Title	**Site Start-up & Running of Trial**
SOP Code	2R2 SOP01_18Sep2019
Effective Date	

Site Approval/Authorization to Adopt

Name, title and role of local personnel (typed or printed)*****	**Signature**	**Date dd/mon/yyyy**

**Note: name of person(s) involved in the approval to use process of the SOP at the site*

1.0 Purpose(s)

The objective of this standard operating procedure (SOP) is to ensure all study sites are properly prepared to begin and run the trial. The SOP focuses on the maintenance of essential documents which permit evaluation of the conduct of the trial and the quality of the data produced. These documents will demonstrate compliance with the standards of Good Clinical Practice and applicable regulatory requirements.

2.0 Scope: Persons/Areas affected

This SOP concerns the co-investigators (and their respective research teams) involved in conducting research with human subjects for the study entitled – 2R2 *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 qualified investigator is responsible for adoption of the processes described in the SOP.

4.0 Definition(s)

BUN: Blood Urea Nitrogen

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.

HCG: Human chorionic gonadotropin, blood test used as pregnancy test.

ICF: Informed consent form.

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.

IRB: Institutional Review Board

5.0 Procedures

5.1. Maintenance of Trial Master Files

Trial master files should be established at the beginning of the trial and maintained throughout the trial. All essential documents need to be printed on paper and kept in binders. No electronic versions are allowed (unless otherwise specified). The trial master files are to be organized in binders and cabinets, as suggested below.
If binder #1 (or binder #2) is not large enough to include all of the documents specified below, please add a sub-binder (for example binder 1.1; 1.2, 1.3 etc. for binder 1 and binder 2.1, 2.2, etc for binder 2). Please follow the order given below as it makes it easier to retrieve documents during monitoring visit or audits.

Binder 1 of Trial Master File for essential documents, should contain the following documents:

1. Revision history of protocol and amendment(s);
2. Original study protocol – Version 1 dated 07June 2018 and amendment: version 1 dated 18 September 2019;
3. Other protocol amendments, if applicable;
4. Information given to participants including:
   - original approved informed consent form (ICF) and amendments
   - any other written information provided to participants
5. Institutional Research Board (IRB) submissions and correspondence - from coordinating center;
6. Local IRB approvals – for the study, amendments (study protocol and information given to participants), interim/annual reviews, and final report;
7. Local IRB committee composition
8. Health Canada NOL (dated 04 July 2019) for Canadian sites, or permission from local regulatory authority (for Indonesia and Vietnam);
9. Site Qualified Investigator Undertaking (only for Canadian sites);
10. Clinical Trial Site Information form (only for Canadian sites);
11. Revision history of Case Report Forms (CRFs) and amendment(s);
12. Sample Case Report Forms for data collection and amendments;
13. Signature sheet/Task delegation log (see Appendix 1 for template and list of personnel who should sign this log).
14. Training log (for training done at site to personnel involved in the trial; see Appendix 2 for a template);
15. Monitoring reports: initiation visit, monitoring visits, trial close-out;
16. Audit certificate if applicable;
17. Relevant communications related to the handling of protocol violations, list of adverse event reporting, trial conduct, (i.e. minutes of meetings, emails etc).

Binder 2 of Trial Master File for essential documents, should contain the following documents:

1. Curriculum vitae (CV) & medical license of co-investigators listed in the Task delegation log (Note: sort the CV and medical licenses by alphabetical order and add a list of all CVs at the beginning of this folder);
2. Site laboratory certification or accreditation;
3. Normal lab values for: liver function tests, complete blood counts with differentials, haemoglobin, hematocrit, creatinine, BUN, HCG;
4. Good clinical practice: consolidated guidelines;
5. Inter-institutional Agreement (the contract) and Transfer of Funds Agreement and any amendments
6. Copy of site insurance, if applicable (note: this is for study sites outside of Canada).

Note: please update these documents as needed (for example, physicians' licence, etc).

Other documents that are considered to be essential documents, but are not included in the binders described above are listed below. These other documents have to kept separately from Binders 1 and 2 and in a locked cabinet.

Part I

1. Signed informed consent forms (refer to Screening, recruitment and randomization SOP02);

   Note: signed consent forms must be kept locked and separate from documents listed in part II below.
2. Participant identification code list (refer to Screening, recruitment and randomization SOP02). This list can be kept in electronic format if the file is kept locked with a password;
3. Participant enrollment log (refer to Screening, recruitment and randomization SOP2). This list can be kept in electronic format if the file is kept locked with a password.

Part II:

1. Original Case Report Forms (CRF) completed. Note that the original CRF must be kept in separate folder for each participant.
2. Participant screening log (please refer to Screening, recruitment and randomization SOP2. Note that, in this study the screening log is captured using CRF1) ;
3. Documentation of CRF corrections (refer to "Note to File" in Management of study data SOP)
4. Notification to coordinating centre of adverse events (refer to Adverse event management SOP9)
5. Notification to local IRB of unexpected serious adverse drug reactions and other safety information (Refer to Adverse event management SOP9)
6. Notification from coordinating centre of safety information (refer to Adverse event management SOP9)

5.2. Maintenance of Standard Operating Procedures (SOP)

A standard operating procedures binder (separate from Binder # 1 and #2 mentioned above) should be established at the beginning of the trial and maintained during the trial. This binder should include paper copies of all trial related SOPs.

5.3. Site Preparation

The following steps must be completed prior to starting the study at your site:

- 5.3.1. **Apply to Institutional Review Board** (IRB) (according to local IRB guidelines)
  - include the most recent version of the study protocol, informed consent form and the information cards that will be given to study participants at the end of the study;
  - modify the informed consent form to meet local IRB and language requirements, but keep changes to a minimum as substantial changes may require central IRB approval ;
  - contact the coordinating centre for assistance with the IRB review/requests if required
- 5.3.2. **Receive IRB approval**
  - once you have approval, send a copy of approval, informed consent form and certification of translations (if applicable) to the coordinating centre.
- 5.3.3. **Receive Institutional approval**
  - once you have approval from your institution to start the trial, send a copy of approval to coordinating centre.
- 5.3.4 **Inter-institutional agreement (contract) and Transfer of Funds Agreement**
  - review, sign and return to the coordinating centre.
- 5.3.5 **Training**
  - receive training from coordinating center on study protocol, case report forms, and
  - use of the trial website.
- 5.3.5 **Site start-up meeting**
  - hold a site start-up meeting to introduce the study to your centre and record the training given to all personnel who will participate in the trial in the trial training log.

5.4. Clinical Conduct of Trial

Clinical conduct of the trial will commence upon completion of site preparation and notification/approval from the coordinating centre. The trial can be broken down into five different aspects: (1) Screening, recruitment and randomization; (2) Follow-up during treatment and; (3) Follow-up post treatment. Two additional steps could be required (4,5): (4) Adverse event reporting and management; (5) Active tuberculosis reporting and management.
Refer to the appropriate standard operating procedure for guidance on each of these five aspects of the trial.

5.5. Trial Termination

- 5.5.1. **Termination of recruitment**
  - Coordinating centre will notify all sites when recruitment should be terminated
  - Site will then notify IRB of termination of recruitment
- 5.5.2. **Termination of trial at site**
  - Trial will terminate upon completion of follow-up post treatment of all recruited study participants and when all study data has been reported to the coordinating centre.

6.0 References

- Health Canada Guidance for Industry. Good Clinical Practice: Consolidated Guideline. ICH Topic E6
- RI-MUHC Standard Operating Procedure SOP-CR-001_07, Administrative Management by Network of Networks, 01-Sept-2018.

APPENDIX 1 – TASK DELEGATION OF RESPONSIBILITES FORM

The Principal Investigator is responsible for: Identifying qualified personnel to be involved in recruitment and follow-up of study participants and documenting delegation of their responsibilities and qualifications.

All qualified personnel who will be involved in the recruitment and follow-up of study participants should be recorded on this form, indicating their assigned responsibilities. The following information should be collected:

Name (block letters)	Title	Signature	Initials	Tasks	Start Date (DD/MMM/YYYY)	End Date (DD/MMM/YYYY)	Principal Investigator's Initials
JOHN DOE	Principal investigator			A, B, C, D, J	02/AUG/2019		

Tasks:
a) Initial contact with participant
b) Access to medical records
c) Participant recruitment
d) Physical exam
e) Participant randomization
f) Participant follow-up
g) CRF entries & corrections
h) Data analysis
i) REB reporting
j) Assessment of AE
k) Drug management, storage and dispensing
l) Other, describe:

APPENDIX 2- TEMPLATE OF TRAINING LOG

The following personnel has attended a session of training on "Higher dose Rifampin for 2 months vs Standard dose Rifampin for Latent TB: a 3-arm randomized trial" .

Name and title	Signature	Attended on (date):

Training was conducted by _____(ex: *site PI, site CTC etc*) **and covered the following aspects of the trial: _____ (**ex. *background, rationale, study design, intervention, outcomes, procedures for screening, enrolment, follow-up, etc*)

7.0. SOP Revision history

SOP code	Effective date	Summary of changes
SOP01_18Sept2019	18 September 2019	NA (original version)