professional recognition, and the provision of supportive supervision activities
- Development and/or strengthening of support systems for DR-TB patients and their families, and staff/treatment providers
- Strengthening linkages with HIV programmes, to ensure appropriate services and care are provided to all HIV-infected DR-TB patients
- Provision of appropriate palliative care for those DR-TB patients who have failed all available curative treatment
- Implementation and/or updating of a, preferably electronic, comprehensive standardized recording and reporting system, which links laboratories, treatment sites, drug stores and programme management units

Further Reading / Resources

This factsheet has been prepared in collaboration with technical partners, using the key
resources below. For details and discussions on the strength of the evidence on the above recommendations, applicants are strongly encouraged to review the following key
resources:

World Health Organization (WHO). *Beijing "Call for Action" on tuberculosis control and*
patient care: Together addressing the global M/XDR-TB epidemic. Beijing, 2009. Available at: http://www.who.int/tb_beijingmeeting/media/en_call_for_action.pdf

WHO. *Guidelines for the programmatic management of drug-resistant tuberculosis: Emergency Update 2008* (WHO/HTM/TB/2008.402). Geneva, Switzerland: WHO, 2008.

WHO. *Guidelines for the programmatic management of drug-resistant tuberculosis - 2011 update* (WHO/HTM/STB/2011.XX). Geneva, Switzerland: WHO, 2011.

WHO. 62nd World Health Assembly. *Prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis*. WHA62.15. Eighth plenary meeting, 22 May 2009. A62/VR/8.

WHO. Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. WHO/HTM/TB/2010.3. Geneva, Switzerland: WHO, 2010. Available at: http://www.who.int/tb/publications/2010/en/index.html).

WHO. *Policy recommendations on the use of liquid culture (2007), second-line drug susceptibility testing (2008), and the use of line probe assays for rapid MDR-TB screening (2008)*. Geneva, Switzerland: World Health Organization, 2007 6 2008. Available at: http://www.who.int/tb/laboratory/policy_statements/en/ index.html.

WHO. *Guidance on ethics of tuberculosis prevention, care and control*. WHO/HTM/TB/2010.16. Geneva, Switzerland: WHO, 2010.. Available at: http://www.who.int/tb/publications/ 2010/en/index.html.

WHO. Guidelines for surveillance of drug resistance in tuberculosis, 4th ed. Geneva, Switzerland: WHO, 2009. Available at: http://whqlibdoc.who.int/publications/2009/9789241598675_eng.pdf.

WHO. *Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach*. Geneva, Switzerland: WHO, 2006 revision. Available at: http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf.

WHO. *Policy on TB Infection Control in Health-care facilities, Congregate Settings and Households*. Geneva, Switzerland: WHO, 2009 (WHO/HTM/TB/2009.419). Available at: http://www.who.int/tb/publications/2009/en/index.html.

Information note

TB/HIV collaborative activities

Introduction

The dramatic spread of human immune deficiency virus (HIV) in the past two decades, in particular in sub-Saharan Africa, has been accompanied by a major increase in the number of new cases of tuberculosis (TB). In 2010, TB killed an estimated 1.68 million people, including 0.38 million deaths among TB patients who were HIV-positive. The interaction of TB with HIV presents additional challenges to TB control. It is crucial to improve and strengthen TB/HIV collaborative activities to reduce the burden of TB among people living with HIV (PLHIV) and reduce the burden of HIV among TB patients.

What is HIV related Tuberculosis?

Together, TB and HIV form a lethal combination. HIV weakens the immune system and promotes the progression of recent and latent *Mycobacterium tuberculosis* infection to active TB disease. A person living with HIV who is also infected with TB is 20 times more likely to become sick with active TB than someone who is HIV negative.

Issues for consideration

In the last two decades the number of new TB cases has tripled in high HIV-prevalence countries. TB is now the leading cause of death among People living with HIV in Africa and a major cause of death elsewhere, accounting for almost 2 million deaths per year globally. It is also the most common presenting illness among People living with HIV.

In the context of proposal for submission to the Global Fund, at its November 2008 meeting, the Board recommended that TB/HIV collaborative activities be included in both HIV and tuberculosis proposals (decision point GF/B18/DP12). The Global Fund recognizes that many HIV and TB control activities are implemented with little interaction between the two programs. As a result, insufficient attention may be given to significant issues related to co-infection. Applicants should therefore explain their plans for scaling up universal TB/HIV collaborative services, including a detailed description of TB/HIV activities, the budget and indicators. Activities may include prevention, treatment, and/or care and support interventions. [2]

In addition, in its report on Round 9 proposals, the TRP recommended "that both HIV and tuberculosis proposals should address TB/HIV collaborative activities unless compelling reasons exist not to do so – even if no funding is sought from the Global Fund for these activities."[1]

Incorporating collaborative TB/HIV activities in Global Fund proposals

The WHO policy[2] on collaborative TB/HIV activities provides guidance on recommended interventions that countries should implement. The Global Fund encourages applicants to work with partners, including WHO and UNAIDS, to determine which activities to include in their TB and HIV proposals based on country context.

Internationally recommended collaborative TB/HIV activities include:

A. Establishing the mechanisms for collaboration

• Setting up coordinating bodies for TB/HIV activities at all levels;
• Conducting surveillance of HIV prevalence among tuberculosis patients;
• Carrying out joint TB/HIV planning; and
• Joint monitoring and evaluation

B. Decreasing the burden of tuberculosis in PLHIV

• Establish intensified tuberculosis case-finding
• Introduction of isoniazid preventive therapy (IPT)
• Ensuring TB infection control in health care and congregate settings

C. Decreasing the burden of HIV in TB patients

• Provision of HIV testing and counseling;
• Introduce HIV prevention methods;
• Introduction of co-trimoxazole preventive therapy among eligible PLHIV;
• Provision of HIV and AIDS care and support; and
• Provision of antiretroviral therapy

New for Round 11:

1. **The latest guidelines on intensified case finding and IPT provision have been published since the last Global Fund round, and these require local adaptation and roll out in many countries applying for Global funds in 2011**

2 **Changes in the WHO recommended initial TB diagnostic test in individuals suspected of HIV/TB** : **Xpert MTB/RIF**

Further details in section D below.

[1] http://www.theglobalfund.org/documents/board/20/GF-BM20-09_TRP_ReportToBoard_and_Annexes1-5-_6.pdf, p.19
[2] http://www.who.int/tb/publications/tbhiv_interim_policy/en/index.html

The following are suggested **general activities** that build on the existing WHO policy and which countries are encouraged to consider:

- Conducting joint annual review meetings by TB and HIV programs and stakeholders at all levels;
- Encouraging maximal use of 'one-stop' services depending on the local context;
- Large-scale training to roll-out the implementation of revised and newly developed policies and guidelines for TB/HIV activities; and
- Development of national guidelines for improved referral systems for TB/HIV.

The following activities/interventions are strongly recommended HIV services for TB patients and those persons presenting signs and symptoms of TB:

- Establishment and implementation of a national HIV testing policy that promotes testing of TB patients and TB suspects, and allows testing by non-lab professionals;
- Revision of National TB Control Program policy, where applicable, to include HIV testing for both TB patients and TB suspects;
- Provision of adequate space and infrastructure for HIV counseling and testing at TB clinics and other health care facilities;
- Provision of regular supervision with respect to national service delivery to ensure providers are consistently providing services;
- When HIV testing is not available on-site at the TB clinic, the patient should be referred to an HIV test site or the specimens brought to the HIV test site. In the case of patient referrals, strict infection control measures should be applied;
- Consistent supply of test kits at all HIV test centers based on national targets, assuring mechanisms for procurement and funding;
- Use of a standardized HIV testing algorithm for patients with TB and protocols for counseling and testing, including a functioning quality assurance program;
- Implementation of a standardized reporting system, including patient identifiers, registers, reporting forms, referral system with common forms, and supervision by the Ministry of Health;
- Standardized initial training, certification and re-testing, and site supervision (i.e. establishment quality assurance) of test providers;
- Increasing human resource capacity through the provision of refresher trainings, adequate pay, motivation of staff, and professional recognition;
- Provision of technical assistance for: supply and procurement systems, quality assurance systems, resource mobilization and operational research;
- Establishment of a policy to decentralize HIV services and shift tasks to nurses and other health cadres with supervision and mentorship; and
- Development of clear national directives on where antiretroviral therapy (ART) for HIV-infected eligible TB patients should start (either in ART or TB service, or in both delivery points).

D. Strengthening and enhancing the nationwide delivery of the *Three I's for TB/HIV*

The *Three I's for HIV/TB*[3] include:

• Isoniazid preventive therapy (IPT)
• Intensified TB case finding, and
• Infection control for TB.

The latest guidelines on ICF and IPT provision have been published since the last Global Fund round and incorporate a new TB screening algorithm and changes to IPT guidelines. These require local adaptation and roll out in most countries applying for Global funds in 2011. [3]

Delivery of the *Three I's for HIV/TB,* services primarily delivered through NAPs, need to be strengthened and enhanced in order to accelerate TB/HIV collaborative activities. Policy barriers around the "Three I's" can be removed by promoting national dialogue and consultation. The development of standardized tools and program guidance4 is essential for ensuring the successful implementation of TB/HIV collaborative activities.

Mention importance of early ART to prevent TB here..

Changes in WHO recommended initial TB diagnostic test in individuals suspected of HIV/TB[5]

WHO has made a strong recommendation that the Xpert MTB/RIF, the new automated DNA test for TB should be used as the initial diagnostic test in individuals suspected of MDRTB or HIV/TB. The expected impact is a doubling in the number of TB/HIV cases diagnosed in areas with high rates of TB and HIV (compared to microscopy diagnosis): National TB programmes worldwide are encouraged to seek additional resources from the Global Fund in support of the adoption of the new TB test in upcoming proposal rounds

Background: The new DNA test for TB is a fully automated diagnostic molecular test that uses modern technology. It has the potential to revolutionize and transform TB care and control. The rapid test simultaneously detects TB and rifampicin drug resistance (a reliable indicator for MDR-TB); provides accurate results in 100 minutes so that patients can be offered proper treatment immediately and has minimal bio-safety requirements, training, and can be housed in non-conventional laboratories.

In high HIV prevalence settings, where Xpert MTB/RIF is available, people living with HIV and with presumptive TB should be tested with it as the primary diagnostic test for TB. For those who are found to be Rifampicin resistant, culture and DST facilities should be planned for.

[3] ***World Health Organization. Guidelines for intensified tuberculosis case finding and isoniazid preventive therapy for people living with HIV in resource constrained settings Geneva, Switzerland: World Health Organization; 2010.*** *http://whqlibdoc.who.int/publications/2011/9789241500708_eng.pdf*

4 TB screening tools, standard operating procedures for TB infection control in HIV, TB and other services, and integrated national public health laboratory networks that include HIV and TB laboratory services such as HIVdiagnostics and monitoring, smear-microscopy, EQA, liquid culture and fluorescence microscopy.

[5] ***Roadmap for rolling out Xpert MTB/RIF for rapid diagnosis of TB and MDR-TB. Geneva, Switzerland:***
World Health Organization 2010.
http://www.who.int/tb/laboratory/roadmap_xpert_mtb-rif.pdf

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E. Monitoring and evaluation

- Develop consensus between National TB Programs and National AIDS Programs and other stakeholders about policy development and data access agreements;
- Set national targets for the implementation of collaborative TB/HIV ^ activities through national consensus;
- Undertake, with advice from WHO, impact evaluations studies to ascertain the benefits of investing in TB control;
- Support TB/HIV monitoring and evaluation through the establishment of TB/HIVteams within the M & E unit/department of the Ministry of Health. Registers (HIV testing, pre-ART and ART care, TB) should be redesigned and develop based on international recommendations:

The two documents for international recommendations are:

For HIV registers:

The updated three interlinked patient monitoring for HIV care/ART,MCH/PMTCT and TB/HIV: standardized minimum data set and illustrative tools WHO 2009, can be accessed at: http://www.who.int/hiv/pub/imai/three_patient_monitor/en/index.html

For TB registers:

Revised TB recording and reporting forms and registers – version 200,; which can be accessed at:
http://www.who.int/tb/dots/r_and_r_forms/en/index.html

- Conduct training with special emphasis on collection and use of HIV/TB-related data;
- Strengthen data collection systems through allocation of adequate human resources, supply and supervision from national to facility level; and Harmonize and standardize the monitoring and evaluation activities including TB/HIV indicators.

Further Reading / Resources

This factsheet has been prepared in collaboration with technical partners, using the key resources below. For details and discussions on the strength of the evidence on the above recommendations, applicants are strongly encouraged to review the following key resources:

- Interim policy on collaborative TB/HIV activities, WHO/HTM/TB/2004.330 http://www.who.int/tb/publications/tbhiv_interim_policy/en/index.html

Global Fund Information Note: TB/HIV Collaborative Activities (May 2011) 5

- Improving the diagnosis and treatment of smear-negative pulmonary and extrapulmonary tuberculosis among adults and adolescents Recommendations for HIV prevalent and resource-constrained settings, WHO/HTM/TB/2007.379 http://whqlibdoc.who.int/hq/2007/WHO_HTM_TB_2007.379_eng.pdf

- Guidelines for intensified tuberculosis case finding and isoniazid preventive therapy for people living with HIV in resource constrained settings Geneva, Switzerland: World Health Organization; 2010 http://whqlibdoc.who.int/publications/2011/9789241500708_eng.pdf

- Roadmap for rolling out Xpert MTB/RIF for rapid diagnosis of TB and MDR-TB.Geneva, Switzerland: World Health Organization 2010. http://www.who.int/tb/laboratory/roadmap_xpert_mtb-rif.pdf

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