# Standard Operating Procedures for Management of Early Termination (withdrawal and treatment discontinuation)

|  |  |
| --- | --- |
| **SOP Number**: SP-028-CT | **Effective Date**: |
| **Version Number and Authorization Date**: 3.0 , 19-Jul-2021 | |

**Table of contents**

[1. PURPOSE 2](#_Toc166246380)

[2. SCOPE 2](#_Toc166246381)

[3. RESPONSIBLE FUNCTIONS 2](#_Toc166246382)

[4. DEFINITIONS and ABBREVIATIONS 2](#_Toc166246383)

[5. PROCEDURE 4](#_Toc166246384)

[5.1 Identification of patients who terminate early the study 4](#_Toc166246385)

[5.2 Management of early termination 4](#_Toc166246386)

[6. REFERENCES 4](#_Toc166246387)

[7. SUPPORTING DOCUMENTS 4](#_Toc166246388)

[8. APPENDIX 4](#_Toc166246389)

# Standard Operating Procedures for Management of Early Termination (withdrawal and treatment discontinuation)

## PURPOSE

|  |
| --- |
| This standard operating procedure (SOP) describes the procedures for the management of patients who terminate the study early due to study withdrawal or permanent study treatment discontinuation. |

## SCOPE

|  |
| --- |
| This SOP is developed for trained healthcare workers in charge of the follow-up of participants enrolled in the endTB clinical trials. |

## RESPONSIBLE FUNCTIONS

|  |  |
| --- | --- |
| **Function** | **Activities** |
| Site Principal Investigator (Site PI) or delegated site clinician | * Identifies patients who meet the criteria for early termination of the study * Manages the termination of the patient’s participation in the study |
| Clinical Advisory Committee (CAC) | * Provides advice regarding the indication to discontinue the treatment * Recommends a non-study treatment for patients who have been discontinued from their study assigned treatment |

## DEFINITIONS and ABBREVIATIONS

**Early termination:** Early termination is the stop of study participation before its planned ending (before or after study treatment completion). Early termination includes both study withdrawal and treatment discontinuation.

**Study withdrawal:**

A participant will be withdrawn from the study if:

* Patient’s initial *M. tuberculosis* strain is determined by confirmatory resistance testing to be resistant to fluoroquinolone (late exclusion; endTB trial only); or
* Patient withdraws consent to participate to the study; or
* Study treatment is permanently discontinued (see below); or
* Patient starts a new anti-TB treatment.

**Permanent study treatment discontinuation:**

A permanent study treatment discontinuation is defined as follows:

* In the experimental arm and in the control arm (shortened regimen):
* permanent discontinuation of two or more investigational drugs; or
* addition or replacement of one or more investigational drugs.
* In the control arm (conventional regimen), addition or replacement of two or more drugs.

Permanent discontinuation of investigational drug(s) or regimen is strongly advised if any of the following occurs:

* An enrolled patient becomes pregnant or begins breastfeeding an infant, and has other treatment options with reasonable chance of success;
* The patient requests to stop study treatment.

Permanent discontinuation of investigational drug(s) or regimen may be considered on a case-by-case basis, in consultation with the Clinical Advisory Committee in the following circumstances:

* Requirement for prohibited concomitant medications;
* Any condition (social or medical) which, in the opinion of the site Principal Investigator, would make study participant unsafe;
* Indications of treatment failure including positive culture at Week 16 or later.

**Suspensions and changes not to be considered for permanent discontinuation assessment:**

For all arms and regimens, modification of dose or frequency or temporary suspension of one or more investigational drugs.

For control arm regimens (conventional and shortened), changes within a drug class (i.e., replacing one member of the fluoroquinolone or thioamide class with another member of the same class).

For control arm (conventional regimen), addition or replacement of two or more drugs to the control arm in order to conform to new WHO guidance—rather than in response to emerging participant safety or efficacy data—might be accepted without qualifying as treatment discontinuation/study withdrawal. This will be assessed on a case-by-case basis by the Clinical Advisory Committee.

NOTE: any permanent treatment change requires advice from the Clinical Advisory Committee.

**Clinical Advisory Committee (CAC):** The CAC serves as an advisory body to endTB site investigators by providing consultation regarding subject eligibility, case management, medical monitoring, and permanent treatment discontinuation.

## PROCEDURE

### Identification of patients who terminate early the study

**The Site PI or delegated site clinician** identifies patients who meet one or more criteria for early study termination, according to the endTB and endTB-Q clinical trials protocols. **Any early study termination should be managed under the supervision of the Site PI.**

### Management of early termination

**The Site PI or delegated site clinician** will manage the patient’s early termination of the study as follows:

* Encourage the patient to undergo an early termination visit. Early termination visit will include tests and procedures as specified in endTB and endTB-Q clinical trials protocols (Protocols - Section 7.4):
* In addition, any patient whose participation is terminated prior to Week 73 (except if due to late exclusion, see above) will be encouraged to complete post-termination follow-up visit(s) (Protocols Section 7.5);
* For patients who did not complete their treatment in the trial, request advice from the CAC on the best subsequent treatment regimen (see ***SOP SP-024-CT Modus Operandi and Communication with CAC***);
  + Refer the patient to the national tuberculosis program for the initiation of a non-study regimen with the guidance given by the **CAC** about optimal subsequent treatment regimen and a referral letter describing the patient’s clinical history, treatment received within the trial, response and tolerability;
* Patients will be followed for safety as described in Protocols - Section 9.6;
* Patients who withdraw consent for further participation prior to completion of the study will not undergo any further study procedures or data collection. In such cases, data collected prior to withdrawal of consent will be kept and analyzed with complete data sets as is appropriate, unless the patient requests otherwise.

## REFERENCES

None

## SUPPORTING DOCUMENTS

* SOP SP-024-CT Modus Operandi and Communication with CAC (endTB Site Study Documents)

## APPENDIX

|  |  |
| --- | --- |
| **Number** | **Title** |
|  | Nil |