Remote study initiation and site monitoring visits
Addendum to SOP12 and SOP13

2R2 SOP23_18Feb2021

Title	**Remote initiation and monitoring visit**
SOP Code	2R2 SOP23_18Feb2021
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1.0 Objective(s)

The objective of this standard operating procedure (SOP) is to ensure how, if initiation visit and monitoring visits cannot be done in person at a study site, for causes independent from the study (as during periods of travel restriction applied for containment of COVID-19 pandemic) these visits can be done as "remote" visits.

The specific objectives of initiation visit can be found in SOP12 and of monitoring visit, in SOP13. This SOP is therefore an addendum to SOP12 and SOP13, which serves to explain how the initiation and remote visits are done remotely.

2.0 Scope: Persons/Areas affected

This SOP concerns the coordinating center and the co-investigators and their respective research teams involved in conducting research with human participant 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. **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.

II. **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).

III. **COVID-19**: Coronavirus Disease, 2019

IV. **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.

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

VI. **Remote (or virtual) visit:** meeting or visit which is not done in person but by use of an electronic/virtual mean (for example a meeting platform as Zoom or TEAMS, a telephone, etc).

VII. **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.

5.0 Procedures

PART I:

5.1 Initiation visit

If site initiation visit, as described in SOP12, cannot be carried out in person, by coordinating center, all elements of the in-person visits will have to be converted in a remote visit.

5.1.1. Agenda of remote site initiation visit

The virtual initiation visit is conducted by the principal investigator and/or the research coordinator from the coordinating center in Montreal, Canada. As for an in-person visit, a draft agenda and training points are sent to the site about two weeks before the virtual visit starts. For each item in the agenda, coordinating center will have to coordinate with site PI and coordinator to agree on the format used for each point.

5.1.2. Tools used for a remote initiation visit

Remote visit can be done using a combination of the following:

1) Video conferences (Skype, Zoom, others): to have group meetings, discussions, training sessions and to discuss specific issues, if needed;

2) Video calls 1:1 (Skype, WhatsApp, Zoom, others): to review and discuss source documents available at study site;

3) Completion of checklist (Appendix 1): for site to describe facility, health care workers force, and services available at each study clinic. **Note**, if needed, pictures of specific items can be included, to show, for example facilities or supplies. Pictures cannot contain any identifying features, faces or names of participants.

Which tool to use for which part of the visit, will be decided by site PI and coordinating center, to fit best the needs of each site and visits.

As for in person visits, in case further preparation is needed, after the initiation visit, another follow-up virtual visit can be done by conference call to discuss the completion of pending issues.

5.1.3. Components of a virtual initiation visit:

Agenda of virtual initiation visits needs to include dates and times.

If site has several clinics/teams to be visited/met, site PI and study coordinating center will decide if there will be a visit of each site or if in the site PI/site coordinator will conduct the training and visit for each clinic, to ensure they are suitable to conduct the study. A report (including the

checklist in appendix 1) for the initiation visits conducted by the site PI/site coordinator, will be sent to coordinating center.

The essential components of a virtual initiation visit are then listed in Table 1 below.

Table 1. Essential parts of a virtual initiation visit:

Session		Tool	Participants	Objective
#[1]	Type			
1	Conference	Phone or platform (as Zoom, etc)	Site investigator(s), site coordinator, study coordinator	Discuss: • Administrative situation at site for study • Review questions/issues at site • Discuss primary objective of virtual visit
2	One-to-one meeting	Video call (for example WhatsApp, Zoom, etc)	Site coordinator/site PI and study coordinator	For coordinating center to review: • Essential documents prepared • Master binder[2]
3	"Virtual tour"	Checklist completed and sent by site coordinator	(done by site coordinator)	Review health care facilities involved in the study (including research office, clinics, radiology, laboratory and PK facilities, study medications and tuberculin storage and dispensing facilities).
4	Conference	A platform (as Zoom, etc) which allows sharing screen, showing slides, etc	All site personnel, as applicable.	Training[3] (refer to SOP12 for the training to be done before study starts).
5	Conference	Phone or platform (as zoom, TEAMS, etc)	Study PI, study coordinator, site investigator(s) and site coordinator	To summaries what learnt on site preparedness and discussion on recommendations and next steps.

Notes:
1.Parts of an in-person visit that the sessions replace**:** 1) Initial meeting with site PI and coordinator; 2) Review of master binder and essential documents; 3) Visit of facilities in which study will take place; 4) Training; 5) Closing meeting with site PI and coordinator.
2. If the site master binder is not yet completed, the coordinating center can help compiling all the essential documentation needed with the research team during the study initiation visit. Please refer to SOP12 for an example of master binder review.
3. The agenda of the training for initiation of the site, will be discussed with site PI and coordinator.

Each session (1 to 5) may actually need to take place in more than one meeting (for example, session #4 training, is likely to imply at least a 3-4 different conference calls), therefore the actual number of calls and videoconferences placed is likely to be more than 5. This implies that the site initiation visit may take several days (over 1-2 weeks).
Coordinating center should be able to meet all research team members with delegated responsibilities at least in one of the calls of the virtual initiation visit.

The order of the items in the visit agenda will be dependent upon availability of staff and timing of visit and is decided with each site.

5.1.4. Documentation

Documentation needed for initiation visit is the same than for in person visit, including Visit report, Training list and Monitoring site visit log. The completed checklist, sent by site coordinator to the coordinating center, will be included in the visit report. Please refer to SOP12 for all documentation needed in initiation visit.

PART II

5.2 Monitoring visit

If a regular in person study monitoring site visit cannot be conducted, the principal investigator or a designed monitor from the coordinating center in Montreal, Canada, can do a remote monitoring visit. Content of the visit will be the same than in person visit, as well as documentation produced after a virtual visit. Please refer to **SOP13** for objectives, essential elements of monitoring visits and documentation needed.

5.2.1 Preparation before performing the regular study monitoring site visit

The monitor will contact the site investigators to have availabilities of the site to conduct a visit. Preparation done by monitor before the virtual visit is that same than for an in-person visit. Agenda for the visit and data to be reviewed will be communicated to the site PI and coordinator about two weeks before the site visit. See SOP13 for points to include in agenda.

5.2.2 Tools to be used during virtual monitoring visits

Tools that can be used are the same than for a virtual initiation visit (see point 5.1.2. above)

5.2.3. Components of a virtual monitoring visit:

Table 2. Essential parts of a virtual monitoring visit, after study started enrollment:

Session		Tool	Participants	Objective
#[1]	Type			
1	Conference	Phone or platform (as Zoom, TEAMS, etc)	Site investigator(s) and coordinator, study coordinator	To review and adjust the agenda, and discuss any issues
2	One-to-one meeting	Video call (for example Zoom, etc)	Site coordinator and study coordinator	To review all consent forms for study participant enrolled since last visit.[2]
3	One-to-one meeting	Video call (for example Zoom, etc)	Site coordinator and study coordinator	To verify that all study participant records, data and source documents identified to be reviewed during the monitoring visit are complete and accurate[3]
4	One-to-one meeting	Video call (for example Zoom, etc)	Site coordinator and study coordinator	To verify all cases of adverse events, active TB and death at the site, to make sure all information needed was obtained
5	One-to-one meeting	Video call (for example Zoom, etc)	Site coordinator and study coordinator	To verify that all study documents are kept in a secure, confidential manner;
6	One-to-one meeting	Video call (for example Zoom, etc).	Site coordinator and study coordinator	To verify the storage and documentation of samples for population PK
7	One-to-one meeting	Video call (for example Zoom, etc)	Site pharmacist (or staff working for 2R[2] as trial pharmacist) and study coordinator	To verify that the study drugs inventories are accurate and study drugs are stored appropriately;
8	Conference	Phone or platform (as zoom, TEAMS, etc)	Site investigator(s) and coordinator, study coordinator	To summaries and discuss findings and recommendations

Notes:
1. Parts of an in -person visit that these sessions replace: 1) Initial meeting with site PI and coordinator; 2-5) Meeting with site coordinator and review of consent forms, CRFs and source documents, master binder, places where documents are kept; 6) Visit of the lab and PK sample storage (and review of relative documentation); 7) Visit or the pharmacy and meeting with pharmacist; 8) Closing meeting with site PI and coordinator.
2. As information verified by coordinating center during this call will be confidential, this part will be conducted with a live video call, without possibility of recording or saving imagine from the site coordinator or the monitor.
3. Monitor will make a list of participants for whom records will be checked during the call and send it before head to the site coordinator;

Each session (1 to 8) may actually need to take place in more than one meeting, or, in case of short sessions, they may be combined in one unique meeting.

Monitor and site staff will work together, before the visit, to plan for best timing and duration of each session.

Remote visit can replace any of the in-person visit previously planned (see SOP13 for monitoring site visits timeline). As soon as travelling can be resumed, subsequent visits can be done in-person.

5.2.4 Study site role

Preparation for regular study monitoring site visit from study sites is the same than for in person visits **(see SOP13).** In addition, connectivity to internet or phone reception need to be checked in advance of the visit to reduce risk of technical issues during the remote visit.

5.2.5. Documentation

Documentation needed for remote monitoring visit is the same than for in person visit. Please refer to SOP13 for all documentation needed.

6.0. References

- Research Institute of McGill University Health Center, "SOP-CR-005_07 Study Initiation/Activation", 01-Sep-2018.
- Research Institute of McGill University Health Center, "SOP-CR-013_07 Study Monitoring and Communication", 01-Sep-2018.

Appendix 1: Checklist for description of clinic(s) participating in the trial.

Introduction: Part I (4 questions) of this list needs to be completed only once for a study sites, as it includes characteristics which apply to all clinics at site. **Part II** (25 questions) needs to be completed for each clinic. If in part II there are sessions which are the same in different clinics, please write "refer to description for clinic ____ " instead of repeating the answer.

Part I: General characteristics of TB care at study site

1. In a TB unit, which are the nurses' tasks (for example: do they make follow-up visits, request exams):
2. In TB units, are there other health care workers, beside nurses and doctors, who works in the TB / LTBI unit? If yes, please describe their tasks:
3. For what concerning the TST: how is, in general, the result of TST documented and how the results will be available, as source document, for the monitoring visits, to check consistency between source document and results of TST reported in CRF5?
4. Please describe how is generally done the follow-up after the beginning of the treatment of LTBI in the TB units:

Part II: Health clinic related characteristics *(to complete for each clinic where study is taking place)*

CLINIC HEALTH CARE WORFORCE

Name of the health unit and city _____

1. How many doctors are working on TB and LTBI in this unit?
2. What days of the week are days dedicated to care for TB and LTBI?
3. How many nurses work at the unit?

TST

4. Is Tuberculin test in the clinic available? ☐Yes ☐No
   4.1 If so, which application days and which reading days: Application: _____ Reading: _____
   4.2 If not, where are patients referred and how are they referred?
5. How many health professionals do the tuberculin skin test (TST) in this unit?
6. Please describe where the tuberculin is stored:

CHEST-X RAY

7. Is there a service of radiography at the clinic? ☐Yes, digital ☐Yes, analogue ☐No
   7.1. If yes, how long does it take to have the result of chest-x ray (CXR) on average?
   7.2. If not, please describe where are potential participants referred to for CXR and how long does it take to book CXR appointment and to have the result back :
8. Is the radiography sent with a report from radiologist? ☐Yes ☐No
   8.1. If not, please describe who is interpreting the radiography:
   8.2. Please describe where is the interpretation of the CXR documented and how can it be accessible during monitoring visits:
9. Please describe how the CXR done at baseline can be available for uploading it in GXT website if needed:

PHARMACY

10. There is a pharmacy in the unit? ☐Yes ☐No
    10.1. If yes, please describe how the medications are stored in the pharmacy, who is in charge of dispensing the medication and the process of dispensing:
11. If there is no pharmacy, describe how are LTBI drugs dispensed and where are they stored:
12. If there is a pharmacy, is the pharmacy involved in patients care? (for example, is the pharmacist consulting patients if they come back to the clinic- or call- for an adverse event?)

MICROBIOLOGY

13. Please describe which are the microbiological tests available at the unit:
    13.1. AFB:
    13.2. Culture:
    13.3. GeneXpert:
    13.4. Is there the possibility to do induced sputum in the unit? ☐Yes ☐No
    If yes, please describe the method used (solution, administration, equipment used, …):
14. For each of the tests mentioned above (13.1 to 13.4), if tests are not available, please describe where are patients referred to; how long it takes to perform the exam; how long to have the results:
15. Please describe where are the results of each microbiological test documented, and how can they be available in a monitoring visit:

LABORATORY

16. Please describe where is the lab that will be used for bloodwork assessment during the study and the process for performing the blood test (who is doing the blood draw, where is it tested, how long before results are reviewed, etc):
17. Please describe where the original blood tests results are documented and how can they be accessible during monitoring visits:
18. Please describe who will be conducting the blood draw for population PK sampling; where will be the samples centrifugated and separated and where they will be stored at -80C before being shipped to Bandung, Indonesia, at the end of the study.

CLINICAL SERVICES

19. In case a participant needs to be referred to an HIV clinic (for example, because diagnosis if HIV infection is done during screening for the study), please describe where is the HIV clinic that you would use as referral clinic:
20. If participants are co-infected with HIV, please describe where is the clinic where they would be in care:
21. Please specify if children and adults are taken care in the same unit for LTBI treatment. If not, please describe the pediatric unit for LTBI:

FACILITIES

22. Is internet network available at the unit? ☐Yes ☐No
23. Does the team think that computers are available for use by the research team? ☐Yes ☐N
24. Please describe the room where the team can meet potential participants, explain the study and obtain informed consent:

25. Please describe the room where research team can place a cabinet or drawer to store research documents and how the documents can be protected:

7.0 SOP Revision history

SOP code	Effective date	Summary of changes
SOP023_18Feb2021		NA (original version)