

WHO/CDS/TB/2001.286 Rev.1

Original: English

Distr: Limited

**INSTRUCTIONS FOR APPLYING
TO THE GREEN LIGHT
COMMITTEE FOR ACCESS TO
SECOND-LINE ANTI-
TUBERCULOSIS DRUGS**

World Health Organization

2002

***Green Light Committee of the Working Group on DOTS-Plus for
Multidrug-Resistant Tuberculosis***

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SUMMARY

DOTS-Plus means DOTS first. Potential DOTS-Plus pilot projects that (1) build on the foundation of a solid DOTS-based TB control programme, (2) design their project within the principles put forth in the *Guidelines for Establishing DOTS-Plus Pilot Projects for the Management of Multidrug-Resistant Tuberculosis (MDR-TB)*, and (3) write their application in the format prescribed in these *Instructions For Applying to the Green Light Committee for Access to Second-Line Anti-Tuberculosis Drugs* (herein after referred to as the *Instructions*) have an excellent likelihood of receiving the “green light” from the Green Light Committee (GLC) to participate in the pooled procurement of second-line anti-TB drugs at preferential prices. Moreover, the application process may lead to enhanced communication between the project site and the WHO, the members of the Working Group, and the GLC. This will benefit all parties involved, but most importantly patients with MDR-TB. The feedback and monitoring process for DOTS-Plus pilot projects incorporating the principles of the *Guidelines for Establishing DOTS-Plus Pilot Projects for the Management of Multidrug-Resistant Tuberculosis (MDR-TB)*, should provide the clinical and programmatic experience needed to develop global standards for the prevention and control of MDR-TB.

WORKING GROUP ON DOTS-PLUS FOR MULTIDRUG-RESISTANT TUBERCULOSIS

Directly Observed Treatment, Short-course (DOTS) is the World Health Organization (WHO)-recommended strategy for tuberculosis (TB) control. However, multidrug-resistant TB (MDR-TB), defined as TB caused by *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin (the two most powerful anti-TB drugs), has become a problem for TB control programmes. The most recent survey of anti-TB drug resistance showed that MDR-TB has reached epidemic proportions in some areas of the world. Unfortunately, short-course chemotherapy with first-line anti-TB drugs, as recommended in the DOTS strategy, does not cure most patients with MDR-TB.

The most effective and least expensive defense against the emergence of epidemic MDR-TB is a well functioning DOTS-based TB control programme. Such programmes cure the large majority of new TB patients and prevent widespread drug resistance. In settings of minimal drug resistance, preventing the spread of drug-resistant TB by effective, complete treatment of new TB patients is more effective and less costly than the treatment of MDR-TB. Therefore, prevention must be the highest priority for TB control programmes. However, programmes that have a significant amount of patients with MDR-TB need to consider direct treatment for MDR-TB.

To address the issue of MDR-TB, WHO and its partners built upon the DOTS strategy and initiated DOTS-Plus, a strategy, under development and testing, designed to manage MDR-TB using second-line anti-TB drugs. In order to further develop the DOTS-Plus strategy, WHO created the Working Group on DOTS-Plus for MDR-TB (herein after referred to as the “Working Group”) and established two subgroups and two committees as part of the Working Group: Subgroup on Drug Procurement, Subgroup on Laboratory Issues, Scientific Panel, and the GLC. Membership of the Working Group includes over twenty non-governmental organizations, agencies, institutions, and National TB Programmes of WHO Member States dedicated to TB control.

Subgroup on Drug Procurement

The Subgroup on Drug Procurement aims to increase access to the second-line anti-TB drugs needed for the management of MDR-TB. One of the major obstacles to implementing DOTS-Plus pilot projects is the high cost of second-line anti-TB drugs. The Subgroup on Drug Procurement has launched a strong effort to negotiate preferential prices with the pharmaceutical industry to reduce the costs of second-line anti-TB drugs. In addition, a pooled procurement mechanism has been organized to facilitate access to these preferentially priced second-line anti-TB drugs. At the same time, TB experts fear that if second-line anti-TB drugs are used under the same circumstances that produced high levels of MDR-TB, resistance to the second-line anti-TB drugs will emerge rapidly, creating incurable forms of TB. Thus, it is imperative that second-line anti-TB drugs are used in programmatically and scientifically sound DOTS-Plus pilot projects so as not to generate further drug resistance.

Subgroup on Laboratory Issues

The Subgroup on Laboratory Issues is devoted to resolving the many complex issues associated with laboratory diagnostics related to MDR-TB management, such as drug-susceptibility testing (DST) standards for second-line anti-TB drugs and use of rapid methods of detecting and testing *M. tuberculosis*. Current recommendations of the Subgroup on Laboratory Issues are available in the WHO document *Guidelines for Drug-Susceptibility Testing of Second-Line Anti-Tuberculosis Drugs for DOTS-Plus* (<http://www.who.int/gtb/policyrd/DOTSplus.htm>).

Scientific Panel

The Scientific Panel, representing leading authorities on TB control, develops programmatic and clinical standards for DOTS-Plus pilot projects. The current recommendations of the Scientific Panel are available in the WHO document *Guidelines for Establishing DOTS-Plus Projects for the Management of Multidrug-Resistant Tuberculosis (MDR-TB)* (herein after referred to as the “*Guidelines*”) (<http://www.who.int/gtb/policyrd/DOTSplus.htm>). The *Guidelines* present some protocols developed in other DOTS Plus Projects. These protocols are presented only as an example as every project applying to the GLC has to come up with a protocol responsive to the characteristics and needs of their patients, and to the resources available in the local context. The Scientific Panel will revise the *Guidelines* regularly based upon evidence generated from DOTS-Plus pilot projects.

Green Light Committee

The GLC was created to foster access to second-line anti-TB drugs to projects that have the greatest chance of programmatic success. The GLC reviews project proposals to determine if they are within the principles presented in the *Guidelines*. Project proposals based on the principles of the *Guidelines* will then have the option of procuring second-line anti-TB drugs at preferential prices via the pooled procurement mechanism. In addition, such projects may benefit from technical assistance provided by the members of the Working Group. The GLC process also includes monitoring visits to help ensure that projects continue to adhere to their original protocols and to the principles of the *Guidelines*.

The GLC is an *independent* group of experts in programmatic, scientific, and clinical aspects of TB that serves WHO in a technical *advisory* capacity. At present, it is composed of six individuals representing two NGOs (Medecins Sans Frontières and the Royal Netherlands TB Association), two NTPs or the equivalent (the National TB Programme – Estonia and the Centers for Disease Control and Prevention - USA), one academic institution (Harvard Medical School) and WHO. An open call for nominations is performed to generate a list of potential new members. Up to three members are replaced every two years. Each institution is allowed one vote, and the GLC freely

consults outside experts as needed. The GLC functions under strict rules to prevent conflicts of interest in its operation. The institutional members and consultants participate entirely on a volunteer basis and receive no financial benefits for participation. Institutional members and consultants are required to adhere to rules of conflict of interest and confidentiality and are, thus, recused for discussion of applications of projects they have or had had direct relation.

OVERVIEW OF APPLICATION PROCESS

DOTS-Plus pilot projects wishing to participate in the pooled procurement process for preferentially priced second-line anti-TB drugs, potential DOTS-Plus pilot projects must submit an application to WHO. The application enables the GLC to understand the structure and performance of the basic TB control programme and the proposed DOTS-Plus pilot project.

The GLC treats all information received in the application process as confidential information and reviews applications within the first four weeks after deadline. Decisions are taken by consensus and communicated to the applicant within the first week after the meeting. In general, WHO will communicate the GLC's initial assessment to the project director within four weeks of the meeting date. It is possible that an application will be approved immediately the first time it is submitted. It is most likely, however, that the GLC will respond to the project director with questions or comments on the application. These questions must be answered within the next three months before the GLC can come to a final decision. If there is no response within the next three months the GLC will assume that the applicant has withdrawn the application.

The GLC may determine after reviewing the application 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 DOTS-Plus pilot project is based on the principles of the *Guidelines*. GLC advises WHO to endorse the project for access to second-line anti-TB drugs at concessionally prices,
- 2.) The application needs further revisions/modifications to incorporate the principles presented in the *Guidelines*, before the project can participate in the pooled procurement process for preferentially priced second-line anti-TB drugs.

or

- 3.) The DOTS-Plus pilot project does not meet at the moment the standards set and the GLC advises WHO not to allow access of this project to second-line anti-TB drugs at concessionally prices.

One of the primary functions of the GLC is to serve DOTS-Plus pilot project proposals as a referral to an expert technical advisory group (such as the Scientific Panel) or as a link to potential technical support (for example, from members of the Working Group). Thus, the GLC may suggest specific training, equipment, or alternative strategies to strengthen the proposed DOTS-Plus pilot project and improve the likelihood of success in a further submission.

Approval of project does not guarantee that it will remain faithful to the principles set in the *Guidelines* the rest of the time. In order to assure that drugs will not be mismanaged monitoring visits will be made throughout the duration of the project. The objective of these visits are to review the implementation of the DOTS strategy and the DOTS-Plus pilot project at the site, and to provide technical assistance (if needed) on behalf of the GLC.

For the sake of the monitoring process, and the building of sound policy on the control of MDR TB the WHO will request some data from the project. It is understood that applicant institution agrees that WHO will be entitled to use these data for the purpose of developing global policy recommendations for the management of MDR-TB. WHO will otherwise treat such data and information as proprietary and confidential to the applicant institution. Any review and analysis of the aforesaid data and information by WHO will be undertaken in consultation with the applicant. WHO will only proceed to the publication of any of the data and information, and/or the review and analysis thereof, in agreement with the applicant.

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

1. Pre-application Phase

Prior to applying to the GLC, the potential DOTS-Plus pilot project site should:

- a. Ensure that the DOTS strategy is in place and is functioning well.
- b. Secure government commitment and adequate funding.
- c. Develop a coordinated project management plan.
- d. Provide adequate laboratory services.
- e. Devise a rational treatment strategy.
- f. Develop an adequate information (data) management system.
- g. Confirm that the drugs requested are registered in the country of the project
- h. Develop a plan for dealing with the local customs procedures for importing the drugs.

2. Application Phase

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

- a. Prepare and submit an application to the GLC according to the *Instructions* in this document.
- b. Respond to GLC comments, questions, or instructions resulting from the review of the application within the next three months, or resubmit after that at the applicant's convenience.
- d. Participate and facilitate a site visit, if requested, by the GLC.
- f. Agree to specific terms and conditions as outlined in a Letter of Agreement with WHO.

3. **Operation Phase**

Once the application is considered to incorporate the principles of the *Guidelines*:

- a. A delivery order for second-line anti-TB drugs is sent by the DOTS-Plus pilot project to WHO and the procurement agent.
- b. Drugs are procured and delivered to the site designated by the DOTS-Plus pilot project.
- c. Technical assistance from members of the Working Group is provided to projects as needed.
- d. Enrollment, treatment, and monitoring of patients begin.
- e. Periodic data and reports are sent to WHO.
- f. Monitoring visits by GLC or consultants are conducted.

These *Instructions* describe primarily the application process itself. The pre-application phase is detailed in the *Guidelines*. The *Guidelines* contains the principles by which the GLC will judge the application. Key elements of the *Guidelines* are summarized in the next section (describing the main body of the application) as they relate to the content of the application. DOTS-Plus pilot projects based on the concepts presented in the *Guidelines* will have the highest likelihood of programmatic success.

Details of the operation phase will be discussed with applicants individually if their application is successful. Applicants should be aware that if their application is reviewed favourably, to receive final approval, the project director will have to agree to specific terms with WHO. These terms include, but are not limited to, periodic data reporting to WHO, on-site monitoring by the GLC or its consultants, rules for procuring the preferentially priced second-line anti-TB drugs, procedures for reporting and resolving problems identified by the GLC or by the project manager(s), and sharing innovative and successful methods between DOTS-Plus pilot project sites.

Some GLC-approved projects may find it necessary to expand their cohorts beyond their approved cohort. In that case projects should submit a request to the GLC according to the timeline for the review cycle for new applications. The chairperson of the GLC will contact the project director directly to resolve any additional issues. It may be necessary for the GLC to conduct a site visit as well. Review of this request will be performed according to the method of review of a new project application as outlined in Annex 1.

INSTRUCTIONS FOR APPLICANTS

There is no official application form¹. The application, in English or translated into English, should conform to the format and include the content described in these *Instructions*. The application should have three major sections:

1. A cover letter (two pages maximum).
2. The main body of the application (thirty pages maximum).
3. Annexes (no page limit).

The GLC makes a final decision on complete applications. If the GLC determines 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 to WHO at the applicants' 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 within the first three months after GLC response. Otherwise, GLC will assume that the applicant has withdrawn the application.

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 DOTS-Plus pilot project should be part of the letter. The cover letter should be signed by the project director and contain the following items in relation to the DOTS-Plus pilot project:

- Location.
- Size of cohort to be treated.
- Anticipated start date and duration.
- Time schedule for inclusion of patients during the pilot project.
- List of all organizations involved.

¹ However, the application should be printed or typed on standard A4 or 8.5"x 11" paper, single-spaced, with 2.5 cm (one inch) margins, characters no smaller than twelve points in height and no more than twelve characters per 2.5 cm. This format applies to all parts of the application prepared originally by the applicants; it does not apply to photocopied annex material.

- Brief justification of the need for a DOTS-Plus pilot project.

Body of the Application

In general, the application should describe in specific terms how the basic TB programme at the pilot project site and the proposed DOTS-Plus pilot project will develop the principles listed in the *Guidelines*. The body of the application should be divided into seven sections:

1. Background.
2. Relevance of the DOTS-Plus pilot project.
3. Government commitment.
4. Organization, management, and coordination.
5. Laboratory issues.
6. Treatment and follow-up strategy.
7. Information systems and data management.

The content of each section should be comprised of the topics and issues highlighted in the *Guidelines*. Although all applications should include these sections, other sections may be added if it would explain the project more clearly. In every case, the applicants should strive for a clear and concise description of the DOTS programme at the site and the proposed DOTS-Plus pilot project to manage and treat MDR-TB.

Background

The background section places the proposed DOTS-Plus pilot project in context. This section should address the following:

- General information on the political or geographic region in which the project will be carried out, including its size, its population and its general governance structure.
- Brief description of the health care system in the region and the TB control programme (including the lines of authority and responsibility), the administrative structure and role of the public (governmental) sector (e.g., an organogram) in the provision of health care services, relationship of the public sector to the private sector, and the relationship of the TB control programme to the rest of the health system.

- Brief description of the structure and performance of the existing DOTS programme: facilities, size of staff, policies (or laws) and regulations governing TB control and prevention, case finding/diagnostic services, treatment and evaluation of treatment outcomes, supervision, drug supply, and the recording and reporting system. This section should be a concise summary of the information requested in Annex 11.
- Epidemiology of TB in the region.
- Reasons for the emergence of MDR-TB in the region and the applicants' assessment of the relative importance of each reason.

Relevance of the DOTS-Plus Pilot Project

This section should provide the justification for a DOTS-Plus pilot project as well as the projected outcomes of the pilot project. This section should state the following:

- All the relevant drug resistance surveillance data for the country as a whole, and/or from the district where the DOTS Plus project will be implemented (see Annex 4).
- Drug resistance profile of the proposed DOTS-Plus treatment cohort.
- Treatment outcome cohort data for the country as a whole, and from the district where the DOTS Plus project will be implemented.
- The expected epidemiological impact of the potential DOTS-Plus pilot project.
- Anticipated long-term strategy to manage MDR-TB in the region (beyond the duration of the DOTS-Plus pilot project).
- Full descriptions of the management programme if the management of MDR-TB cases is already occurring within the TB control programme of the proposed DOTS-Plus pilot project (see Annex 12).

Government Commitment

The governing authorities, leadership of the health department, and the leadership of the TB control programme in the region must be firmly committed to TB control as this is one of the most important elements for the success of TB prevention and control activities. This section must present credible evidence of such commitment. It should also verify that treatment of MDR-TB is provided free of charge to the patients. This section should include:

- Evidence of commitment to TB control such as the budget for TB services and changes in the budget in recent years (see Annex 3), costs or charges to patients for TB services, development of TB services and supportive social services in recent years, and recent responses of the authorities to the TB situation.
- Commitment of funds or contributions in kind to support the DOTS-Plus pilot project from the local government or health system authority.
- Original letters of support (see Annex 1) for the proposed DOTS-Plus pilot project from the ranking authority in the region with responsibility over the health system and the TB control programme. For example, for a countrywide programme, letters would be appropriate from the Minister of Health and the National TB Programme manager. For regional or local programmes, letters would be appropriate from these same individuals plus letters from the corresponding individuals at the state, provincial, regional or oblast level.
- Commitment of the TB control system to regulate and account for the distribution of second line anti-TB drugs according to specific guidelines.
- Original letters of support (see Annex 2) from each of the collaborating institutions by individuals with sufficient authority to commit the institution (and specific individuals in the institution) to its role and responsibility in the project.

Organization, Management and Coordination

The organization and operation of the proposed DOTS-Plus pilot project is crucial, as is the relation of the two to the TB control system in the region. Roles and responsibilities of each participating component of the TB system, including specific individuals, must be delineated to prevent overlap and to ensure all aspects of the pilot 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 pilot project. This section should provide a detailed description of:

- Local facilities of the TB control system (including specialized units) that will be involved in the treatment of MDR-TB patients and the roles and responsibilities of each of them.
- Local personnel in the TB control system who will be responsible for the treatment of MDR-TB patients, and their training / experience in the management of MDR-TB and use of second-line anti-TB drugs.
- Local facilities outside the TB control system that will be involved in the management of MDR-TB patients, including roles and responsibilities of each (e.g., prisons, general medical services, social services, psychiatric facilities, alcohol and drug abuse treatment programmes, social services, etc.).

- Local, national and international collaborating agencies and the roles and responsibilities of each of them.
- Plan for implementation of the DOTS-Plus pilot project.
- Management and coordination of the DOTS-Plus pilot project.
- Management system for anti-TB drugs, especially the second-line anti-TB drugs to be procured as a result of this application, including storage, distribution, monitoring, reporting, and accountability.
- Monitoring and supervision of the DOTS-Plus pilot project by both an internal and external body.
- Training programme for all health care personnel, laboratory technicians, and information systems/data management personnel.
- Plan for sustainability of MDR-TB management beyond the DOTS-Plus pilot project period.

Laboratory Issues

This section should clearly identify all laboratories involved in the DOTS-Plus pilot project and the capabilities of each one. Specify the number and types of specimens processed; the techniques used for smear-microscopy, culture and DST; biosafety procedures for laboratory workers; and the structure of the laboratory supervision. This section should provide a list and brief description of:

- Local reference laboratory(s) performing smear-microscopy, culture, and/or DST.
- Quality assurance system and supervisory activities of the local reference laboratory(s), and the results of the most recent quality assurance evaluations.
- Any other laboratories performing culture and DST.
- Laboratory network performing smear-microscopy only.

This section should provide a more detailed description of:

- Collaboration with an international reference laboratory and the quality assurance system associated with this laboratory.
- Process and infrastructure for specimen collection, transport and referral.
- Development of laboratory capacity in recent years.

- Problems with laboratory operations such as shortage of reagents and supplies, quality of reagents and media, shortages of sputum specimen containers, outdated or inadequate equipment.

Case-finding Strategies

This section should clearly describe the case-finding strategies to be employed for enrolling the patients in the cohort. Some projects have already identified the MDR TB patients to be included in the cohort. Some other may have also additional plans for enrolling patients which at the time of the application have not being identified yet. This section should provide a list and brief description of:

- Stage in the diagnostic assessment at which the TB patient receives a DST (a flowchart will help).
- Inclusion / exclusion criteria to be employed for selecting, out of the total of MDR TB cases identified by the project, those to be enrolled in the cohort of the DOTS Plus project.
- Health care institutions/bodies in charge of elaborating and applying those inclusion/exclusion criteria.

Treatment and Follow-up Strategy

This section should clearly describe all aspects of the management of patients with the proposed treatment cohort, from case finding and selection through post-treatment follow-up. Key baseline, monitoring, outcome variables, and outcome analyses should be specified according to WHO criteria.² This section should include the strategy/plan (with justification) for:

- Treatment regimens for both intensive and continuation phases according to specific drug resistance patterns.
- Transfer of patients and patient information from hospital/dispensary (inpatient) settings to the ambulatory or polyclinic setting, and in the reverse direction if necessary.
- Other transfers of patients and patient information such as transfer between the prison and the civilian sectors, to long-term care or specialized housing facilities, sanatoria, or to other hospitals.

² *Tuberculosis Handbook*. WHO/TB/98.253
Guidelines for the Management of Drug-Resistant Tuberculosis. WHO/TB/96.210
Treatment of Tuberculosis: Guidelines for National Tuberculosis Control Programmes. WHO/TB/97.220

- Monitoring schedule for patients and evaluations/tests to be performed at each point.
- Direct observation of drug ingestion.
- Ensuring complete treatment and follow up of all patients (case management).
- Detailed management of adverse reactions and collection of adverse reaction data.
- Provision of social services and support needed by patients.

Information Systems and Data Management

The ability to accurately record and report data covering all aspects of case finding, diagnosis, treatment, outcome, and programme performance is crucial to all DOTS-Plus pilot projects. These DOTS-Plus pilot projects are considered pilot projects because sufficient data do not exist to provide definitive evidence-based policy guidelines. The DOTS-Plus pilot project must commit to training all participants and to record the required information accurately and completely, including supervision and quality assurance. The training requirements may be intensive. The individuals responsible for the DOTS-Plus pilot project must also commit to recording for each patient, at a minimum, the data specified in Annex 9 of the *Guidelines*, "Standard Data Collection Set" and report these data to WHO on a regular basis. In addition to the standard data set, this section should specify:

- Case finding and notification system and forms (see Annex 7).
- System of data recording and management in the hospital, dispensary, polyclinic or clinic 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 databases.
- Laboratory data recording and reporting system.
- Format for aggregate quarterly and annual reporting.
- The indicators and analyses to be used for project outcome and case management, point of collection of these data, and the justification for the specific variables.

Application Procedure for Cohort Expansion

Those GLC-approved projects finding it necessary to expand their cohorts beyond their approved cohort should send a formal request to the GLC. The request should include the following items:

- Cover letter justifying the need for cohort expansion;
- Case finding and cohort data of all TB patients;
- Case finding and cohort data (or preliminary outcome data) of all MDR-TB patients;
- Documentation of secured funding for the additional patients;
- Description of any changes to the programme made or planned since the submission of the original application;
- DST patterns of all patients and changes in DST patterns from the original application;
- Procurement order to cover the complete treatment of the additional patients according to DST patterns; and
- Accounting of the use of all GLC-provided second-line drugs used in the project (if applicable).

Annexes

The annexes of the application should contain all letters of support and relevant data related to the project. Specifically, this section should contain the following items in separate annexes:

1. Original letters of endorsement for the project from National TB Programme, Ministry of Health (or appropriate authority, such as Ministry of Justice), and local health authorities.
2. Original letters of commitment from representatives of each organization involved in the potential DOTS-Plus pilot project verifying the organization's proposed role.
3. Detailed budget (in USD) and documentation of funding committed to potential DOTS-Plus pilot project.
4. Drug-resistance surveillance data and standard WHO/IUATLD analysis of this data.
5. Proposed therapeutic protocols and the proposed number of patients in each treatment scheme.
6. Results of quality assurance programmes performed for each laboratory (and each procedure) involved in the DOTS-Plus pilot project.

7. All data collection and reporting forms to be used.
8. Programme evaluation data used to determine efficacy of the present TB control programme and standard WHO/IUATLD analysis of this data.
9. Specific procurement request, in six-month intervals and cumulative total, for second-line anti-TB drugs to complete treatment of the proposed cohort including, the generic name, formulation, unit dose, number of unit doses, cumulative weight of each drug, and the timing for delivery (see below form for drug procurement request). Changes to the procurement request after GLC approval requires a satisfactory justification to be assessed by the GLC.

Form for Drug Procurement Request.

Name of the Project _____

Duration of the project (years) _____

Timing for delivery of the first drug request (covering six months treatment) _____

Size of the cohort _____

Request	DRUG	Km 1 g vials	Am 1 g vials	Cm 1 gr vials	Pth 250 mg Tab	Eth 250 mg Tab	Cip 500 mg Tab	Ofl 200 mg Comp	PAS 4 g sachets	Cs 250 mg caps
Quantity for each treatment course	—									
Total quantity unit doses for first drug request covering first 6 months										
Total drug request for the total cohort										

10. Examples of aggregate case finding and programme performance reports from the previous two years (if possible) according to the following reporting form:

COUNTRY: _____

COUNTRY ADMINISTRATIVE OFFICE: _____

OPERATIONAL DATA

NATIONAL TUBERCULOSIS PROGRAMME OF _____

	Year / Quarter Number		Year / Quarter Number		Year / Quarter Number		Year / Quarter Number		Year / Quarter Number	
RESULTS OF TREATMENT IN NEW SMEAR POSITIVE PULMONARY TUBERCULOSIS PATIENTS										
Number (N°) of Registered patients										
	N°	%	N°	%	N°	%	N°	%	N°	%
Patients Included in Cohort		100		100		100		100		100
Cured										

Treatment Completed										
Failures										
Defaulters										
Transfer Outs										
Deaths										

Chief of National Tuberculosis Programme

11. Successful implementation of the DOTS strategy is one of the primary criteria in determining whether or not a pilot project is capable of handling the complex issues associated with DOTS-Plus. It is critical that the application provides a comprehensive and detailed description of the implementation of the DOTS strategy in the project region. This includes addressing the following topics (in reference to DOTS implementation):

- Size and description of health care facility, including bed occupancy rate in the TB ward.
- Infection control measures to prevent nosocomial transmission, including isolation measures, disposal of waste, use of masks, etc.
- Description of treatment delivery (via direct observation) for the intensive and continuation phases of treatment, respectively.
- Percentage of TB cases (of the total number of TB cases) under direct observation during the intensive and continuation phases of treatment, respectively.
- Quarterly reporting of percentage of retreatment TB cases and chronic TB cases of all TB cases, respectively.
- Regulation of anti-TB drugs distribution/sale in the region.
- Drug supply mechanism (including funding source and any problems associated with distribution, such as stockouts).
- Cost of care to patients, including direct (ex. drugs) and indirect (ex. cost of transport to health care facility) costs.
- Standard case definitions used in the cohort analysis.
- Percentage of smear-negative and extra-pulmonary TB cases of the total number of TB cases.
- Treatment strategy for TB cases (regimens and method for determining what regimen a patient receives).
- Method for case finding, contact tracing, and defaulter tracing system.
- Number and type (nurse, physician, laboratory technician, etc.) of all staff involved including their roles and responsibilities.
- List of all partners and consultants including their roles and responsibilities.

12. If the management of MDR-TB cases is already occurring within the TB control programme of the proposed DOTS-Plus pilot project, then data from the management programme must be included. Information included in the cover letter and body of the application does not need to be repeated in this annex. However, as a minimum, this annex should contain (in reference to the MDR-TB cohort managed under the current TB programme):

- number of MDR-TB cases registered per year,
- number of MDR-TB cases treated under current TB control programme,
- treatment regimen(s) utilized (stratified by drug-resistance pattern),
- time to sputum and culture conversion,
- treatment outcomes, and
- adverse reactions encountered.

ADDRESS AND SCHEDULE FOR SUBMITTING APPLICATIONS

Completed applications should be delivered to:

**World Health Organization
Communicable Diseases
Green Light Committee of the Working Group on DOTS-Plus for Multidrug-Resistant Tuberculosis
20 Avenue Appia
CH-1211
Geneva 27
SWITZERLAND**

E-mail: dotsplus@who.ch

In order to ensure timely consideration, the application must be received by WHO in advance of the corresponding meeting date. Although a hard copy of the application must be sent to meet the deadline for the respective GLC meeting, a version sent through electronic mail will facilitate the timely review of the application. Incomplete applications and unclear information are the main reasons explaining the GLC delay in providing a definitive answer to the applicant. But please, do not hesitate in contacting the GLC Secretariat (dotsplus@who.ch) if you have any question regarding the application. The GLC plans to meet the third week of even months and receive applications by the 20th of the preceding month. The following table gives GLC meeting dates and application due dates for 2002.

GLC Meeting Date	Application Due Date
21 February 2002	20 January 2002
13 April 2002	20 March 2002
21 June 2002	20 May 2002
21 August	20 July 2002
21 October 2002	20 September 2002
20 December 2002	20 November 2002

References

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- World Health Organization. Guidelines for Establishing DOTS-Plus Pilot Projects for the Management of Multidrug-Resistant Tuberculosis (MDR-TB). Gupta R, Arnadottir T, eds. WHO/CDS/TB/2000.279. Geneva: WHO, 2000.
- Gupta R, Espinal M A. Progress in DOTS-Plus and the Management of Drug-resistant Tuberculosis: Proceedings of the Meeting of the Stop TB Working Group on DOTS-Plus for MDR-TB. 25–27 January 2001. WHO/CDS/TB/2001.292. Geneva: WHO, 2001.
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- Gupta R, Kim J Y, Espinal M A, et al. Responding to market failures in tuberculosis. *Science* 2001; 293: 1049–1051.
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- Gupta R, Brenner JG, Henry CL, Kim JT, Shin S, Espinal M, Raviglione MC (Eds). Procurement of second line anti-tuberculosis drugs for DOTS Plus pilot projects. Proceedings of a meeting . Cambridge, USA, 5-6 July 1999. WHO/CDS/TB/2000.276. Geneva: WHO, 2001.
- Espinal M (Ed). Basis for the development of an evidence –based case-management strategy for MDR TB within the WHO’s DOTS strategy. Proceedings of 1998 meetings and protocol recommendations. WHO/TB/99. 260. Geneva: WHO, 2001.