Title	Study Initiation Monitoring Site Visit
SOP Code	2R2 SOP12_06Jul2020
Effective Date	06 July 2020

1.0 Objective(s)

The objective of this standard operating procedure (SOP) is to ensure that all the sites who are conducting $2R^2$ study have facilities that are suitable to conduct the study, and that the study procedures have been reviewed with the site investigators and research team responsible for the study.

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 – $2R^2$: *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 qualified investigator is responsible for adoption of the processes described in the SOP.

4.0 Definition(s)

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

II. **Monitor:** Research staff from coordinating center who will conduct site visit to direct assess compliance with the protocol and applicable regulations and guidelines.

III. **Site Investigator**: A person responsible for the conduct of the research study at a study site. If a study is conducted by a team of investigators at the same study site, the Site Investigator is the responsible leader of the team.

IV. **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 participant in a clinical research study.

V. **Good clinical practice (GCP):** An international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human participant.

5.0 Procedures

5.1 General information

The coordinating center will do a study initiation & protocol training visit to each participating center, as a final assessment of the site's readiness to start the clinical trial. This visit is done just before the study start at the site. In case further preparation is needed before the trial can start at the site, a follow-up virtual visit can be done by conference call to discuss the completion of pending issues.

5.2. Study initiation monitoring site visit

One study initiation monitoring site visit should be done before the study start. This visit is conducted by the principal investigator and/or the research coordinator form the coordinating center in Montreal, Canada.

A draft agenda and training points are sent to the site about 2 weeks before the visit takes place, to ensure the site will properly prepare for the needs of the visit. The order of the agenda will dependent upon availability of staff and timing of visit. In **Appendix 1** an example of site visit agenda.

The site investigator and all research team members with delegated responsibilities should be present during the initiation visit. All staff who has been trained during the initiation visit or during other study training sessions held by the monitoring center of the site PI, has to be documented in the Training list (see example of training list in 2R2 **SOP01-**Appendix 2 "Site start-up and running of a trial"). The Training list must be retained with the essential documents in the master binder, as described in 2R2 SOP01 **"**Study Start-up and running of a trial**"**. Topics of training given during initiation visit will be reported in the visit report. See an example of training summary report in **Appendix 2.**

The review that takes place during the initiation visit will include, but will not be limited to, the following items:

- Discussion and review of study protocol, background, objectives;
- Description of how study procedures will be implemented at the site;
- Participant's inclusion and exclusion criteria and how will they be evaluated;
- GCP, legal, and regulatory obligations of the research team;
- How management of adverse events and ascertainment of active TB and death will be carried out;
- Completion and storage of Case Report Forms (CRF);
- Management of study essential documents (in master binder);
- Participant informed consent form procedures;
- All study SOPs;
- Data management and use of trial specific website database;
- Management of biological samples;
- Management/storage of study medications;
- Any other protocol-specific item.

The monitor will also:

- visit the facility to ensure that there is the proper capacity and equipment to conduct the study at that centre;
- visit all the appropriate departments (clinics, medications storage, radiology, laboratory etc).

Note: if a physical initiation training is not possible on sites due to a major impeding cause, independent from the study, and the site is ready to start the study, a training and visit by distance must be take in account, by use of technology which allows virtual visit (as for example Zoom, Skype, TEAMS platforms). All the items of training and review must be covered in the virtual visit, including, for what possible the walk through the physical site/clinic/laboratory. The PI of the coordinating center must be confident that the sites

have the appropriate capacity to conduct the study before they start. The physical visit will be done at a later time, as soon as the circumstances will allow the travel.

5.3 Study initiation report

Principal investigator/research coordinator will confirm if the team at site is ready and the facilities are suitable to conduct the study, and that the study procedures have been reviewed with the site investigators and research team responsible for the study. The coordinating centre will prepare a detailed site initiation report including the following: (1) Agenda & training points (example in **Appendix 1**); (2) Research team list (**Appendix 3**); (3) Summary of site initiation visit training (**Appendix 2**); (4) Review of Master Binder (essential study documents) (**Appendix 4**); (5) Summaries of individual center visits (if applicable) (**Appendix 5**).

A draft report will be sent to the site investigator, who will review and complete it. Once finalized by the coordinating center, the report is sent back to the site investigators. A copy of the final report has to be placed in the master binder.

The coordinating centre will follow-up with the study site to ensure that all the recommendations have been followed.

5.3.1 Agenda and training points

The agenda & training points that was used at the visit has to be included in the report that will be sent to the site.

This will include the following:

- Meetings with site investigator (at least one to discuss administrative and project issues, questions and plan the final agenda; and one to summarize the findings of the visit)
- Dates and times of visit's activities
- If more than one clinic to be visited, list of name of the clinic / dates / time for each clinic
- Training points

See example in **Appendix 1**.

5.3.2 List of all research staff involved in 2R^2 study (name & title)

This list include all research staff who are involved in the 2R^2 study and who are listed in the task delegation of responsibilities form **(2R2 SOP01**-appendix 1 "Site start-up and running of a trial"), specifying who has been met during the site visit.

It could also include administrative and clinical staff if they have important role in the study (ex: nurse who will be in charge of referring patient to the research team, etc). See example in **Appendix 3.**

5.3.3 Summary of site initiation training session

The coordinating centre will review all the task that need to be done during the visit, as specified in section 5.2, and will write the action that was taken, and any comment or recommendation needed. See **Appendix 2** for more details.

5.3.4 Review of essential study documents (Master Binder)

The coordinating centre will look at the master binder to ensure that all the essential documentation is properly placed in this binder, as per GCP recommendations. For Master Binder description, see 2R2 **SOP01** "Site start-up and running of trial".

If the site does not have a master binder or did not yet completed it, the coordinating centre can help compiling all the essential documentation needed with the research team during the study initiation visit. The master binder review can be summarized following the example in **Appendix 4.**

5.3.5 Summaries of individual centers (if applicable)

If there is more then one clinic in the same study site that will participate in the study, the coordinating centre has to go at each clinic to ensure they are suitable to conduct the study.

A short training on the study must be done also to clinical team:

- Visit the department (clinic, CXR, laboratory, study drugs, etc);
- Verification of medication storage and dispensing procedures;
- If they have a proper room for research staff to meet the participant;
- If they have access to a computer with internet to be able to do the randomization of participant.

A summary for each clinic must be done with the action that was done and any comments and recommendations (see example **Appendix 5** for more details).

5.4 Monitoring site visit log

The monitoring site visit log must be signed by the coordinating centre (monitor) and the site investigator (refer to **Appendix 6** for more details).

- Site date visit (from/to)
- Type of monitoring site visit (e.i. Study initiation visit, Regular study monitoring site visit, etc)
- Coordinating center (monitor) name and signature
- Site personnel name and signature

This form has to be signed also at any further monitoring site visit and kept in the master binder.

6.0 Reference

Research Institute of McGill University Health Center, "SOP-CR-005_07 Study Initiation/Activation", 01-Sep-2018.

7.0 SOP Revision history

SOP code	Effective date	Summary of changes
SOP012_22Jun2020	22 June 2020	NA (original version)

APPENDIX 1

Example of an agenda/schedule and training points for visit

[*include dates & times, if the site has several clinics to be visited a list of the times & dates for each clinic visit should be included. The order of the agenda will be dependent upon availability of staff and timing of visit]*

Meet with the site investigator & study coordinator if applicable
- Review administrative
- Review questions/issues at site
- Discuss primary objective of visit

Review essential documents, Master binder (regulatory review as required)

Facilities visit (research office, clinics, radiology (if applicable), Laboratory and PK facilities, study medications storage and dispensing facilities)

Presentation of the overview of the study

CRFs and SOP training

Training on study medication blinding and dispending in clinics

Any other topics, issues, questions can be added to the agenda

Summary meeting (findings, recommendations, next step, etc)

TRAINING POINTS

Protocol review & questions
Primary & Secondary outcomes

Review Site Start-up Procedures & Requirements
Review Good Clinical Practice
Master binder & essential documents

Screening & recruitment procedures for potential patients
Screening - Inclusion & exclusion criteria
Inform consent/assent/parental
Data collection – case report form (CRF) & website
Contact information (identification form)
Randomization on website & Manual randomization

Follow-up during treatment
Medical examination and investigations needed during follow-up
Data collection – case report form (CRF) & website
Maintenance of contact information

Compliance, Adverse events, Other medications

Adverse event management & reporting
Data collection – case report form (CRF) & website

Follow-up post treatment
Screening for active TB
Maintenance of contact information

End of treatment
Data collection – case report form (CRF) & website

Follow-up post treatment
Data collection – case report form (CRF) & website

Active TB management & reporting
Data collection – case report form (CRF) & website

Death management & reporting
Data collection – case report form (CRF) & website

End of follow-up post treatment
Data collection – case report form (CRF) & website

PK sub-study
Population, blood collection, storage & shipping
Data collection – case report form (CRF) & website

Summary & next steps

RESOURCES
1. Resources/procedures: study medication blinding and storage, laboratory testing, medications, dispensing, internet access
2. Facility tour (research room, clinic, pharmacy, Lab, CXR if applicable)

APPENDIX 2 - Summary of site initiation training session for <*Name of the site*>

SITE INTITIATION TRAINING		
Task and supportive documents	**Action**	**Comments/Recommendations**
Site initiation visit – agenda (2R2 SOP12, Appendix 4)		
Review of protocol & study outcomes		
Site Start Up & Running of Trial Procedures (2R2 SOP01) training		
Initial screening CRF-1 & Procedure (2R2 SOP02) training		
Eligibility & Inform Consent CRF-2 & Procedure (2R2 SOP02) training		
Evaluation and randomization CRF-3 & Procedure (2R2 SOP02) training **Identification form** CRF-4 training		
Manual randomization Procedure (2R2 SOP03) training		
Follow-up during treatment CRF-5 & Procedures (2R2 SOP05_Follow-up and 2R2 SOP15_Follow-up in special populations) training		
End of treatment CRF-6 & Procedures (2R2 SOP06) training		
Follow-up evaluation post treatment CRF-7 & Procedures (2R2 SOP07) training		
End of post follow-up CRF-8 & Procedures (2R2 SOP07) training		
Adverse Event CRF-9 initial report / CRF-10 final report & Procedures (2R2 SOP09) training		

SITE INTITIATION TRAINING		
Task and supportive documents	**Action**	**Comments/Recommendations**
Active TB CRF-11 Initial report / CRF-12 Final report & Procedures (2R2 SOP08) training		
Death CRF-14 & Procedures (2R2 SOP07) training		
Population PK CRF-13 & Procedures (2R2 SOP11) training		
Sample shipment for Pharmacokinetic and GLP Procedures (2R2 SOP20) and GLP documents at the site lab		
Storage and transportation of study drugs Procedures (2R2 SOP13) training		
Website training and access - Data collection and functionality for follow-ups		
Review of resources		
Computer (Laptop/desktop) and internet connection		

APPENDIX 3 - Research staff involved in 2R2

Name of site:		
Date:		
Name and title	**Role in the trial**	**Met during visit?**

APPENDIX 4 - Master Binder review - Essential documents for the study at <*Name of the site*>

Document/Function	Version	Copy sent from the coordinating center	Comments
Ethical approval at coordinating center			
Original Protocol form RI-MUHC			
Original Consent			
Ethic committee approval			
MUHC authorization			
Health Canada Approbation (NOL)			
Health Canada - Qualified investigator undertaking (Canada sites only)			
Clinical trial site information form (Canada sites only)			
Ethical approval at site	**Version**	**Copy sent to the coordinating center**	**Comments**
Original protocol translated			
Consent (translation)			
IRB application & correspondence			
IRB Approval			
IRB composition			

Sample case report forms (CRFs)			
Task delegation of responsibilities form/Signature sheet			
CV & copy of medical license (or diploma) of investigators			
Contract/transfer of funds agreement			
Patients insurance			
Laboratory certificate			
Normal lab values			
Good clinical practice guidelines			
Certification GCP			
SOPs			

APPENDIX 5- Summary of individual center visits for <*Name of the site*>- if applicable

SITE INITIATION VISIT – <*Name of the center*>		
Task	**Action**	**Comments/Recommendations**
Protocol		
Resources/recruitment targets		
Training session		
Clinic tour		
Laboratory		
Medications		
Information technology		

APPENDIX 6

MONITORING SITE VISIT LOG

2R2: Higher dose Rifampin for 2 months vs Standard dose Rifampin for Latent TB: a 3-arm randomized trial.

Site name:
Site investigator:
Study Coordinator:

Site Visit Date		Type of monitoring visit	Names/ Signatures	
From	To		Monitor	Site Personnel