End of Treatment

Title	**End of treatment**
SOP Code	2R2 SOP06_25Nov2019
Effective Date	

1.0 Objective

The objective of this standard operating procedure (SOP) is to ensure judgement of, and recording of end of treatment outcomes after the study participant stopped the study medication.

The SOP will ensure:

- these actions are in compliance with the standards of Good Clinical Practice
- the safety and protection of study participant
- the quality of the data produced by the study

2.0 Persons affected

This SOP concerns the site principal investigators (and their respective research teams) involved in conducting research with human subjects for the study entitled - *Higher dose Rifampin for 2 months vs Standard dose Rifampin for Latent TB: a 3-arm randomized trial.*

3.0 Responsibilities.

The trial coordinating center is responsible for developing and maintaining this SOP and for making it available at the clinical research site. At the clinical trial site, the site principal investigator is responsible for adoption of the processes described in this SOP.

4.0 Definition(s) and abbreviations

Adverse Event (AE): Adverse event as defined in SOP09_Managment and report of Adverse events.

Coordinating centre: research staff involved in running the $2R^2$ study who are based at Research Institute of McGill University Health Centre (RI-MUHC)

Case Report Form (CRF): A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the Sponsor on each trial participant in a clinical research study.

ICH International council for harmonisation of technical requirements for pharmaceuticals for human use. Section E of the ICH are the reference for good clinical practice (GCP) used in the trial's SOPs.

INH: Isoniazid.

IRB: Institutional Review Board

5.0 Procedures

General information

The END OF TREATMENT FORM (CRF-6) must be filled out for each study participant who is randomized, once study medication has been stopped permanently. This can be because treatment was completed, as specified in the protocol, or if treatment was stopped early, for any reason (adverse event, participant's decision, death, occurrence of active TB, etc). In case of adverse event remind to complete CRF9 and CRF10 and in case of active TB, complete CRF11

and CRF12. Please refer to SOP09 for Adverse Event reporting and to SOP08 for Active TB reporting.

5.1. Reasons for stopping the study medication

5.1.1 "Study participant completed therapy" means participant completed therapy (i.e. took 60 daily doses for the 2-month high dose regimens and 120 daily doses within 144 days for the standard regimen)

5.1.2 "Study medication stopped due to an adverse event": this answer is chosen if study medication has been permanently stopped due to an adverse event. If study medication has been held temporarily due to a possible adverse event complete End of Treatment form CRF6 only when it is clear that the medication will not be restarted but rather is stopped permanently. Please refer to "**SOP09** Adverse event management and reporting", for guidance on how to report adverse events.

5.1.3."Study participant decided to stop therapy (participant's decision)": this answer is chosen if study participants who have started the medication made their own decision to stop taking the treatment . The treating team should discuss with the participant possible alternatives (other LTBI treatment, or follow-up). If the participant decides to take an alternative LTBI treatment, this still means the study medication is stopped. Specify that alternative treatment has been started in section **"**T5.General comments "of CRF6

Note: do not choose this option for study participants who never came back to any follow-up visits (see below).

5.1.4 " Treating team decided it was futile to continue (patient non-compliance)" : this answer is chosen if treating team or research team decided that it is futile to continue study medication as the study participant has demonstrated very poor compliance with treatment and follow-up visits. It is for situations in which it is not the study participant who decides to stop but the medical staff.

5.1.5. "Participant started a new drug, which has potential drug interaction" : this answer is chosen if a new medication was prescribed to the study participant and there is new potential drug interaction which the treating team feels is not manageable. In this case, REPORT also an INITIAL Adverse Event (CRF 9), refer to **SOP09** for guidance on AE reporting.

5.1.6 "Study participant has decided to withdraw COMPLETELY from study". This answer is chosen if someone actively requests to be removed from the study. This is not the same as someone who has decided to no longer take study medication but is willing to be followed post treatment or has been lost to follow-up. This is generally considered an indication that the consent procedure was not adequate. The coordinating centre will receive an automatic notification. All withdrawals must be notified to the IRB of the coordinating center. In case of withdrawals, the coordinating centre will contact the site to learn more about this event.

5.1.7 "Pregnancy": If study participant became pregnant during the treatment, HCG blood test must be done to document pregnancy and Adverse event initial report (CRF-9) should be completed. Please refer to **SOP09** for guidance on AE reporting.

5.1.8 "Active TB suspected": If active TB treatment is initiated, the study medication is considered permanently stopped and this option " Active TB suspected" can be chosen. If study participant is suspected to have active TB, an active TB initial evaluation form (CRF-11) need to be completed. Please refer to **SOP08** _Active TB reporting for guidance on how to complete CRF-11.

5.1.9 "**Study participant has died" :** if study participant died during the treatment, an adverse event initial evaluation form (CRF-9) must be completed- refer to SOP9 for guidance on AE reporting.

5.1.10 "Study participant never started treatment": This is the case of participants who never came back and, when called, they confirmed they never took any study drug; or of participants who came back for a visit and said they never took any study drug and do not want to start study treatment. Treating team needs to discuss with these participants alternative treatments (as INH) and follow-up. If an alternative treatment is given for LTBI, report it in the answer *T5.General comment* in CRF6.

5.1.11."Study participant never came back after randomization, but reported by phone they took some treatment". If participants never came back to the clinic, the research staff must verify whether participants started the treatment - defined as taking at least ONE dose. This will be used for the analysis of adverse events (to identify if they were 'exposed' to the study drug). If they report having taken at least one dose, please write the number of daily doses taken in *T2.For how many days the participant said he/she took treatment?* of CRF6. It is very important to contact participants who never came back, by telephone or in person, to find out if they took any doses of study drug (please refer to **SOP05**_"Follow-up during treatment" for guidance on how to deal with "no-show").

5.2. Date of Last dose taken

5.2.1. Record in CRF6, the date on which the participant took the study medication for the last time. If participant never started, do not fill this date. If you do not know the date because participant did not complete treatment yet, wait to complete this form. You can complete the form once you are sure participant has taken the last dose.

5.2.2. When the treating team does not require the study participant to come to the clinic at the end of treatment, and the last scheduled visit for 4R is at 14 weeks or 15 weeks, call participant just after the date the treatment was supposed to be completed and ask participant the exact date of the last dose intake. Fill out an End of Treatment form with the real date of last dose intake. Also, ask participant how many pills of study medication does he/she still have at home and report them in CRF5, specifying that this was not a visit at the clinic but participant was reached by phone.

5.2.3. If a study participant does not attend a SCHEDULED visit for the end of treatment (i.e. they were scheduled for a visit at 16 weeks for 4RIF and did not show-up), contact the participant by phone and try to schedule a visit. The last pill count should be done at that visit.
If not possible to schedule the visit: ask the participant when was the last drug intake and complete the End of Treatment form using that date. Also, ask the number of remaining pills at home and complete a Follow-up visit form CRF5, specifying that this was not a visit at the clinic but that participant was reached by phone.

NOTE: After treatment is permanently stopped, for any reasons, the follow-up post treatment starts. Please refer to **SOP07** "Follow-up post treatment" for instructions. Remind that, for 30 days following the end of treatment, adverse events still need to be reported as during treatment.

5.3. Data entering in $2R^2$ website

5.3.1. The end of treatment information must be entered into the study website in order for this information to be available to the Coordinating Centre. Log on to the website (http://2r2.crc.chus.qc.ca) and choose the participant's study ID number, then click on "End of treatment" on the left menu. (Note – after 20 minutes of inactivity users will be automatically logged off of the website). If unable to log on to the site, the Coordinating centre should be notified and the information should be entered into the website when it becomes available.

5.3.2. Enter the end of treatment information into the website and at the end of the section click on the "save" button at the bottom of the screen. The data will be saved and can be modified as required. The website will provide the estimated date of the first post treatment follow-up call. Record this information on the End of Treatment form. At any point during data entry you may exit this section by clicking on the left menu. It is advisable to always click on the "save" key prior to this in order to save any data that has been entered or modified.

5.3.3. To return to the end of treatment information to modify previously entered data, choose the participant's study ID number (Add/Select participants) and then click on "Select participant", then click on "CRF-6 End of treatment" on the left menu. Modify the appropriate information and click on the "save" button at the bottom of the screen. Note: once participant has completed the post-treatment follow-up (and CRF6 has been completed), it will not be possible anymore to modify CRF6.

6.0 References

INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE
E6(R2), Current Step 4, version dated 9 November 2016.

7.0. SOP Revision history

SOP code	Effective date	Summary of changes
SOP06_25Nov2019	25 November 2019	NA (original version)