REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH

THE NATIONAL TB/LEPROSY CONTROL PROGRAMME

GUIDELINES FOR THE PROGRAMMATIC MANAGEMENT OF DRUG - RESISTANT TUBERCULOSIS

FOREWORD

The publication of the first edition of the National Tuberculosis and Leprosy Programme (NTLP) manual on the programmatic management of drug resistant TB marks a big step forward for the Ministry of Health and it underscores the Programme's commitment to providing the latest knowledge and developments in TB control in Zambia.

A case of drug-resistant TB excretes bacilli resistant to one or more anti-TB drugs. Multidrug – Resistant TB or MDR TB refers to Mycobacterium Tuberculosis isolates that are resistant to at least both isoniazid and rifampicin, the two most powerful anti-TB drugs. This is a very serious problem and people with MDR TB can only be treated with reserve or second line drugs. These drugs are not as effective as the first line drugs and they cause more side effects.

The Ministry of Health has developed the guidelines to ensure that patients with MDR TB are well treated with second line drugs that are usually used to treat such patients; these drugs are very difficult to administer as they have to be given for a longer period and it is important that people have to take them appropriately and monitored as they may have a lot of side effects. Since MDR TB is also transmitted through airdrops just like the normal drug susceptible TB, it is important that these patients are not generally mixed with the other patients in the general medical wards who may stand the risk of getting infected.

Tuberculosis is a major health problem in Zambia and the emergence of drug-resistant TB has become a worldwide problem. It is important to note that good TB control prevents and reverses high levels of drug resistant TB in communities; therefore the national TB control programme will ensure to guarantee good DOTS implementation.
This manual provides information on management of drug resistant TB diagnosed throughout the country within the NTLP services and it is complementary to the national TB and TB/HIV manual. The guidelines on programmatic management of drug resistant TB is also in line with the stop TB strategy in ensuring that MDR TB challenges are addressed.

It should be realized that drug resistant TB is a notifiable disease in accordance with the Public Health Act, Chapter 295 of the laws of Zambia and all care providers attending to TB clients are expected to ensure that such cases are notified in line with the Government policies and guidelines.

Lastly, I wish to thank the Directorate of Public Health and Research and all the cooperating partners for making it possible to produce the first edition of this manual. It is my hope that this tool will find the widest use in our institutions for a long time to come and that it will continue to be updated as new knowledge is added to the efforts in the fight against tuberculosis.

Hon. Kapembwa Simbao, MP

MINISTER OF HEALTH

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Finally, at the Ministry of Health, I would like to thank Dr Victor Mukonka (Director – Public Health and research) the TB/Leprosy Specialist (National TB/Leprosy Programme Manager) Dr Nathan Kapata and all staff in the TB unit namely, Dr Carlistus Kaayunga, Mrs. L. M Zulu, Mr. M. Malukutu, Ms. Chanda Chikwanda and Mr. C Munyandi for their dedication to ensuring the smooth running of the TB control Programme and ensuring the finalization of this manual.

Dr V. Mtonga

Permanent Secretary
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CHAPTER 1

1. BACKGROUND

Tuberculosis is one of the major public health problems in Zambia. The notification rate which was 105 per 100,000 population in 1985 increased to 545/100,000 in 2006, mainly due to association with the HIV/AIDS epidemic. Significant progress is being made in the fight against TB. In 2001 the cure rate was 58% and increased to 64% in 2002, 73% in 2003 and 76% in 2007. Likewise, the treatment success rate improved from 77% in 2002 to 85% in 2007. These important achievements have been due to the strengthening of the national TB control programme and the scaling up of the Directly Observed Treatment Short Course (DOTS) Strategy to all the districts.

National TB Control Programme (NTP)

The structure of the national TB control programme consists of the central, provincial and district levels and works in close collaboration with the national TB reference laboratory network.

Smear microscopy is routinely used for TB diagnosis and is provided free of charge by the National TB Programme to all patients with signs or symptoms of pulmonary tuberculosis in all public facilities.
Zambia has 156 laboratories with the capacity to perform quality assured TB microscopy. Three of these (Chest Disease Laboratory, University Teaching Hospital Laboratory, and Tropical Disease Research Centre) perform culture and drug susceptibility testing.

All TB patients are treated with first line drugs Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol in fixed dose combinations free of charge.

Drug Resistance TB

When patients are not prescribed their drugs properly or do not take their medicines as prescribed, TB bacilli become resistant to a certain drug/s. this means that that drug is no longer effective against the TB bacillus. Multidrug-resistant tuberculosis or MDR TB refers to Mycobacterium Tuberculosis isolates that are resistant to at least isoniazid and rifampicin, the two most powerful anti-TB drugs. People who have spent time with someone sick with MDR TB disease can become infected TB bacilli that are resistant to several drugs. Close contacts of patients therefore must be carefully examined for active disease and treated accordingly. This is particularly important for people who are at high risk of developing MDR TB disease, such as children and HIV-infected people.

Multidrug-resistant TB is in most cases, entirely man-made; the common causes of MDR TB are:

- The prescription of inadequate chemotherapy
- Poor management of drug supply leading to patients having difficulty in obtaining all the drugs they need
- The use of drugs of unproven bioavailability, and
- Poor case management or when treatment is not directly observed

The prevalence of MDR TB, in new patients is estimated at 1.8% and 2.3% in previously treated cases, based on the 2001 Drug Resistance Survey. This translates in approximately 265 new cases of MDR TB in Zambia each year. Currently the National TB control Programme is recording a number of confirmed MDR TB cases from selected parts of the country.

Appropriate management of MDR TB cases would allow the NTP to achieve good cure rates and at the same time reduce the risk of transmission of resistant strains.

The TB/HIV co-infection, in an important factor to take into account in the management of MDR TB.

Note: *It is important to remember that MDR TB can best be prevented by rigorous adherence to the principles of the Tuberculosis Control Programme (the DOTS Strategy) and by building strong partnerships with patients, their families and communities to cure TB at the first attempt.*

MDR TB Programme Management

Treatment of patients with MDR TB involves second line, reserve drugs; these are much more expensive, less effective and have more side effects than standard first line TB drugs. It is therefore recommended that confirmed MDR TB patients will be managed in designated health facilities by qualified health care providers.

The framework of management should be organized around the five components of the DOTS Strategy because the underlying principles are the same:

1. Sustained political commitment
2. A rational case-finding strategy including accurate, timely diagnosis through 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 anti-tuberculosis drugs
5. Standardized recording and reporting system

Note: *MDR TB is a notifiable disease*

CHAPTER 2

2. Case finding, diagnosis and definitions

Case Finding:

The diagnosis of MDR-TB should be suspected when a patient has persistent positive acid-fast bacilli smear or culture (beyond five months of treatment with Category I) or clinical progression of tuberculosis while on standard chemotherapy.

Patient Group	**Risk**	**Send sputum sample for Culture & DST?**
TB Patients who remain or turn positive after five months of TB treatment and/or at the end of treatment (CAT I failures)	Low	√
TB patients previously defaulted from CAT I regimen	Low	√
TB Patients who were previously treated for TB with CAT I and relapses	Low	√
TB Patients who have a contact who died while on CAT I directly observed therapy for TB.	Low	√
TB patients who defaulted on a CAT II regimen	Moderate	√
TB Patients who relapsed after CAT II regimen	Moderate	√
Health workers who are exposed to MDR TB cases	Moderate	√
TB Patients with HIV who are clinically progressing on CAT I TB treatment.	Moderate	√
TB Patients who failed treatment on a CAT II regimen	High	√
Persons from facilities with high rates of MDR-TB, including prisons	High	√
TB Patients who have a contact with known MDR-TB case	High	√

Children, pregnant women and patients with co-morbidities including HIV should be treated with guidance from MDR TB experts.

Prior to starting therapy all patients should be appropriately informed and should understand implications of treatment and also receive appropriate health education.

CHAPTER 3

3. DEFINITIONS: CASE REGISTRATION, BACTERIOLOGY AND TREATMENT OUTCOMES

3.1 General definitions of resistance

The Category IV diagnostic criteria is defined as “chronic cases” i.e. still sputum smear-positive after supervised re-treatment; proven or suspected MDR-TB. For the definitions of diagnostic Categories I, II and III refer to the national TB and TB/HIV Manual.

A patient is determined to have drug-resistant TB only through laboratory confirmation (culture and drug susceptibility testing) of resistance to one or more first-line anti-tuberculosis drugs.
Anti-tuberculosis drug resistance is classified according to the following definitions:

Drug resistance: Drug-resistant tuberculosis refers to a patient with pulmonary TB coughing-out bacilli resistant to one or more anti-tuberculosis drugs.

Primary resistance*:* Primary resistance refers to a patient with pulmonary TB coughing-out bacilli resistant to TB drugs, but who has no prior history of treatment with anti-tuberculosis drugs.

Initial resistance*:* Initial resistance occurs when doubt exists whether the patient with resistant TB has received prior treatment with anti-TB drugs. Initial resistance is a mixture of primary resistance and undisclosed acquired resistance.

Acquired resistance: Acquired resistance refers to a patient with drug-resistant TB with a history of previous treatment with anti-TB drugs. Resistance can develop within four weeks with mono-therapy or treatment with inappropriate drug combinations. This is why we can safely assume that any patient who has received at least four weeks of TB therapy is no longer a “new” patient and should be managed as a patient who has been treated before and potentially has some form of TB drug resistance.

Mono-resistance: Tuberculosis that is resistant to one anti-tuberculosis drug.

Poly-resistance: Tuberculosis that is resistant to more than one anti-tuberculosis drug, other than both isoniazid and rifampicin.

Multi-drug resistance (MDR-TB): Tuberculosis that is resistant to at least isoniazid and rifampicin.

Extensive drug resistance: resistance to any fluoroquinolone and at least one of three injectable second-line drugs (kanamycin, amikacin and capreomycin) in addition to multidrug-resistance.

Note: confirmed drug resistance must always be based on laboratory evidence.

While laboratory confirmation of MDR-TB is being obtained, patients may be included in diagnostic Category IV only by specialized physicians.

In general, recommended treatment regimens for drug-resistant forms of TB are similar, irrespective of site (pulmonary or extrapulmonary). Defining site is important primarily for recording and reporting purposes.

3.2 Bacteriology and sputum conversion (Diagnosis)

Bacteriological examinations in patients with drug-resistant TB should include sputum smear microscopy and culture. All patients suspected of having MDR-TB must have two sputum samples collected at the health facility. Direct smear can be analyzed at the nearest diagnostic facility; however, one sample must be sent for culture and DST.

Sputum conversion is defined as two sets of consecutive negative smears and cultures taken 30 days apart.

Both smear and culture are used to monitor patients throughout therapy. The date of the first set of negative cultures and smears should be used as the date of conversion (and date to determine the length of the initial phase and treatment)

The frequency and timing of smear and culture conversion among smear- and/or culture-positive patients receiving Category IV treatment should be as indicators of programme performance.

In order for a patient to be considered culture- or sputum smear-positive at the start of treatment, the following criteria must be met: at least one pretreatment culture or smear was positive; the collection date of the sample on which the culture or smear was performed was less than 30 days before, or 7 days after, initiation of Category IV treatment.

Time	Sputum Smear	Culture	DST
Beginning of treatment	√	√	√
Monthly until three cultures are consecutively negative	√	√	-
Every three months until cure/treatment completion	√	√	If culture positive

3.3 Registration based on history of previous anti-tuberculosis treatment

Before enrolling a patient in a Category IV regimen with second-line drugs, it is important to determine whether the patient has previously received anti-tuberculosis treatment and, if so, to record the drugs that were taken and the treatment outcome.

It is also important to record whether the patient ever previously received second-line drugs. These registration groups are essential for epidemiological monitoring of the TB epidemic and help in the management of MDR TB patients.

Before enrolling a patient, a detailed history taking is necessary, especially in respect to determine whether s/he has previously received anti-tuberculosis treatment and if so, record the treatment outcome and prior usage of second-line TB drugs. History taking should include the following points:

1. Demographic data
   a. Name, age, sex
   b. Address
   c. Patient Type: new, failure, treatment after interruption, relapse, transfer in, or other (which includes chronic case)

2. TB history
   a. Date of initial diagnosis
   b. Start and end date of all previous treatments; compliance with treatment regimens; outcomes
   c. Microscopy and culture results
   d. DST results
   e. Adverse effects and allergies
   f. Surgical treatments (resections, chest tubes)
   g. Complications (pneumothorax, empyema, massive hemoptysis)
   h. Type of TB: pulmonary, extrapulmonary, or both (if extrapulmonary, indicate site)

3. Past medical and social history
   a. Chronic medical conditions, including HIV, diabetes, renal insufficiency, chronic liver disease, chronic heart disease
   b. Prior psychiatric history
   c. Current non antituberculosis medications
   d. Allergies
   e. Alcohol, drug, and tobacco use
   f. Incarceration history
   g. Last menstrual period and method of contraception

4. Documented and suspected MDR TB contacts
   a. Treatment history of contacts
   b. Current status
   c. DST data
   d. Assessment of how closely the patient interacted with the contact

5. Review of symptoms: cough, sputum production, fever, night sweats, weight loss (include previous weight when healthy, with date), dyspnea, appetite, abdominal pain, nausea, vomiting, diarrhea, constipation, headache, peripheral, leg pain, hearing loss, depression, anxiety,

Category IV patients are classified in two different ways:

1. Classification according to history of previous drug use mainly used to assign appropriate treatment regimen

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- **New Category IV patients.**
  Category IV patients who have never received Anti-tuberculosis treatment or who have received anti-tuberculosis treatment for less than one month. (Note: patients who had DST at the start of a WHO Category I regimen and are then switched to a Category IV regimen because of resistance are placed in this group, even if they received more than one month of Category I treatment.)

- **Category IV patients previously treated with first-line drugs only.**
  Category IV patients who have been treated for one month or more with First-line drugs only.

- **Category IV patients previously treated with second-line drugs.**
  Category IV patients who have been treated for one month or more with one or more second-line drugs, with or without first-line drugs.

2. Classification according to history of their previous treatment (referred to as the patient's 'registration group')

1. **New**: A patient who has never received anti-tuberculosis treatment, or who has received treatment for less than one month.

2. **Relapse**: A patient previously treated for tuberculosis who has been declared cured or treatment completed, and who is subsequently diagnosed with bacteriologically positive TB by sputum smear or culture.

3. **Treatment after default**: A patient who returns to treatment, bacteriologically positive TB by sputum smear or culture after interruption of treatment for two or more consecutive months.

4. **Treatment after failure of Category 1**: A patient who returns after Category I treatment has failed (positive sputum smear at 5 months and/or at the end of treatment).

5. **Treatment after failure of re-treatment**: A patient who returns after the r e-treatment has failed.

6. **Transfer in**: A patient who has transferred from another register for treatment of drug-resistant TB to continue Category IV treatment. Their outcomes should be reported to the transferring unit so that it can report their outcomes in the cohort in which they originally started Category IV treatment. This group is excluded from the quarterly reports of the receiving unit on registration and treatment result.

7. **Other**: Category IV patients who do not fit the above definition. This group includes sputum smear positive patients with unknown treatment outcome; sputum smear positive patients who receive treatment other than Category I or II and Category IV patients who were treated outside DOTS programmes.

If DST is carried out at the start of Category I or II treatment and the patient is later switched to a Category IV regimen because of resistance (without meeting the formal criteria of failure), he or she should be included in the outcome analysis of Category I or II – under the category "Change to Category IV" and noted as such in the facility TB register.

It is important to track the number of patients who do not meet the traditional definition of failure and are switched to Category IV regimens because of resistance.
The Category IV Treatment Card provides for documentation of history of previous anti-tuberculosis treatment and therefore facilitates the determination of the group registrations as described above (see Form 01).

3.4 Treatment outcome definitions

Cured: A Category IV patient who has completed treatment according to the programme's protocol and has at least five consecutive negative cultures from samples collected at least 30 days apart in the final 12 months of treatment. If only one positive culture is reported during that time, and there is no concomitant clinical evidence of deterioration, a patient may still be considered cured, provided that this positive culture is followed by a minimum of three consecutive negative cultures taken at least 30 days apart.

Treatment completed: A Category IV patient who has completed treatment according to the programme's protocol but does not meet the definition for cure because of lack of bacteriological results (i.e. fewer than five cultures were performed in the final 12 months of treatment).

Died: A Category IV patient who dies for any reason during the course of MDR-TB treatment.

Failed: Treatment will be considered to have failed if two or more of the five cultures recorded in the final 12 months of therapy are positive, or if any one of the final three cultures is positive. (Treatment will also be considered to have failed if a clinical decision has been made to terminate treatment early because of poor response or adverse effects.

Defaulted: A Category IV patient whose treatment was interrupted for two or more consecutive months for any reason.

Transferred out: A Category IV patient who has been transferred to another reporting and recording unit and whose treatment outcome is unknown.

3.5 Cohort analysis

A Category IV treatment cohort is defined as a group of patients who start Category IV treatment during a defined time period. The Category IV treatment cohort will consist of a subset of patients recorded in the Category IV Register, i.e. those who actually started Category IV treatment during the specified period of time.

To allow adequate analysis of all patients who meet the criteria of diagnostic Category IV, three dates should be recorded (these dates are recorded in both Forms 01 and 02):

1. **Date of initial registration as a TB case** (most commonly obtained from the District Tuberculosis Register)
2. Date of registration in Category IV
3. Date of starting Category IV treatment

Treatment cohort analysis focuses on treatment outcomes among patients who actually started Category IV treatment.

The diagnostic cohort includes patients diagnosed with MDR-TB (identified in the DST register by date of DST result) during a specific period of time. It is used to assess the number of patients with MDR-TB in subgroups and over time. It allows the programme to evaluate delays in starting treatment and proportion of patients who started treatment.

The recommended time frame for Category IV treatment cohort analysis reflects the long duration of Category IV regimens. Cohort analyses should be carried out at 24 months and repeated at 36 months after the last patient starts treatment.

The analysis is done at 24 months because most of the patients will have finished treatment, allowing preliminary assessment of cure rates. Since a few patients may be on treatment longer than 24 months, the cohort analysis is repeated at 36 months after the last patient starts treatment. The 36-month evaluation is considered the final treatment cohort analysis result.

All patients should be assigned the first outcome they experience for recording and reporting purposes. Programmes may wish to record subsequent outcomes among patients followed systematically. (For example, a patient defaults on the first Category IV treatment and then returns 14 months later to be re-registered and is cured with a second Category IV treatment. This patient should receive a final outcome of “defaulted” in the cohort in which he or she was first registered and “cured” in the second cohort.)

Patients who remain on treatment at the end of a designated cohort treatment period must be identified as “still on treatment”.

For each cohort, an interim status should be assessed at 6 months after the start of treatment to monitor programme progress (see Chapter 18 and Form 08).

CHAPTER 4

4. ORGANIZATION OF TREATMENT AND FOLLOW-UP

The management of MDR TB is based on the fact that Zambia is a low prevalence and incidence country. A centralized management system and standardized treatment regimes should be used in the care of MDR TB patients.

The treatment facilities for MDR TB patients will be scaled up in a phased manner. Initially patients will be treated at the University Teaching Hospital (UTH) and then will move to other facilities based on the lessons learnt from UTH.

The functioning MDR TB Sub Committee comprising of UTH, ZAMBART, USAID, TB CAP, MSH, CDL, CDC Zambia, School of Medicine, WHO Country Office and Under the stewardship of the NTP (MOH) will be involved in the monitoring and evaluation of the MDR TB activities in the country.

Note: Individualized treatment regimens may be used in specific situations only by specialized physicians.

The trained physician may change the regimen after the consultation with the Central Unit or the MDR-TB Subcommittee, since they will be monitoring the proper use of the second line medications. All these medications will be provided by the central pharmacy for the intensive phase. In the continuation phase the health centers will receive a three month supply of the medicine in the areas where storage assures good temperature and humidity control. If this is not possible, then NTLP will provide only one month supply to the health center, in this way a large volume of the stock will be kept in better conditions at the central pharmacy.

The treatment is in two phases – the initial phase for a minimum of 6 months and a continuation phase for a minimum of 18 months.

Standard treatment regimen for Category IV: 6 Km-Levo-Eto-Cs-Z/18 Levo-Eto-Cs-Z

Phase	Duration	Comments
Initial Phase (6 months) - Kanamycin (Km) - Levofloxacin (Levo) - Ethionamide (Eto) - Cycloserine (Cs) - Pyrazinamide	Minimum of 6 months and until sputum smears and cultures are negative	• Directly observation of treatment should be applied • Close monitoring for side effects • At least five drugs • Includes at least one injectable drug
Continuation Phase (18 months) - Levofloxacin - Ethionamide	Minimum of 18 months	• Less side effects • Usually oral drugs

- Cycloserine - Pyrazinamide		

It is **strongly recommended** that all MDR TB patients **must** be put on this standard regimen as the first choice. However, in special cases the regimen can be selected after consulting the detailed results of susceptibility testing **(individualized regimen).**

Individualized treatment regimen for category IV

To adjust category IV regimen according to drug susceptibility testing (DST) results the following general principles must apply:

1. Include at least 5 drugs
2. Include any first-line drug to which the strain is susceptible
3. Include an injectable for prolonged period (until smear and/or culture conversion)
4. Include a quinolone
5. Consider drug resistance data (of individual) and patient treatment history when designing the regimen.

However, designing an appropriate regimen needs experience and skill. It is necessary to summarize previous treatment(s), drug susceptibility results, adherence history, clinical course and adverse reactions to drugs used previously. It is therefore strongly recommended that this approach should only be done by specialized physicians with the appropriate expertise, who in turn will make recommendations to the MDR TB Subcommittee.

Table: Suggested regimens for mono- and poly-drug resistance (when further acquired resistance is not a factor and laboratory results are highly reliable)

DRUG RESISTANCE PATTERN	SUGGESTED REGIMEN	TREATMENT DURATION (months)	COMMENTS
E (± S)	H, R, Z	6	
H (± S)	R, Z, E	6–9	A fluoroquinolone may strengthen the regimen for patients with extensive disease
H and Z	R, E, Fluoroquinolones	9–12	A longer duration of treatment should be used for patients with extensive disease
H and E	R, Z and Fluoroquinolones	9–12	A longer duration of treatment should be used for patients with extensive disease
R	H, E, Fluoroquinolones + at least 2 months of Z	12–18	An injectable agent may strengthen the regimen for patients with extensive disease
R and E (± S)	H, Z, Fluoroquinolones + injectable agent for at least the first 2-3 months	18	A longer course (6 months) of an injectable agent may strengthen the regimen for patients with extensive disease *or Refer to specialist physician if there is resistance to S
R and Z (± S)	H, E, Fluoroquinolones + injectable agent for at least the first 2-3 months	18	A longer course (6 months) of an injectable agent may strengthen the regimen for patients with extensive disease *or Refer to specialist physician if there is resistance to S
H, E, Z (± S)	R, Fluoroquinolones + oral second-line agent + injectable agent for the first 2-3 months	18	Patient needs referral to specialist physician

Adapted from Drug-resistant tuberculosis: a survival guide for clinicians

Note: It is <u>strongly recommended</u> that when first line drugs are used they must be given in <u>maximum dosages</u>.

Follow-up:

Discontinuation of the parenteral agent (Kanamycin)

The decision to stop the parenteral agent should be made upon:

- Review of the cultures, smear, X-rays and clinical status of the patient.
- Patient completing a minimum of six months of documented smear or culture negativity.
- There being four remaining drugs to which the isolate has documented sensitivity.

Recurrence/persistence of positive culture after four months of treatment

- In most cases culture conversion occurs between months two and four of the MDR TB treatment.
- DST results should be compared to determine if the newly positive culture has the same susceptibility pattern as the initial strain or whether amplification of the resistance pattern has occurred.
- Re-appearance of single or multiple positive smears or cultures should be considered as possible evidence for treatment failure, and all such cases must be evaluated for the possibility of changing therapy.

Treatment support

All patients should be hospitalized at the MDR TB treatment facility in the initial phase until the sputum/culture converts to negative. The continuation phase should be provided on out-patient basis; review visits should be conducted at least every second month at designated health facilities.

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Direct Observation of Therapy (DOT):

All doses of MDR TB medicines will be directly observed. The choice of DOT provider should be agreed with the patient and or his/her family before discharge. The DOT provider during the continuation phase may be a health care worker, a workmate, a family member or a community volunteer but they make every effort to accord the patient respect and dignity and maintain confidentiality. The continuation phase of treatment must be continued until the patient is declared cured, or treatment completed, according to the definitions

All patients **must** be assigned an observer (community health worker) when receiving out patient care. It is recommended that the observer:

- Is chosen by/or acceptable to the patient
- Is committed to support the patient for a long time
- Should receive MDR TB specific training
- Should be trained in the recognition of side effects and report serious ones to the health facility
- Is available to observe the patient taking medication
- Is available to accompany patients to clinic and lab appointments

Note: CHWs, nurses and doctors should all be part of a united team that takes care of the patients on clinical aspects, but also in other issues that may affect the adherence to treatment.

MDR TB patients should be monitored closely for adverse drug effects and appropriate actions should be taken at once. As far as possible, all necessary patient and family support should be put in place to increase adherence to treatment. These may include patient support groups, psychological counseling, transportation, subsidy, food baskets etc. All MDR TB patients, their families and communities health education, including stigma reduction.

All the doses for second line should be observed by the health care worker and confirmed as swallowed on a weekly basis.

Treatment delivery and adherence

Treatment of MDR TB should aim to ensure maximum adherence. The prevention of non–adherence and default from treatment will be emphasized as it's more important than default retrieval measures. It is important to understand that many patients with MDR TB may have been non adherent to previous treatment and could become non-adherent to current treatment if not strongly supported. To prevent non adherence and default from treatment the following measures are essential:

Education of patients

All patients with MDR TB and their families should receive education about MDRTB, its treatment, potential adverse drug effects and the need for adherence to treatment from start of treatment and reinforced throughout the period of treatment. This can be done by health care workers (clinicians, nurses), lay health care workers, community health care workers and current or former TB patients. Interpersonal Communication (IPC), the most effective way of communication, should be used to educate patients and their families complimented with use of IEC including pamphlets and brochures in various languages.

Assessment for risk factors for non–adherence

All patients started on treatment will be assessed for their risk factors for non – adherence.

Referral and community-based DOT for a patient with MDR

All patients after completion of the initial phase will be linked or referred to a community based DOT programme within the National TB Control Programme.

Default Retrieval

All patients started on MDR TB treatment will be linked to a network of the treatment facility, community based DOT programme and members of the family. Contact details will be kept by all involved in the treatment of the patient and regular contact with the patient maintained to follow up on progress and ensure the patient does not default. In the unlikely event that a patient defaults, all necessary measure will be taken to ensure that the patient is traced and retrieved. Upon retrieval and assessment for treatment the patient will be admitted for treatment for the duration of treatment in line with the Public Health act as regards communicable diseases.

CRITERIA AND ALGORITHM FOR REINITIATING THERAPY AFTER DEFAULT

Length of treatment received prior to abandoning therapy	Result of last culture prior to abandoning therapy OR result of smear upon return to therapy	Action
Less than 3 Months	Positive or Negative	All patients with less than three months of treatment are restarted on a new course of treatment using their previous DST
Between 3 and 12 Months	Positive	Restart treatment and send for DST. Adjust regimen when DST arrives. (If patient was a suspected failure at time of abandonment, consider designing a new regimen instead of restarting original regimen.)
	Negative	Restart patient with the injectable until two cultures return. All patients in this category should get a minimum of 24 months therapy total past initial conversion.
Greater than 12 months	Positive	Send for DST and start a completely new course of treatment.
	Negative	If the patient was off the injectable at the time of the interruption and has no evidence of clinical deterioration, then all oral medications can be restarted without restarting the injectable.

Completion of therapy

The full treatment course is a minimum of 24 months of regular supervision and monitoring.

Follow up after completion of therapy

- The follow-up visits should assess symptoms and signs of relapse.
- Smear and culture must be performed every three months for a year.
- Clinical and radiographic evaluation should be done as needed for assessment of respiratory symptoms.
- All co-infected HIV patients should have regular periodic TB screening
- Ancillary medicines such as bronchodilators should be continued in patients after tuberculosis therapy is completed if needed.

CHAPTER 5

SIDE EFFECTS

Management of side effects

ADVERSE REACTION	SUSPECTED DRUG	MANAGEMENT
Hepatitis	Z, H, R, Of, L, Cx, PAS	1) Stop therapy 2) Rule out other potential causes of hepatitis 3) Re-introduce drugs grouped serially while monitoring liver function, with most likely agent introduced last
Renal failure	S, Km, Am, Cm	1) Discontinue suspected agent 2) Consider using Cm if an amino-glycoside had been prior parenteral in regimen
Arthralgias	Z, Of, L, Cx	1) Therapy with non-steroidal anti-inflammatory drugs 2) Initiate exercise regimen 3) Lower dose of suspected agent, if this can be done without compromising regimen 4) Discontinue suspected agent if this can be done without compromising regimen
Gastritis	PAS, H, E, Cfz, Z	1) Antacids (e.g. calcium carbonate, H2-blockers, proton-pump isoniazid ibitors) (antacids should preferably not be taken at the same time as TB drugs as they may impair absorption) 2) Hold suspected agent(s) for short periods of time (e.g. one to seven days) 3) Lower dose of suspected agent, if this can be done without compromising regimen 4) Discontinue suspected agent if this can be done without compromising regimen
Nausea and vomiting[1]	PAS, H, E, Cfz, Z	1) Rehydration 2) Initiate anti-emetic therapy 3) Lower dose of suspected agent, if this can be done without compromising regimen 4) Discontinue suspected agent if this can be done without compromising regimen
Seizures[2]	Cs, H, Of, L, Cx	1) Initiate anti-convulsant therapy (e.g. phenytoin, valproic acid) 2) Increase pyridoxine to 300mg daily 3) Lower dose of suspected agent, if this can be done without compromising regimen 4) Discontinue suspected agent if this can be done without compromising regimen
Peripheral Neuropathy[3]	S, Km, Am, Cm, M, Cs, E, Of, L, Cx	1) Increase pyridoxine to 300mg daily 2) Change parenteral to Cm if patient has documented susceptibility Cm 3) Begin exercise regimen, focusing on affected regions 4) Initiate therapy with tricyclic anti-depressant drugs 5) Lower dose of suspected agent, if this can be done without compromising regimen 6) Discontinue suspected agent if this can be done without compromising regimen 7) Initiate therapy with neurontin
Hearing loss	S, Km, Am, Cm, Clr	1) Change parenteral to Cm if patient has documented susceptibility Cm 2) Lower dose of suspected agent, if this can be done without compromising regimen 3) Discontinue suspected agent if this can be done without compromising regimen

Psychotic symptoms4	Cs, Of, L, Cx, H	1) Initiate anti-psychotic drugs 2) Hold suspected agent for short period of time (one to four weeks) while psychotic symptoms brought under control 3) Lower dose of suspected agent, if this can be done without compromising regimen 4) Discontinue suspected agent if this can be done without compromising regimen
Depression5	Cs, Of, L, Cx, H	1) Group or individual supportive counselling 2) Initiate anti-depressant drugs 3) Lower dose of suspected agent, if this can be done without compromising regimen 4) Discontinue suspected agent if this can be done without compromising regimen
Hypothyroidism	PAS, Tha, especially when given in combination	1) Initiate thyroxine therapy 2) Substitute equally efficacious agent for Tha or PAS Comments - Completely reversible upon discontinuation of PAS or Tha

Comments on some side effects

[1]Nausea and vomiting common in early weeks of therapy and usually abate with supportive therapy; Electrolytes should be monitored and replaced if vomiting severe; Reversible upon discontinuation of suspected agent

[2]Anti-convulsant is generally continued until MDR-TB treatment completed or suspected agent discontinued; History of prior seizure disorder is not a contraindication to the use of agents listed here if patient's seizures are well controlled and/or patient is receiving anti-convulsant therapy; Patients with history of prior seizures may be at increased risk for development of seizures during MDR-TB therapy; Seizures not a permanent squealer of MDRTB treatment Seizures

[3]Patients with co-morbid disease (e.g. diabetes, HIV, alcoholism) may be more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here; Neuropathy is generally not reversible, although only a minority (approximately 10%) of patients require continued intervention to keep symptoms controlled once MDR-TB treatment completed

4Some patients will need to continue anti-psychotic treatment throughout MDR-TB therapy; Prior history of psychiatric disease is not a contraindication to the use of agents listed here but may increase the likelihood of development of psychotic symptoms; Psychotic symptoms generally reversible upon MDR-TB treatment completion or discontinuation of offending agent

5Importance of socio-economic conditions should not be underestimated as contributing factor to depression; Depression and depressive symptoms may fluctuate during therapy; History of prior depression is not a contraindication to the use of the agents listed here; however, these patients may be at increased risk for developing depression during MDR-TB treatment

CHAPTER 6

Information systems and data management

Recording and reporting system

Aims of the information system

The aims of the information system are two fold:

1. To allow managers of national TB control programmes at different levels to monitor overall programme performance as a basis for programme and policy developments. Performance indicators include:

    - The outcome of patients with drug-resistant TB, including MDR-TB,
    - The results of Category IV treatment, and in the subgroups.

2. To aid staff in treatment facilities to provide adequate management of individual patients.

The information system for treatment of drug-resistant TB is based upon, and is an extension of, the basic DOTS information system (1–4). The forms have therefore been designed to be as similar as possible to the standard forms used in DOTS programmes. The records for all individual patients should be kept and filed according to the requirements of standard NTP in the following formats:

a) MDR TB Suspect Register
b) MDR TB Laboratory Request Form for Microscopy
c) MDR TB Laboratory Request Form for Culture and Drug susceptibility testing
d) MDR Laboratory Register for Microscopy
e) MDR Laboratory Register for Culture and Drug susceptibility testing
f) MDR TB Patient Identity Card
g) MDR TB Treatment Card
h) MDR Health Facility TB Register
i) MDR TB Transfer Form
j) Quarterly Report on MDR TB Case Registration
k) Quarterly Order Form For MDR TB Drugs at Health Facility
l) Quarterly Report On MDR TB/HIV Activities
m) Quarterly Report On MDR TB Outcomes

ANNEXES

ANNEX 1. GROUPING OF ANTI TB DRUGS USED FOR MDR TB TREATMENT

Group 1: Oral first-line agents (HREZ)

- **All first line drugs to which patient's isolate is sensitive will be used**

  First line agents should be used whenever possible, since they are more powerful and better tolerated than second-line drugs. They should be used at maximum doses (25 mg/kg for Ethambutol and 30 mg/kg for Pyrazinamide).

Group 2: Injectables(Sm, Km, Cm)

- **All patients should be given an injectable agent until their bacillary burden is demonstrably lower (defined as 6 months of documented negative smear and/or cultures)**

The history of previous treatment, drug susceptibility data, relative efficacy and cross-resistance between parenteral drugs will influence the choice of parenteral therapy. A number of factors will be considered in the choice of injectable:

- The Injectables should be used in a hierarchy based on efficacy, side effects, and cost. If susceptible, streptomycin is the usual injectable of choice. If resistant to streptomycin then kanamycin or capreomycin should be used.
- If creatinine clearance is significantly reduced, the dose of the drug should be adjusted.
- If patient is diabetic or has renal failure, capreomycin should be always the option

Group 3: Quinolones (Cpx, Ofx, Lfx, Moxi, Gati)

- **All patients sensitive to this class of drugs should receive a quinolone.**

Because it is the only class of second-line drugs that is oral and bactericidal, whenever possible, a Fluoroquinolones (FQ) should be included in the regimen. Due to economic and dosing considerations the initial choice of a Fluoroquinolones (FQ) will be Ofloxacin. If DST to FQ shows resistance then should be considered the use of Moxifloxacin.

Group 4: Other second-line drugs (Ethio, Prothio, Cs, PAS, Terizidone)

- **These second-line drugs have a long history of use in the treatment of MDR-TB but are bacteriostatic and not as well tolerated as first-line drugs and quinolones.**

One or more of these agents should be added to MDR-TB regimens based on efficacy, tolerability, resistance pattern and cost. Ethionamide is the most widely available and often the first of these agents added. Cycloserine is a potent and proven anti-tuberculosis drug but with neuropsychiatric side-effects which, though manageable, need careful monitoring. Terizidone is an early generation of CS and is felt to have fewer side effects. In any of this option, Piridoxine should be added in order to reduce side effects. PAS has shown to be a poorly tolerated drug, regardless of its presentation and is costly. However if need it, should be added last due to these factors.

Group 5: Possible reinforcing agents (High dose INH, Amx/Clv, Clofazimine, clarithromycin, thiazetazone)

- **Drugs in group five have come in vitro data or animal data but scant clinical data supporting their use for the treatment of MDR-TB**

If there are sufficient number of standard anti-tuberculosis drugs to constitute a five-drug regimen to which a patient is sensitive, the use of additional drugs should not be considered. However, in clinically advanced cases or in cases with suspected or confirmed high-grade drug resistance, reinforcement of the regimen should be done with agents from this group. High dose INH (900 mg twice a week) can be used if the strain demonstrates in vitro susceptibility to it.

ANNEX 2.

Weight-based dosing of anti- TB drugs for adults

The drugs in the table are divided into four categories based on drug efficacy and drug properties (or drug classes)

GROUP 1: INJECTABLE ANTI-TB DRUGS

Drug	<33kg	33-50kg	51-70kg	>70kg
Streptomycin (S) 1 g vial	15-20mg/kg daily	500-750mg	1000mg	1000mg
Kanamycin (Km) 1 g vial	15-20mg/kg daily	500-750mg	1000mg	1000mg
Amikacin (Am) 1 g vial	15-20mg/kg daily	500-750mg	1000mg	1000mg
Capreomycin (Cm) 1 g vial	15-20mg/kg daily	500-750mg	1000mg	1000mg

GROUP 2: FLUOROQUINOLONES

Drug	<33kg	33-50	51-70	>70
Ofloxacin (Ofx) (200, 300,400mg)	15-20mg/kg daily	800mg	800mg	800-1000mg
Levofloxacin (Lfx) (250, 500mg)	7.5-10mg/kg daily	750mg	750mg	750-1000mg
Moxifloxacin (Mfx) (400mg)	7.5-10mg/kg daily	400mg	400mg	400mg

GROUP 3: ORAL BACTERIOSTATIC SECOND LINE ANTI-TB DRUGS

Drug	<33kg	33-50	51-70	>70
Ethionamide (Eto) (250mg)	15-20mg/kg daily	500mg	750mg	750-1000mg
Protionamide (Pto) (250mg)	15-20mg/kg daily	500mg	750mg	750-1000mg
Cycloserine (Cs) (250mg)	15-20mg/kg daily	500mg	750mg	750-1000mg
Terizidone (Trd) (300mg)	15-20mg/kg daily	600mg	600mg	900mg
P-aminosalicylic acis (PAS) (4 g sachets)	150mg/kg daily	8g	8g	8-12g

Paediatric dosing of second line anti-TB drugs

Drug	Daily dose (mg/kg)	Frequency	Maximum daily dose
Streptomycin	20-40	once daily	1 g
Kanamycin	15-30	once daily	1 g
Amikacin	15-22.5	once daily	1 g
Capreomycin	15-30	once daily	1 g
Ofloxacin	15-20	twice daily	800mg
Levofloxacin	7.5-10	once daily	750mg
Moxifloxacin	7.5-10	once daily	400mg
Ethionamide	15-20	twice daily	1g
Protionamide	15-20	twice daily	1g
Cycloserine	10-20	once or twice daily	1g
P-aminosalicylic acid	150	once or twice daily	12g

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Patient Identity Card

Name: _____

Address (in full): _____

_____

_____

_____

Sex: ☐ M ☐ F Date of birth: / /

District TB unit: _____

Health unit: _____

Disease classification	**Date treatment**
Pulmonary ☐ Extrapulmonary ☐ Site……	Day Month Year

Type of patient

New	☐	Treatment after default	☐
Transfer in	☐	Relapse	☐
Treatment after failure	☐	Other (specify)	☐

Treatment Category **I** **II** **III** **IV**

Initial treatment
Change in treatment

Allergies: _____

Severe adverse reaction: _____

_____

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Appointment dates

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

REMEMBER

1. Take care of your card.
2. You can be cured if you follow your treatment regimen by taking your prescribed drugs regularly.
3. Tuberculosis can spread to other people if you do not take your medication.

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Category IV Treatment Card

Name: _____

Category IV registration number: _____

Date of Category IV registration: ____/____/____

District TB registration number: _____

Date of district TB registration: ____/____/____

Address: _____

District: _____

Treatment Centre: _____

Sex: ☐ M ☐ F

Age: _____ Date of birth: ____/____/____

Initial weight (kg): _____ Height (cm): _____

Site: ☐ Pulmonary ☐ Extrapulmonary ☐ Both

If extrapulmonary, specific site: _____

No.	Registration group	Select one only
1.	**New**	
2.	**Relapse**	
3.	**After default**	
4.	**After failure of first treatment**	
5.	**After failure of re-treatment**	
6.	***Transfer in*** (from another Category IV treatment site)	
7.	***Other*** (previously treated without known outcome status)	

HIV Information
HIV testing done ☐ Y ☐ N
Date of test: ____/____/____ Results
Started on ART: ☐ Y ☐ N Date: ___/____/____
Started on CPT: ☐ Y ☐ N Date: ___/____/____

Previous tuberculosis treatment

No.	Start date (if unknown put year)	Regimen (write regimen in drug abbreviations)	Outcome

Drug abbreviations

First-line drugs

H = Isoniazid
R = Rifampicin
E = Ethambutol
Z = Pyrazinamide
S = Streptomycin
(Th = Thiocetazone)

Second-line drugs

Am = Amikacin
Km = Kanamycin
Cm = Capreomycin
Cfx = Ciprofloxacin
Ofx = Ofloxacin
Lfx = Levofloxacin
Mfx = Moxifloxacin
Gfx = Gatifloxacin
Pto = Protionamide
Eto = Ethionamide
Cs = Cycloserine
PAS = p-aminosalicylic acid

Review panel meetings: dates and decisions

Date	Decision	Next date

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Patient name: _____

Month #	Sputum smear microscopy		
	Date *	Sample No.	Result
Prior**			
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			
11.			
12.			
13.			
14.			
15.			
16.			
17.			
18.			
19.			
20.			
21.			
22.			
23.			
24.			

Month #	Culture		
	Date *	Sample No.	Result
Prior**			
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			
11.			
12.			
13.			
14.			
15.			
16.			
17.			
18.			
19.			
20.			
21.			
22.			
23.			
24.			

Notes:

* All dates in the tables that report smears, culture and DST are dates the specimen was collected from the patient

** The date the sputum was collected led to the patient being registered with MDR-TB (if performed)

Notation method for recording smears (for non-centrifuged specimens)

No. AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation method for recording

Notation method for DST

R = resistant
S = susceptible
C = contaminated

Drug susceptibility testing (DST) results

Date*	S	H	R	E	Z	Km	Am	Cm	Fq	Pto/Eto	PAS	Cs	Other	Other

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Patient name: _____

CATEGORY IV REGIMEN *(date treatment started and dosage (mg), change of dosage, cessation of drugs):*

Date*	S	H	R	E	Z	Km	Am	Cm	Fq	Pto/Eto	PAS	Cs	Other	Comments

Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	**Weight (kg). Lab, X-ray**

Administration of Drugs (one line per month)

Mark in the boxes: **O** = directly observed
N = not supervised
Ø = drugs not taken

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Patient name: _____

Administration of Drugs (one line per month)

Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Weight (kg). Lab, X-ray

Mark in the boxes: **O** = directly observed
N = not supervised
Ø = drugs not taken

Comments _____
_____
_____
_____
_____
_____

Outcome	Mark one	Date
Cured		
Completed		
Died		
Failed		
Defaulted		
Transferred out		

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Category IV Register

Unique Cat.IV Register No.	Date entered in Cat. IV Register	Names (in full)	Sex M/F	Age Date of birth D/m/y	Address	District TB Register number /Date of Registration	Site of disease (P/EP)	Registration group*	**Result of drug susceptibility testing (DST)** **(Enter the DST that resulted in the patient being registered as a Category IV patient; if the DST is pending it should be filled in when the results are known. See treatment card for full history or DST data)** R = resistant S = susceptible C = contaminated											Date sample taken for DST	Second line drugs already received
									R	H	E	S	Km	Cm	Fq	Pto/Eto	Other	Other	Other		
1.																					
				/ /																	
2.																					
				/ /																	
3.																					
				/ /																	
4.																					
				/ /																	
5.																					
				/ /																	
6.																					
				/ /																	
7.																					
				/ /																	
8.																					
				/ /																	
9.																					
				/ /																	
10.																					
				/ /																	

* 1 New
2 Relapse
3 After default
4 After failure of first treatment
5 After failure of re-treatment
6 Transfer in (from another Category IV treatment site)
7 Other

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Smear (S) and culture (C) results during treatment

(if more than one smear or culture done in a month, enter the most recent positive result

Reasons for entering in Category IV Register		**Category IV treatment**	Start of treatment month 0		Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7		Month 8		Month 9		Month 10		Month 11		Month 12		Month 13		Month 14	
MDR-TB documented	MDR-TB suspected (determined by country protocol)	**Regimen (in drug initials) Date started**	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C
			d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y	
		Date	/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /	
		Date	/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /		/ /	
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ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Month 16		Month 17		Month 18		Month 19		Month 20		Month 21		Month 22		Month 23		Month 24		Month 25		Month 26		Month 27		Month 28		Month 29		Month 30		Month 31		Month 32		Month 33		Month 34	
S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C
d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y		d/m/y	
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ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Outcome Cured Completed Failed Died Defaulted Transferred out	***TB/HIV activities***					**Comments**
Date outcome given	HIV testing			ART Y/N Start date	CPT Y/N Start date	
	Testing done (Y/N/unknown)	Date of test	Result			
/ /						
/ /						
/ /						
/ /						
/						
/ /						
/ /						
/ /						
/ /						
/ /						

Notation method for recording smears (for non-centrifuged specimens)

No. AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation method for recording cultures

No growth reported	0
Fewer than 10 colonies	Report number of colonies
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++

Drug abbreviations

First-line drugs	**Second line drugs**
H = Isoniazid	Am = Amikacin
R = Rifampicin	Km = Kanamycin
E = Ethambutol	Cm = Capreomycin
Z = Pyrazinamide	Cfx = Ciproflaxin
S = Streptomycin	Ofx = Ofloxacin
(Th = Thiocetazone)	Lfx = Levofloxacin
	Mfx = Moxifloxacin
	Gfx = Gatifloxacin
	Pto = Protionamide
	Eto = Ethionamide
	Cs = Cycloserine
	PAS = *P*-aminosalicylic acid

ZAMBIA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAM

Quarterly report on Category IV case registration

Name of District: _____

District No: _____

Name of district coordinator: _____

Signature: _____

Patients registered in the Category IV Register during _____ quarter of year _____

Date of completing this form: _____

Block 1: Patients registered in Category IV treatment

Patients	Confirmed MDR-TB	Suspected MDR-TB
Registered in category IV diagnostic group		
Started on Category IV Treatment during The quarter		

Block 2: Confirmed MDR-TB cases registered during the quarter

Pulmonary							
New	Previously treated				New extrapulmonary	Other*	Total
	Relapse	After default	After failure of Category I treatment	After failure of Category II treatment			

*** Other cases include previously treated pulmonary patients without known outcome status, and all previously treated extrapulmonary TB patients**