Title	Screening, Recruitment and Randomization
SOP Code	2R2 SOP02_13Oct2021
Effective Date	

1.0 Purpose(s)

The objective of this standard operating procedure (SOP) is to ensure appropriate screening, recruitment and randomization of study participants.
The SOP will ensure:

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

2.0 Scope: Persons affected

This SOP concerns the co-investigators and their respective research teams involved in conducting research with human participants for the study entitled $2R^2$: *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 the SOP.

4.0 Definition(s)

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

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

ICF: Informed consent form.

ICH: International council for harmonization 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. Responsibilities of the site Principal Investigator

The site principal investigator is responsible for: **1)** Identifying qualified personnel to be involved in recruitment, and documenting delegation of their responsibilities and qualifications (see

physician but this is dependent on the site specific IRB. If the treating physician is the person obtaining consent, they may need to explain to the IRB why it is necessary. If the IRB approves this, the physician must disclose his dual role to the participant.

5.2.3. No research activity should be conducted before the participant has signed the informed consent form

5.3 Step 1: Initial screening

5.3.1. The fist step is an initial screening that is performed by completing CRF-1. This is an initial quick check for general eligibility. See detailed instructions to complete CRF1 in **Appendix 1**.

5.3.2. If after this first check potential participant seems eligible, then the consent process can take place. Otherwise, it this initial check reveals reasons for which potential participant is not eligible then the recruitment process ends here, thank the potential participant and direct them to the treating team for them to receive standard care.

5.3.3. The completed **CRF1**, for both eligible and ineligible potential participants for whom this first step was done, **constitutes the screening log of this study**.

5.4. Step 2: Informed consent process

5.4.1. Only the most recent version of the informed consent form (ICF) approved by the IRB should be used for participant consent.

5.4.2. The ICF should provide the participant with all necessary pertinent information. They should have ample time and opportunity to inquire about the details of the study and to decide whether or not to participate.

5.4.3. During the course of discussion concerning the informed consent, all elements

- The intermediary has translated the consent form or approved an existing translation of the information relevant to the participant.
- The intermediary has assisted the participant in the discussion of the study.
- The participant has acknowledged in his or her own language, that he or she understands the study, the nature and extent of his or her participation, including the risks involved, and freely gives consent.

5.4.8. Prior to participating in the study, the participant or the participant's legal representative should receive a copy of the signed and dated ICF and any other written information

they have been correctly recorded by participants. An impartial witness must be present during the consent and sign it, if required by the local ethic committee.

5.5.Step 3: In depth assessment of eligibility

The following procedures are specific to the third step of recruitment for this trial: the collection of

of randomization- and HIV testing -if HIV status and is not known at the time of randomization). Note that for each of these tests, the date in which the laboratory test has been ordered has to be filled in for randomization to take place. Once the participant has been randomized, any other changes to data must be done by submitting a request to the coordinating center (refer to Management of Study data SOP). Once randomization is complete, please refer to SOP4 "Blinding and Dispending study medication" for procedures of dispensing study medications.

5.7.5. Although participants are given their study medication (or a prescription for their medication) on the day of randomization, the results of laboratory test for all participants and pregnancy test (if applicable) are usually not available on the same day. Therefore participants should be advised **they must wait for a call from study staff before they actually start to take their medication**. Research staff should ensure that laboratory results are reviewed 24-48 hours after randomization, so that participants can be called and told to start their study medication

SOP-CR-009_07 _Subject Recruitment and Screening_01-Sept-2018 – Research Institute of the McGill University Health Centre

SOP-CR-002_07_Research Team Roles and Responsibilities_01-Sept-2018 – Research Institute of the McGill University Health Centre

SOP-CR-008_07 _Inform Consent Process _01-Sept-2018- Research Institute of the McGill University Health Centre

7.0. SOP Revision history

SOP code	Effective date	Summary of changes
SOP02_25Nov2019	25 November 2019	NA (original version)
SOP02_06Jul2020	06 July 2020	Update exclusion criteria and exclusion post-randomization, as per Protocol v2_15March2020 (in Appendix 1 and 2).
SOP02_21Jun2021		- Correction of exclusion criteria (Appendix 1 and 2); -Procedures when COVID-19 related measures are in place (page 5 and Appendix 2)

Appendix 2 – Instruction to fill CRF 3 (Initial evaluation)

General note: all information in CRF3 are obligatory (i.e. if left blank participant file will appear as incomplete on the website). There are though some information which absolutely need to be filled in before randomization can take place and others which

D10 **Viral load** (at randomization) _____

Note: if CD4 is not know, write 9999. Note: if viral load is not know, write 9999 and

. **perform viral load test.** __

If susceptibility test in index patient has been requested but results are not available yet, leave D15 blank. Come back to fill D15 as soon as results become available. When the DST the results are available, if there is resistance to rifampin, call the participant to stop study medication and refer them to the treating team. Also, inform the coordinating center as this is a per-protocol exclusion post-randomization.

D16 Does the study participant have any immunosuppressive conditions or therapy?

C **No** C **Yes**

D. 17-24. **If Yes, which are the conditions or therapies causing immuno suppression in this participant** (check all that apply)**?** *Tick more than one if participant has more than one condition*

C **Diabetes** C **Renal failure (dialysis)** C **Transplant anti-rejection therapy** C **TNFa inhibitory therapy**

C **Other immunosuppressive conditions,** D22. **Specify**_____

C **Other immunosuppressive therapy** D24. **Specify**_____

D25. Smoking status (choose one)

C Never smoke C Current smoker C Ex- smoker

If current or ex-smoker D26.**Age started** C C D27. **Packs/day** C C . C

If ex-smoker D28.**Age stopped** C C

Write approximate age for starting and stopping and packs per day if participant cannot remember with precision.

D29. Alcohol: How often do you have a drink containing alcohol? (choose one)

C Never C Less than once a month C 1-3 times per month C Once a week C 2-3 times a week

C 4 or more times a week

D30. How many drinks containing alcohol do you have on a typical day when you are drinking? (choose one)

C Not applicable C 1 or 2 C 3 or 4 C 5 or 6 C 7 to 13 C 14 or more

D31. How often do you have six or more drinks on one occasion? (choose one)

C Not applicable C Never C < Monthly C Monthly C Weekly C More than once a week

D32. Do you use any recreational drug more than once a month? C **No** C **Yes**

If Yes, **choose any that apply (D33-D34):**

C **D33.Cannabis** (marijuana, hashish, etc) C **D34.Other,** D35. **If other, specify** _____

_____

HISTORY OF TB

M18.Other medical conditions C **None** C **Any,** M19,

Specify_____

MEDICAL EVALUATION

M20. Respiratory symptoms C **None** C **Any,**

M21.**Specify**_____

M22. Other symptoms: C **None** C **Any,** M23.

Specify_____

M24. Physical exam C **Normal** C **Abnormal,**

M25.**Specify**_____

M26 . Comments (for all the above sections):

If enrolment is done at distance for COVID-19 related measures: ask participant by phone if they have respiratory symptoms or any other symptoms. Ask them if a recent medical examination has been done, if possible, retrieve the report of this evaluation from participant's medical file. If not possible, report is as ***Abnormal*** *at M24 and Specify:* ***NOT DONE because of at-distance enrolment for COVID-19 related measures*** *at M25****.***

SECTION -3 Initial investigations

INVESTIGATIONS
CHEST X RAY
L1.Date of chest-x ray

A chest-x ray has to be done prior to randomization, and the result should be "normal" or "abnormal but not TB" in order to exclude active TB. ***The chest x ray can be used if it was done less than 6 months prior to the date of randomization.***

L2. Chest-x ray results (select one only)
☐ Normal
☐ Abnormal possible active TB. NOTE: If possible active TB complete section on microbiology :L8 to L18)
☐ Abnormal not TB. L3. Specify:
_____

If the chest-x ray report is "abnormal possible active TB", then microbiological investigations

L7. **If any, Results** _____

MICROBIOLOGY

L8. Microbiology: ☐Not required ☐Done

L9**. If Done, date of 1st test**

Microbiology test is "not required" if active TB is not suspected on basis of medical history, physical exam and chest-x ray. Otherwise, if active TB is suspected on the basis of medical history, physical exam, or chest-x ray - then microbiological tests are required. If microbiological tests are done, ***date in L9 has to be less than 6 months prior to the date of randomization.*** *If answer to L8 is "Not required" then questions L9-L18 are not necessary for randomization.*

L10 **Number of spontaneous sputum samples obtained** C

L11**. Number of induced sputum samples obtained** C

L12. **Number of gastric aspirate samples obtained** C

L13. **AFB smear: Number done** C L14.**Results: C All contaminated C All Negative C At least one positive** (if at least one positive, STOP HERE)

L21.1. L20.0 Upper normal limit for AST c c c . c UL

Write the upper normal limit for the AST and ALT result reported. Please note that just one of these two tests (AST or ALT) is sufficient to randomize. If you testes both, please report both AST and ALT.

If AST or ALT results, which become available after randomization, are ≥ 3 times higher than upper limit of normal, call participants immediately to tell them to NOT START their study medication This is a case of post-randomization exclusion per protocol: fill a note to file in the 2R2 database to inform coordinating center. Coordinating center will confirm with you once the exclusion is completed.

L22. Total bilirubin c c c . c umol/L

L22.1 Upper normal limit for **Total bilirubin c c c . c umol**

L30**. If Yes, date test was performed**

L31. **HIV Test Results** c **Positive** c **Negative** c **Unknown**

If results of the HIV test that have been requested is not yet available, randomization can take place but you need to fill Line 31 as soon as the result is available after randomization. Remember that if a participant needs to start a new treatment, such as for HIV, during follow-up; this new treatment should be reported in the CRF-5- follow-up during treatment.

L32. Pregnancy test : c **Positive** c **Negative** c **N/A**
If results of pregnancy test become available after randomization, and is positive, call participants immediately to tell them to NOT START their study medication