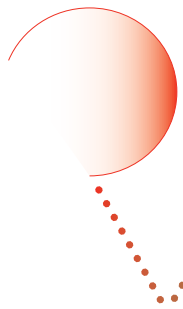


GREEN LIGHT COMMITTEE
THE STOP TB PARTNERSHIP WORKING GROUP



GREEN LIGHT COMMITTEE APPLICATION INSTRUCTIONS

Subgroup of the stop tb partnership working group on multidrug-resistant tuberculosis

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Introduction

Management of drug-resistant tuberculosis (DR-TB) under programmatic conditions is a complex intervention in public health, not yet fully established in many countries. The treatment that does not meet international standards, however, risks amplifying and spreading multidrug-resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB) further. The global response to MDR-TB and XDR-TB, embedded in the Global Plan to Stop TB 2006-2015¹, has the target of achieving universal access to diagnosis and treatment of MDR-TB by 2015. The WHO *Guidelines For The Programmatic Management Of Drug Resistant Tuberculosis* (herein after referred to as the WHO Guidelines)² provide recommendations for appropriate management of DR-TB to control it, avoid generation of further drug resistance and taking into consideration community based / ambulatory and patient centered care. The Green Light Committee (GLC) was created by WHO and its partners in January 2000 with the objective to help programmes/projects³ develop and implement strategies for the management of DR-TB,

The GLC a subgroup of the Stop TB Partnership's Working Group on MDR-TB and serves both WHO and the Stop TB Partnership (STP) as an advisory body. The GLC has the following functions:

- Evaluates applications for access to second-line anti-TB drugs (SLD) in relation to current WHO guidelines, available evidence, and collective experience;
- Advises WHO and the STP as to the outcome of each application;
- Monitors the progress and performance of GLC-approved programmes/projects;
- Promotes the development of programme/project capacity to manage DR-TB;
- Promotes capacity development for expert technical assistance and consultation on DR-TB;
- Promotes and participates in the analysis of data from GLC-approved programs and in the dissemination of new data-driven information on treatment of DR-TB.

Today GLC forms part of the Green Light Committee Initiative ("GLC Initiative"), which is a mechanism that:

- Establishes compliance of country MDR-TB programmes/projects with the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis and other international standards set in the field of TB care and control;
- Enables access to affordable, high-quality, second-line anti-TB drugs for the treatment of MDR-TB;
- Provides monitoring and technical assistance to countries in scaling up their MDR-TB programmes/projects;

¹ <http://www.stoptb.org/globalplan/>

² WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis, emergency update 2008 (WHO/HTM/TB/2008.402 http://www.who.int/tb/publications/2008/programmatic_guidelines_for_mdrtb/en/index.html.)

³ The GLC encourages countries to scale up their MDR-TB response by changing initial projects with small patient cohorts into nation-wide MDR-TB programmes.

- Advises WHO on policy-related matters to effectively prevent and control MDR-TB based on the best available scientific evidence;
- Fosters research to strengthen the evidence base for the programmatic management of DR-TB.

The GLC consists of nine member institutions⁴ that are drawn from the Stop TB Partnership Working Group on MDR-TB and chosen based on a competitive selection process which is regulated by the GLC Operating Procedures. The member institutions have a demonstrated leadership in public health and are active in TB care and control internationally. Each member institution is represented by two experts in programmatic, scientific, clinical, or microbiological aspects of TB who serve WHO in an advisory capacity. The GLC freely consults outside experts as needed. All members are required to adhere to rules of conflict of interest and confidentiality and, thus, cannot participate in the decision-making on applications from programmes/projects, in relation to which they have or had a direct or perceived conflict of interest. Each institution is allowed one vote, and all decisions are taken on the basis of consensus.

The services offered by the GLC include the following:

- Pre-application assistance with DR-TB programme/project development and needs assessment;
- Expert technical review of applications;
- Evaluation of proposed programmes/projects;
- Regular monitoring of approved programmes/projects;
- Peer support and knowledge sharing with other GLC-approved programmes/projects;
- Promotion of training and technical assistance;
- Contribution to the evidence base for the programmatic management of DR-TB.

The Global Drug Facility (GDF) is presently the procurement arm of the GLC Initiative, with the Secretariat housed at WHO, which, together with its procurement agent(s) coordinates and implements drug order processes. Currently, all GLC approved programmes/projects are required to use the GDF procurement mechanism. GDF can begin providing services after a programme/project has received approval from the GLC in the so called operation phase. For detailed instructions on procurement, please refer to the Procurement Manual for MDR-TB Projects under the Green Light Committee Mechanism⁵.

To benefit from the services of the GLC and, more broadly, of the GLC Initiative, programmes/projects must: (1) build on the foundation of a solid DOTS-based TB care and control programme/project; (2) design their programme/project within the principles put forth in the most recent WHO *Guidelines*; and (3) write their application in the format prescribed in these *Green Light Committee Application Instructions* (herein after referred to as the *Instructions*). Programmes/projects receiving approval can benefit from the pooled procurement of WHO prequalified quality assured SLD at preferential prices. Moreover, the application process leads to enhanced communication between programme/project sites, WHO, other public health agencies and the GLC Initiative. It also facilitates technical assistance to the programmes/projects. Feedback from programmes/projects provides important clinical and programmatic experience needed to develop global standards for the prevention and control of DR-TB.

The Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund) at its Third Board Meeting⁶ recognized that the GLC provides a package of services for MDR-TB care and control that cannot be disaggregated. It further determined that Principal Recipients of Global Fund grants would be required to procure SLD through the GLC Initiative, including the pooled procurement mechanism (Third Board Decision).

⁴ The current GLC member institutions are Partners In Health (PIH), KNCV Tuberculosis Foundation, International Union Against Tuberculosis & Lung Disease (IUATLD), Infectious Diseases Hospital F. J. Muñiz (HFJM), U.S. Centers for Disease Control and Prevention (CDC), State Agency for TB & Lung Disease, Latvia, Médecins sans Frontières (MSF), World Health Organization (WHO), Indus Hospital.

⁵ http://whqlibdoc.who.int/hq/2008/WHO_HTM_STB_2008.51.pdf

⁶ GF/B4/2 (January 2003).



The Global Fund at its Thirteenth Board Meeting⁷ determined that Country Coordination Mechanisms (CCMs) applying for funding of MDR-TB care and control activities in a Proposal under Round 6 and subsequent rounds of funding, or in a Request for Continued Funding, must include in their Proposals or Requests for Continued Funding provision to share the cost of the GLC Initiative and reaffirmed the Third Board Decision. The Global Fund, in consultation with the GLC, has defined the cost-sharing element for GLC services as a flat rate per grant per year that will not exceed \$50,000 per grant per calendar year (ending 31 December) (the "Cost-Sharing Element"). Countries using the GLC mechanism and basing themselves on the Global Fund funding must include this flat-rate payment in their Global Fund grant application budgets.

These Instructions were designed and written to be used in conjunction with the following source material, available at no cost from WHO in paper or the world wide web:

World Health Organization. Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis, emergency update 2008 (WHO/HTM/TB/2008.402)

http://www.who.int/tb/publications/2008/programmatic_guidelines_for_mdrtb/en/index.html

World Health Organization. Treatment of TB Guidelines - 4th Edition (WHO/HTM/TB/2009.420);

http://www.who.int/tb/publications/2009/who_htm_tb_2009_420_beforeprint.pdf

World Health Organization. Procurement Manual for MDR-TB projects under the Green Light Committee mechanism, September 2008, (WHO/HTM/STB/2008.51);

http://whqlibdoc.who.int/hq/2008/WHO_HTM_STB_2008.51.pdf

WHO policy on TB infection control in health-care facilities, congregate settings and households;

http://whqlibdoc.who.int/publications/2009/9789241598323_eng.pdf

⁷ GF/B13/8 (27-28 April 2006).



Overview of application process

Programmes/projects⁸ wishing to apply may request the GLC Secretariat to organize a pre-application visit of GLC consultants in order to help prepare the application and provide assistance on any relevant technical issues. This pre-application assistance is not mandatory, however is recommended to ensure the programme/project is well prepared with its application. Programmes/projects should submit their application to the GLC Secretariat. The application enables GLC to understand the existing TB care and control programme/project and the proposed programme/project for DR-TB.

Programme/project implementation status will be listed on the GLC website. Decisions are taken by consensus during the GLC meeting and the GLC Secretariat, hosted by the WHO, will communicate the GLC's initial assessment to the programme/project director within six weeks of the meeting date. In cases when the GLC needs additional information, a letter with questions and comments is sent to the programme/project director. These questions must be answered within three months; otherwise, the GLC will suspend consideration of the application. In some cases, after reviewing an application, the GLC may decide that a site visit is necessary before it can make an informed decision.

After one or more rounds of correspondence and a site visit (when needed), the GLC may reach one of the following decisions:

1. The GLC advises WHO to approve the programme/project to procure SLD through the procurement agent(s) of the GLC Initiative at reduced prices;
2. The application needs modifications to incorporate the recommendations in the WHO Guidelines before the GLC will advise WHO to approve the programme/project;
3. The programme/project lacks basic elements for successful management of drug-resistant tuberculosis in accordance with the *WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis*.

In cases when the GLC is unable to extend its approval, the GLC Secretariat will work with the programme/project to provide the necessary technical assistance which would lead to eventual approval in future.

The GLC treats all information received during the application process as confidential. To help develop sound policy on DR-TB, the GLC Secretariat will request data from the programme/project in the post-approval stage. It is understood the applicant agrees that GLC Secretariat will be entitled to use aggregate level data in its publicly available reports and other communications and for the purpose of developing global policy recommendations for the management of DR-TB. The GLC Secretariat will otherwise treat such data and information as confidential and proprietary to the applicant. Any review, analysis, and/or publication of the aforesaid data by the GLC Secretariat will be undertaken only in consultation and agreement with the applicant.

⁸ This includes smaller projects from non-governmental entities.

The GLC approved programmes/projects have the responsibility to consider and respect the rights of patients as per Chapter 19 of the WHO Guidelines.

Phases of the application process

The application process has four phases. Each phase has several steps:

1. Pre-application Phase

Prior to applying to the GLC, the potential applicant should:

- a. Analyze the scope/extent of the DR-TB problem;
- b. Ensure that an adequate TB care and control programme/project is in place and functioning well;
- c. Secure government commitment and adequate funding;
- d. Develop a coordinated and funded programme/project management plan with an implementation timeline, as an integral part of the TB care and control management plan;
- e. Assure adequate TB external quality-assured TB laboratory services are in place;
- f. Devise an appropriate treatment and monitoring strategy;
- g. Develop a plan for protection of patient rights and definition of patient responsibilities;
- h. Develop an adequate information (data) management system;
- i. Confirm that the drugs needed are registered in the country of the programme/project or that they can be imported and distributed (any existing limitations of drug registration and /or importation and distribution have to be notified to the GLC at this stage);
- j. Develop a plan for dealing with the local customs procedures for importing the drugs;
- k. Develop a strategy for TB infection control;
- l. Develop a strategy to ensure access to diagnosis and treatment by vulnerable groups like prisoners, minorities, homeless etc.;
- m. Develop a strategy to ensure the availability of adequate social support.

Programme/project managers may contact the GLC Secretariat, the WHO country and/or Regional offices, a Stop TB Partnership technical partner working in the country, or any of the GLC member institutions to request assistance including a pre-application assessment. The main objectives of a pre-application assessment mission are to evaluate the proposed programme/project site, its preparedness to start a programme/project, and advise the programme/project personnel on how to best prepare an application to the GLC.

2. Application Phase

Once the foundation of the programme/project is in place, the applicants should:

- a. Prepare and submit an application to the GLC according to the Instructions (this document);
- b. Respond to the GLC comments, questions, or instructions within three months (if a timely response is not possible, the applicant may resubmit a new application at the applicant's convenience);
- c. Facilitate a site visit, if requested by the GLC;
- d. Applicants should be aware that if their application is reviewed favorably, to receive final approval, the programme/project director will have to agree to specific terms with WHO. These terms include, but are not limited to, periodic data reporting to GLC Secretariat, on-site monitoring by the GLC or its consultants, rules for procuring the preferentially priced SLDs, procedures for reporting and resolving problems identified by the GLC or by the programme/project manager(s), and sharing innovative and successful methods between similar programme/project sites.



3. Approval Phase

Once the application is approved:

- a. A Letter of Approval is sent to the programme/project by the GLC Secretariat with a copy to GDF and its procurement agent.
- b. An Agreement is reached between the programme/project and the WHO on specific terms and conditions regulating GLC procurement mechanism (Letter of Agreement).
- c. The programme/project will send a procurement form to the GDF⁹ specifying the exact quantities and requested delivery times of each drug to be purchased. It is advisable to send an advance procurement form to the GDF during the application phase in order to facilitate the procurement process.
- d. The GDF sends procurement data to the drug procurement agent based on the number of patients approved and the amounts indicated in the procurement form.

4. Operational Phase

After a programme/project is approved by the GLC and all preparations are made, the following steps have to be taken:

- a. The programme/project sends a delivery order for SLDs to the procurement agent and a copy to GDF Secretariat.
- b. After receipt of an order from a project, the procurement agent prepares a quotation and sends it to the programme/project within 10 working days.
- c. Procurement agent and the programme/project negotiate and sign a contract for delivery of the SLDs, copying the GLC Secretariat and GDF.
- d. After the programme/project confirms the delivery order, it makes the payment to the procurement agent and informs the GDF accordingly.
- e. Once payment is received by the procurement agent, it will confirm the order and delivery schedule.
- f. Through the Order Management System¹⁰, a web-based order tracking system, the programme/projects are informed about each step in the supply process, including order placement, receipt of payment, expected delivery dates, as well as the relevant shipping details and necessary documentation.
- g. The procurement agent procures the drugs and arranges their delivery to the site designated by the programme/project; N.B. The programme/project carries the responsibility for importation of the drugs in country, including customs clearances and any other pertinent formalities.
- h. The programme/project begins enrollment, treatment, and monitoring of patients.
- i. The programme/project sends annual reports to the GLC Secretariat using the annual reporting forms in the *WHO Guidelines*.
- j. The approved programmes/projects agree to assume the responsibility of accepting and facilitating monitoring and technical assistance visits, and especially implementing the recommendations made by the visiting consultants after the monitoring report is approved by the GLC and officially sent to the programme/project.

The GLC takes the following steps:

- k. GLC Secretariat (glc_secretariat@who.int) coordinates and accepts requests for technical assistance, including drug management technical assistance to the programme/project as needed, involving Members of the Stop TB Partnership Working Group on MDR-TB;

⁹ For GDF contact information and relevant procedure please refer to the Procurement Manual for MDR-TB Projects under the Green Light Committee Mechanism http://whqlibdoc.who.int/hq/2008/WHO_HTM_STB_2008.51.pdf

¹⁰ See page 12 of the Procurement Manual for MDR-TB Projects under the Green Light Committee Mechanism, http://whqlibdoc.who.int/hq/2008/WHO_HTM_STB_2008.51.pdf

- I. The GLC or its consultants conduct periodic monitoring and evaluation visits and provide technical assistance (as needed).

These *Instructions* describe primarily the application process itself. The pre-application phase is detailed in the WHO *Guidelines*. The WHO *Guidelines* contain principles by which GLC will judge the application. Programmes/projects based on the WHO *Guidelines* will have the highest likelihood of GLC approval and programmatic success. Details of the approval and operation phases will be discussed with applicants individually if their application is successful.

Application Procedure for Programme/Project Expansion

GLC-approved programmes/projects may find it necessary to expand beyond the cohort approved initially. There are two procedures for doing this:

1. Full expansion application

Programmes/projects should submit a formal request to GLC according to the timeline for review cycle for new applications. The review of this request will be performed according to the method of review of a new programme/project application. The request should include following items:

- a. Cover letter justifying the need for programme/project expansion;
- b. Case finding and cohort data of all TB patients, including new patients and available data on different categories of re-treatment patients (failure of Category I, failure of re-treatment, default and relapse);
- c. Case finding and cohort data (or preliminary outcome data) of all MDR-TB patients;
- d. Documentation of funding for the additional patients;
- e. Description of any changes to the programme/project made or planned since the submission of the original application;
- f. Updated drug resistance surveillance data or patients' drug susceptibility testing (DST) patterns;
- g. Drug request and procurement order/procurement plan to cover the complete treatment of the additional patients.

2. Expansion request based on the GLC monitoring mission report

Decision to expand the GLC programmes/projects can be also taken on the basis of the GLC monitoring reports. If the GLC consultant rates the implementation of the GLC programme/project as successful and makes a recommendation for expansion in the report accordingly, following the approval of the monitoring report by the GLC, the decision to expand the programme/project can be taken with immediate effect by the Chair of the Committee in consultation with the Secretariat. To initiate request of expansion under this option, programme/project has to submit to the GLC Secretariat a simple formal letter of request.

Programmes/projects for small numbers of patients

Programmes/projects intending to treat a small number of patients (generally less than 50) can minimize the time required for the application process. Such programmes/projects are welcome to contact the GLC Secretariat for further details and instructions for the simplified application (see Annex A). The time of the GLC review is substantially reduced, and the application can be submitted outside the regular review cycles. It is important to note that although the process of the application is simplified, the requirements for approval of the programme/project remain the same: evidence of sound TB care and control based on all elements of DOTS, and the ability to provide DR-TB treatment and management according to WHO *Guidelines*. All cohort extensions will follow the full application requirements of the GLC.



Instructions for applicants

The application can be submitted in any of the WHO official languages (English, Russian, Chinese, Arabic, Spanish, and French), and should conform to the format and include the content described in these *Instructions*. Applications submitted in languages other than English will require additional time and incur costs for professional translation. A complete application has four major sections:

1. Cover letter (two pages maximum).
2. Main body of the application (30 page maximum; 12 pt font).
3. Annexes (no page limit; attached to the main body of application if possible).
4. Additional information/guidelines/DRS surveys (published or unpublished) may be provided as attachments as appropriate.

The GLC makes a final decision on **complete** applications. The GLC Secretariat will contact the applicant within seven days after the receipt of an application to confirm receipt and request any missing data before review. If the GLC determines during its review that the application is incomplete or incorrect in form or content, the application will be returned with an explanation of the specific deficiencies. Applicants may revise and resubmit applications at their own convenience. The revised application should include a new cover letter responding to each of the GLC's comments, point-by-point, indicating how each specific deficiency was remedied.

An electronic version of the application, including all supporting documents and annexes are necessary and will greatly facilitate the review process. However, the original paper letters of support must be received by the GLC Secretariat before an application can be approved. Please note that WHO and Stop TB technical partners can provide technical assistance necessary for the applicant to meet the conditions set by the GLC.

Cover Letter

The cover letter should be typed or printed on the applicant organization's original letterhead. It should be addressed to the "Green Light Committee". A formal request to the GLC to review the potential programme/project for treatment of DR-TB cases should be part of the letter. The cover letter should be signed by the programme/project director and contain the following items:

1. Size of cohort to be treated;
2. Location of the programme/project;
3. Anticipated start date and duration;
4. Time schedule for inclusion of patients;
5. Intention to use GLC Initiative pooled procurement mechanism;
6. List of all organizations involved ;
7. Brief justification of the need for a programme/project.

Body of the Application


The application should describe in specific terms how the basic TB programme/project and the proposed programme/project have implemented or plan to implement the principles and recommendations in the *WHO Guidelines*. The body of the application is divided into the following sections:

1. Background
2. Existing TB care and control programme/project
3. Information on DR-TB in the area and past use of SLD
4. Government commitment and partnerships
5. Organization, management, and coordination
6. Case finding, diagnosis and definitions
7. Laboratory aspects
8. Infection control aspects
9. Treatment and follow-up strategy
10. Side effects monitoring and management
11. Treatment delivery and adherence
12. Patient rights and responsibilities
13. Drug management
14. Information systems and data management
15. Annexes to the application.

Each section should include the topics and issues as described in the *WHO Guidelines*. Although all applications should include these sections, other sections may be added if it would explain the programme/project more clearly. In every case, the applicants should strive for a clear and concise description of the TB care and control programme/project at the site and the proposed programme/project to detect, treat, and manage DR-TB. To facilitate the review process, the application and annexes must follow the format, coding and section titles in these *Instructions*.

1. Background

- 1.1 General and brief information on the political or geographic region in which the programme/project will be carried out, including its size, population and general governance structure.
- 1.2 Brief description of the health care system in the region and the TB care and control programme/project (including the lines of authority and responsibility):
 - a. administrative structure and role of the public (governmental) and private sectors in the provision of TB related health care services;
 - b. relationship of the TB care and control programme/project to the rest of the healthcare system; and
 - c. TB situation and TB care and control in prisons.
- 1.3 Epidemiology of TB in the country and programme/project region.
- 1.4 Epidemiology of HIV in the country and programme/project region.
- 1.5 Reasons for the emergence of DR-TB in the region and the applicant's assessment of the relative importance of each reason.

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- 1.6 Brief description of the existing pharmaceutical regulations including registration and importation of anti-TB drugs into the country. In the case of existing restrictions for registration and importation of SLDs, please provide a description of options for obtaining a waiver or exemption under national legislation/regulations/decrees, e.g. based on humanitarian group treatment under a United Nations special agency programme.

2. Existing TB care and control programme/project

Successful implementation of the DOTS strategy is one of the primary criteria in determining whether or not a programme/project is capable of handling the complex issues associated with diagnosis and treatment of DR-TB.

- 2.1 DOTS programme/project performance in the country/region with aggregate data and regional/sector (for example prison-civilian) breakdown according to standard WHO case registration, reporting, and cohort analysis formats and definitions.
- 2.2 Quarterly reports generated by the DOTS based TB care and control programme/project for at least the last two years.
- 2.3 Among all TB cases, percentage of re-treatment TB cases, percentage of chronic TB cases, and percentage of pulmonary smear-negative and extra-pulmonary TB cases.
- 2.4 Strategies and methods for case finding and contact tracing.
- 2.5 Treatment strategy for TB cases (regimens and method for determining what regimen a patient receives).
- 2.6 Description of treatment delivery for the intensive and continuation phases of treatment.
- 2.7 Defaulter tracing system and measures to assure adherence to treatment.
- 2.8 Drug supply mechanism (including funding source and any problems associated with distribution, such as stock-outs).
- 2.9 Number and type (nurse, physician, laboratory technician, etc.) of professional staff involved including their roles and responsibilities.
- 2.10 Present TB infection control strategy.

3. Information on DR-TB in the area and past and future use of SLD

- 3.1 Any available drug resistance surveillance data for the country and/or the area(s) where this programme/project will be implemented. Data should be separated for new patients and re-treatment patients. Whenever possible, data for re-treatment cases should be separated for each of the re-treatment subgroups: Failures of Category I, Relapses after Category I, Return after Default from Category I, Failures of Category II, Relapses after Category II, and Return after Default from Category II.
- 3.2 In case representative drug resistance surveillance data are not available, any available drug resistance data from the programme/project area should be provided with a clear explanation of the nature of the group of patients represented by the data.
- 3.3 Drug resistance profile of the proposed treatment cohort if known.
- 3.4 Full description of the management of DR-TB cases within the TB care and control programme/project prior to the application to the GLC.
- 3.5 Availability and use of SLDs in the country and programme/project area prior to the application to the GLC, such as availability for purchase with or without doctor's prescription, on the open (legal) or black market, outside the TB care and control programme/project and in the private medical sector.
- 3.6 Medium-term (3 to 5 year) tentative forecast of patient enrolment.

4. Government Commitment and Partnerships

The governing authorities, leadership of the health department, and the leadership of the TB care and control programme/project in the region must be firmly committed to TB care and control as this is one of the most important elements for the success of TB prevention and control activities. This section should include:

- 4.1 Confirmation that diagnosis, treatment, and follow-up of DR-TB is provided free of charge to the patients, including ancillary tests and medications;
- 4.2 Name of local, national and international collaborating agencies, partners, consultants and NGOs including their roles, commitment and responsibilities;
- 4.3 Description of legal framework, if any, regulating the use of first- and second-line anti-TB drugs in the country/project area;
- 4.4 Anticipated long-term strategy to manage DR-TB in the region/country;
- 4.5 Describe any sources of funding that you anticipate will be used for the DR-TB treatment programme/project.

5. *Organization, Management and Coordination*

Roles and responsibilities of each participating component of the TB care and control system, including specific individuals, must be delineated to prevent overlap and to ensure all aspects of the programme/project are covered. Local institutions, the general medical services, and the social services system as well as outside donors or collaborators should be integrated into the programme/project. This section should provide a detailed description of the following.

- 5.1 Anticipated start date and number of patients planned for enrollment. If the project is of limited duration, please indicate this in this section.
- 5.2 Local facilities **of the TB care and control system** (including specialized units) that will be involved in the treatment of patients with DR-TB and the roles and responsibilities.
- 5.3 Local personnel in the TB care and control system who will be responsible for the treatment of patients affected by DR-TB, and their training/experience in the management of such cases and use of SLDs.
- 5.4 Local facilities **outside the TB care and control system** that will be involved in the management of patients with DR-TB, including roles and responsibilities of each (e.g., prisons, general medical services, social services, psychiatric facilities, alcohol and drug abuse treatment programmes, patient support groups, NGOs and FBOs etc.).
- 5.5 Plan for the monitoring and supervision of the programme/project by the programme/project itself and by any external organizations.
- 5.6 Training programme for health care personnel, laboratory technicians, and information systems/data management personnel.
- 5.7 Collaboration established with the prison system for management of the DR-TB.
- 5.8 Programme/project advocacy and social mobilization around DR-TB treatment and management.
- 5.9 Plan for sustainability beyond the programme/project period.

6. *Case finding, diagnosis and definitions*

This section should clearly describe case-finding strategies to be employed for enrolling patients in the programme/project cohort. Some programmes/projects have already identified patients with DR-TB waiting to be treated; others may plan to enroll patients as they are diagnosed in the future.

- 6.1 Case finding strategies and methods; including policies for use of culture and DST (flow charts are encouraged, including which drugs will be tested and at what stage in the diagnostic assessment).
- 6.2 Inclusion/exclusion criteria for selecting, out of all cases with DR-TB identified by the programme/project, those to be enrolled in the programme/project cohort, including a description of health care institutions/bodies in charge of elaborating and applying the criteria (for example, the responsible clinician, an expert committee, etc.).
- 6.3 Case definitions for patients with DR-TB according to the WHO *Guidelines* with brief description for each and rationale behind using them within a framework of this programme/project.
- 6.4 Detailed definitions of DR-TB treatment outcomes according to the Guidelines.
- 6.5 HIV testing and counseling policy and percentage of HIV-infected persons among those with DR-TB.



7. Laboratory Aspects

Although DR-TB may be suspected on clinical grounds, it is diagnosed with certainty only by the bacteriology laboratory. Ultimately, definitive treatment is based on accurate, timely DST results.¹¹ Well-functioning bacteriology laboratory services that provide, at minimum, accurate, timely drug susceptibility testing, at minimum, for isoniazid and rifampicin are mandatory. The application should describe the following.

- 7.1 Laboratory network and main laboratories that will serve the programme/project (national or regional reference laboratory(ies), culture laboratory(ies), microscopy services, for example), including the number and types of personnel, the number of sputum specimens processed, the techniques used for culture and DST, availability of molecular tests for MDR-TB screening of suspects, bio-safety procedures.
- 7.2 Schedule, frequency, and extent of bacteriological evaluation of patients during treatment and follow-up.
- 7.3 Quality control and quality assurance systems and supervisory activities of the local reference laboratory(s), results of the most recent quality assurance evaluations of sputum smears, cultures, DSTs, and rapid molecular tests; structure of supervision in the laboratory network;
- 7.4 Collaboration with an international reference laboratory and the quality assurance system associated with this laboratory.
- 7.5 External quality control results of Proficiency Testing and DST and molecular testing data by the supranational reference laboratory (SRL).
- 7.6 Process and infrastructure for specimen collection, transport and referral.
- 7.7 Information management (recording and reporting) system.
- 7.8 TB infection control physical provisions, organization and monitoring.

8. Infection control aspects

Applications should describe existing and proposed strategies to ensure that TB infection control measures are in place in settings where patients with DR-TB and/or people suspected of having DR-TB are diagnosed and managed. This includes laboratories, health care settings and households where community/ambulatory-care approaches are promoted. This section should provide information regarding:

- 8.1 A plan for the implementation/reinforcement, monitoring and evaluation of TB infection control measures; this should include administrative, environmental and engineering controls in the situations described above.
- 8.2 Description of the managerial and monitoring activities at national and local levels aimed at facilitating the implementation of administrative controls, environmental controls and the use of particulate respirators.
- 8.3 Physical provisions, organization and monitoring of TB infection control at MDR-TB treatment sites (home/policlinic / hospital).

9. Treatment and Follow-up Strategy

This section should clearly describe all aspects of treatment with anti-TB drugs within the proposed programme/project and post-treatment follow-up, including:

- 9.1 Use of standardized, empiric, or individualized treatment regimens and rationale behind their use;

¹¹TB treatment that is based on the best educated guess or probability of drug resistance in an individual patient is considered empiric treatment, for example, a patient in whom category II treatment is failing but whose sputum DST results have not yet been reported.

- 9.2 Treatment regimens and algorithms for their design for both intensive and continuation phases;
- 9.3 Criteria to change the treatment regimen from intensive to continuation phases and other modifications in the regimen;
- 9.4 Experience of the medical staff in using SLD;
- 9.5 Transfer of patients and patient information from inpatient to outpatient settings and in the reverse direction, transfers between the prison and the civilian sectors, between long-term care or specialized housing facilities, sanatoria, other regions, and other hospitals, including community/ambulatory follow-up;
- 9.6 Monitoring for the effectiveness of treatment with bacteriological and other tests;
- 9.7 Management of patients with associated problems such alcohol or drug abuse, poverty, TB related loss of job, homelessness, diabetes mellitus, and HIV infection; and
- 9.8 Availability and use of surgery for diagnosis and treatment.

10. Side effects monitoring and management

Second-line drugs cause side effects much more frequently than first line drugs. The side effects must be detected promptly and managed skillfully to ensure adequate treatment. The application should include a detailed plan to monitor for and manage adverse drug reactions.

- 10.1 Schedule for monitoring for adverse reactions including the clinical evaluations and laboratory tests to be performed at baseline and periodically.
- 10.2 Experience of the medical staff, patient counsellors and treatment supporters in managing side-effects or training activities planned in this regard.
- 10.3 Ancillary drugs and other therapies available to manage side effects.
- 10.4 Strategy and algorithms for the management of the most frequently occurring/expected side effects.

11. Treatment delivery and adherence

Applications should describe existing and proposed strategies and measures to assure adherence to the long duration of treatment under direct observation of therapy by a health worker.

- 11.1 Plan for follow up of all patients (case management) at all levels of care.
- 11.2 Plan for provision of social support (including financial support, incentives and enablers) to all patients.
- 11.3 Plan for follow up of patients defaulting treatment.
- 11.4 Plan for peer and community support.

12. Patient rights and responsibilities

The GLC expects applicants to address the rights and responsibilities of patients as per Chapter 19 of the WHO *Guidelines, The Patients' Charter for Tuberculosis Care, Patients Rights and Responsibilities* (www.patientscharter.org) (1) has been developed to inform this process.¹⁴

¹²For further detail please refer to WHO policy on TB infection control in health-care facilities, congregate settings and households, WHO/HTM/TB/2009.419, http://www.who.int/publications/2009/9789241598323_eng.pdf

¹³Standardized treatment means the same drug regimen is used for all patients (for example, category I treatment for new pulmonary cases). Empiric treatment means drugs for an individual patient are selected based on the best guess or probability of drug susceptibility. Individualized treatment means drugs are selected based on DST results. These definitions refer to general concepts and not necessarily to individual clinical circumstances. A treatment regimen may mix these approaches, for example, in programmes/projects that test for resistance to some drugs but not others.

¹⁴Applicants are encouraged to review the charter in its entirety. The Charter's provisions include:



Application should describe existing and proposed strategies including:

- 12.1 Plan for respecting patient rights and encouraging patient responsibility;
- 12.2 Plan for distribution of the Patient's Charter to all patients.

13. Drug management

This part of the application should describe how SLD will be imported, managed (including drug distribution system and storage, stock rotation) and accounted for from the time they are ordered through the GLC Mechanism and the designated procurement agent until the medications have been received by the patient.

This part of the application should also provide a written and signed confirmation that GLC-approved quality-assured SLD have been registered or can be imported into the country. Any existing limitations to the registration and/or importation of any of these drugs have to be clearly identified and suggestions should be made on how to resolve the problem. This will be required in order to be able to effectively place an order through the GLC mechanism. If you envision any problems with registration or importation, please refer to Annex B to provide as detailed information as possible to facilitate the resolution of the drug registration/importation problem).

14. Information Systems and Data Management

The programme/project must train all necessary participants to record and report the required information accurately and completely, at a minimum, for the data specified in the WHO *Guidelines*, including supervision and quality assurance, and report these data to the GLC Secretariat annually.

- 14.1 System of data recording and management in the hospital, dispensary, and out-patient setting for the clinical management of each patient (specify the data to be recorded in a standard format in the medical record and in computerized electronic database).
- 14.2 Laboratory data recording and reporting system.
- 14.3 Format for aggregate quarterly and annual reporting.

15. Annexes of the application

The annexes of the application should contain all letters of support and relevant data related to the programme/project. Fax or scanned copies are acceptable with the electronic submission, but the original paper letters of support must be received by the GLC Secretariat before an application can be approved. Specifically, this section should contain the following items in separate annexes:

- 15.1 Original letters of:
 - a. endorsement for the programme/project from National TB Programme, Ministry of Health (or appropriate authority, such as Ministry of Justice), and local health authorities. For regional or local programmes/projects, letters would be appropriate from these same individuals plus letters from the corresponding authorities at the state, provincial, or regional level;
 - b. commitment from representatives of **each** organization involved in the potential programme/project verifying the organization's proposed role and responsibilities.
- 15.2 The budget (in USD).
- 15.3 Documentation of funding committed (if available).
- 15.4 Drug Resistance Survey results or other DST data not included in the main body of the application.
- 15.5 Results of external quality assurance performed for each laboratory (and each diagnostic modality) involved in the provision of DR-TB diagnosis. Results of external quality assurance are required both from the national reference laboratory (for control of the national laboratory network) and also from the SRL (for control of the NRL).

- 15.6 Data collection and reporting forms to be used.
- 15.7 Programme evaluation data for the present TB care and control programme/project and according to standard WHO/IUATLD reporting system for case registration, reporting, and cohort analysis.
- 15.8 Estimated Second-Line Drug Needs For Program Year 1 Enrolment Form¹⁵ to complete treatment of the proposed cohort including, the generic name, formulation, unit dose, number of unit doses, daily dosage, number of patients per each drug, and total quantity for the full period of treatment. The final drug order (with consideration of delivery timing) must be submitted after final GLC approval (see section 4 Operation Phase above) after which changes to the procurement request requires satisfactory justification to be assessed by the GLC. Drugs should be shipped no more than every quarter and no less than every year. Please consult WHO *Guidelines* and the *Procurement manual*¹⁶ for GLC approved programmes/projects while preparing this annex.
- 15.9 Other annexes may be included as needed.

Applicants are encouraged to review the charter in its entirety. The Charter's provisions include:

Patient Rights:

- To be treated with respect and dignity and without discrimination
- To receive TB education and information about my case and my treatment in my language and to ask questions
- To receive quality TB care meeting International Standards using quality assured drugs, free of charge
- To have all personal information treated with confidentiality
- To have protection through the use of infection control measures

Patient Responsibilities:

- To inform health care providers of all relevant information about my case and my contacts
- To take all TB medications under direct observation and remain available to fully participate in follow-up
- To help prevent the transmission of TB and fully comply with infection control measures
- To avoid the use of substances that may diminish the chance for TB cure

¹⁵Please refer to the form in Annex C

¹⁶http://whqlibdoc.who.int/hq/2008/WHO_HTM_STB_2008.51.pdf



Address and schedule for submitting applications

Completed applications should be delivered to:

**Green Light Committee Secretariat
World Health Organization
Stop TB Department
20 avenue Appia
CH-1211 Geneva 27
SWITZERLAND**

Electronic copy of the application itself, annexes and all supporting documents should be sent to the following email address: glc_secretariat@who.int

Incomplete applications will not be reviewed by the Committee until all information requested is submitted.

The GLC Secretariat (glc_secretariat@who.int) can be contacted with any question regarding the application .

Applications are due on 20th day of January, March, May, July, September, and November. The GLC meets and will discuss each application on approximately the 20th of the following month.

¹⁷Samples of GLC applications can be made available to applicants upon request.



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<http://www.worldcarecouncil.org/content/patients-charter-tuberculosis-care>



Annexes

ANNEX 1:

Instructions for Fast-Track Applications

INSTRUCTIONS FOR FAST-TRACK APPLICATIONS ARE CURRENTLY UNDER REVISION, IN THE MEANTIME THE APPLICANTS ARE ADVISED TO REFER TO THE OLD VERSION OF THIS PROCEDURE WHICH CAN BE FOUND UNDER THE FOLLOWING LINK:

http://www.who.int/entity/tb/challenges/mdr/greenlightcommittee/glc_fasttrack_application.pdf

ANNEX 2:

Important additional information on drug management

- 1.1. National legal framework for public and/or donor funding procurement to purchase drugs (**brief description** on key issues related to procurement of SLD);
- 1.2. National drug registration regulations existing in the country (**brief description** on key issues related to procurement of SLD);
- 1.3. Fast-track procedure for registration foreseen in the national pharmaceutical law;
- 1.4. Provisions for drug registration waivers in the national pharmaceutical law. Possibility of importing and distributing drugs in the country prior to registration;
- 1.5. Host Agreements with WHO whereby WHO benefits from simplified import procedures and is exempt from taxes as well as some of the regulatory requirements (e.g. drug registration)¹⁸;
- 1.6. SLD registered in the country (INN name, pharmaceutical form, strengths, manufacturer, manufacturing site, country of origin);
- 1.7. SLD produced or available in the country other than through the GLC mechanism;
- 1.8. Provide evidence of commitment to facilitate the importation of SLD from: NDRA¹⁹, customs, and/or from any other relevant national authority.

¹⁸The Host Agreement between the country and WHO defines, among other things, which "privileges and immunities" and other exemptions WHO will enjoy in the country concerned. This is specific to the country/organization concerned, has the status of International Treaty and is registered as such in the United Nations Treaty Series. **WHO does not have host agreements with all the countries where it holds an office.**

¹⁹National Drug Regulatory Authority

ANNEX 3:

Projects are strongly advised to consult the Procurement manual and contact Global Drug Facility (GDF) for additional details on preparation of the drug procurement using the GLC mechanism.

ESTIMATED SECOND-LINE DRUG NEEDS FOR PROGRAM YEAR 1 ENROLMENT

SECTION A. CONSIGNEE DETAILS

Country:	
Consignee:	
Position:	
Address:	
Telephone:	
Fax:	
Email:	

SECTION B. PROJECT DATA

Number of patients to be treated	Treatment Regimen For MDR-TB patient
Total Patients:	

Please fill out the following for the two full years of treatment:

Drug Product	Units/Day (Months) Patient will take the drug	No. of Days Patient	Total Units/ Patients	Total No. of Receiving the Drug	Total Estimated Need <small>(for the full two years of treatment for the cohort enrolled in the first year)</small>
Kanamycin 1 gr vial					
Capreomycin 1 gr vial					
Amikacin 500 mg/2 ml					
Levofloxacin 250 mg					
Levofloxacin 500 mg					
Levofloxacin 750 mg					
Moxifloxacin 400 mg tabs ²⁰					
Ethionamide 250 mg tabs					
Prothionamide 250 mg tabs					
Cycloserin 250 mg capsule					
Paminosalicylic acid (PAS) 4 gr. Sachet (requires refrigeration)					
PAS Sodium 100 mg jars					

* units: tablets, capsules, injections, sachets

²⁰The WHO guidelines recommends that projects use levofloxacin as their fluoroquinolone of choice given the drug's anti-TB activity.

