Study site closure

Title	**Study Site Closure**
SOP Code	2R2 SOP18_27Jun2023
Effective Date	26Sep2022

1.0 Objective(s)

The objective of this standard operating procedure (SOP) is to ensure adequate site close-out of clinical trial sites participating in $2R^2$ study.

2.0 Scope: Persons/Areas 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 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. **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.

III. **Essential Study Documents**: Essential Study Documents are those documents that collectively permit the evaluation of the conduct of a trial and the quality of data produced. Essential Study Documents serve to demonstrate compliance with standards of Good Clinical Practice and with all applicable regulatory requirements. They are contained in the Regulatory Binder (Master Binder).

IV. **Site close-out:** Site close-out is integral to the quality of a trial and is designed to ensure that all necessary documents are available should a site be queried or inspected once all participants at a site have completed their investigations. A site may be deemed "closed-out" once all study-related activities at the site are reconciled and/or complete.

V. **Source documents**: Original documents, data, and records (e.g. hospital health records, clinical and office charts, laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the study, and any other material applicable to the study).

VI. **Study closure**: Study closure is the act of ensuring that all clinical trial related activities have been appropriately reconciled. These activities include securing all the lab specimens collected and

ensuring that all accounts payable and receivable have been dealt with. Lock of the trial database, final analysis of the data, and study report writing may occur after formal study closure. Study closure only occurs after all sites have been closed out (refer to **SOP21** Study closure).

5.0 Procedures

5.1 General information

A study site must be closed out as soon as it is practicable to do so:

- The coordinating centre will inform each study site of their respective projected date of close-out based on recruitment information;
- Study sites must develop operational and staffing plans for completion of all required close-out procedures as listed in this SOP;
- No study records are permitted to be destroyed without prior written authorization from the coordinating centre;
- If a study participant specifically requests for their samples to be removed from the study and destroyed, the coordinating centre must be notified.

5.2 Responsibilities of the site investigator prior to Site Close-Out Monitoring Visit

- Confirm that all Essential Study Documents and the study-related correspondence are in the Regulatory Binder (master binder);
- Ensure that all protocol-required data have been collected, entered in the website, and validated;
- All necessary corrections to the data should have been carried out, according to correspondence with coordinating center or note to file. Ensure that all participant files have been closed as per **SOP17** Closing participant files;
- Make sure that all adverse events have been properly reported and dealt with (refer to **SOP09** Adverse Event reporting & Management);
- Make sure that all Active TB cases have been properly reported and dealt with (refer to **SOP08** Active TB reporting);
- Make sure that all Death have been properly reported and dealt with (refer to **SOP07** Follow-up post treatment and **SOP09** Adverse Event reporting & Management);
- Make sure that: 1) All site samples for population PK (i.e. boxes A and B) have been shipped to : Montreal -for Canadian sites other than Montreal; to Ho Chi Minh City- for Vietnam sites in Ha Noi; 2) Boxes A have been shipped to Bandung, Indonesia for Montreal and Ho Chi Minh City sites;
- Make sure that all remaining study medications at site have been used or destroyed following communication from coordinating center, and as per site pharmacy SOP.
- Verify that all data queries have been appropriately resolved or addressed;

- Check that all issues from previous monitoring, auditing, or inspection visits have been resolved and were documented;
- Collect any outstanding required signatures;
- Confirm that all financial matters are in good standing;
    - For example, verify that all site payments have been processed as agreed in the study contracts.
- Read over the publication policy;
- Confirm archiving arrangements for at least one copy of the Essential Study Documents for a minimum of 15 years after publication, as calculated by the coordinating centre. In all cases:
    - A site's plan for archiving must meet all applicable regulations and standards – including *Good Clinical Practice;*
    - Storage should guarantee safety against disasters (e.g.: fire, floods) and confidentiality of the information contained in the participant file (i.e. it must be under lock);
    - All non-identifiable information regarding each individual participant in a study must be grouped together (**SOP17** "Closing participant files");
    - Data must be retrievable in such a fashion that all information regarding each individual participant in a study is attributable to that participant specifically;
    - The site investigator must make sure that the persons in charge of the archive understand that participant files must not be destroyed;
    - The plan must detail the transfer of responsibility for record retention in the event the investigator retires, dies, , or, for any other reason, must withdraw from assuming their record retention role.
- Plan for the Site Close-Out Monitoring Visit and submit the closing site check list (in **Appendix 1**) to coordinating center. Note if n person Monitoring Visit is not possible, a virtual visit will be done to review actions specified in the check list.

5.3 Responsibilities of site investigator during the Site Close-Out Monitoring Visit

Assist the Monitor during the Site Close-Out Monitoring Visit and ensure cooperation from study site staff. In case an in person visit is not done: supervise the preparation of the closing site check list.

5.4 Responsibilities of site investigator following the Site Close-Out Monitoring Visit

Notify the research ethics board overseeing the study site of the site close-out using their procedures;

- For instance, submit a summary report of the study activities to the research ethics board if required;
- Archive all required documents as per the plan approved by the coordinating centre;

- Remain available for queries from the coordinating center.

Important: as analyses on the data collected during the trial may continue for some years after study is closed at sites, annual renewal from local REB must be asked every year, if applicable to your site, until no more analyses will be planned. Site investigator needs to appoint a person (and a backup) to ensure annual approvals are asked and specify in the checklist (Appendix 1), where renewals are stored once trial master binder has been archived.

5.5. Responsibilities of coordinating center for Site Close-Out Monitoring Visit

Coordinating center will organize the Site Close-Out Monitoring Visit, in accordance with site investigator availability.

During the Close-Out visit, monitor will verify all documents as specified in the checklist in appendix 1.

Note: if a closing in-person visit is not possible, site will complete check list in appendix 1 and send it to coordinate center. Coordinating center will organize a conference call with the site to go through the checklist with sites investigator, and make sure all necessary information are included.

Monitor will also verify the pharmacy documentation for the study and the study medication remaining at site. Decision on how to dispose of remaining study medication will be discussed during the visit with site investigator and communicated with Close-Out visit report, from coordinating center.

The monitor will send a written summary of key discussions and conclusions made during the study close-out visit, including the procedure for disposing of remaining study medications.

6.0. References

Health Canada, Food and Drug Regulations, Part C, Division 5, Drugs for Clinical Trials Involving Human Subjects, (Schedule 1024), June 20, 2001 .

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), ICH Harmonised Guideline, Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice, E6(R2), November 9, 2016.

Research Institute of McGill University Health Center, SOP-CR-016_07 Study Close-Out, 01-Sep-2018.

7.0 SOP Revision history

SOP code	Effective date	Summary of changes
SOP018_01Sep2022	26 Sep 2022	NA (original version)
SOP018_27Jun2023		Specification on virtual closing visit, need for REB renewal after site closure, updated appendix 1, update N of years for archiving.

APPENDIX 1

$2R^2$

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

CLOSING STUDY SITE IN *<site name>*
<date>

CLOSING STUDY SITES:

The objective of this check list is to ensure adequate site close-out of this clinical trial at each site participating in $2R^2$ study. We must ensure that no essential documents were missing, all participant file were well completed and entered in the $2R^2$ website data base. All Adverse Event, active TB and death were properly reported on the $2R^2$ website, all participant files were closed and stored in an appropriate place.

All sites must develop operational and staffing plans for completion of all required study closure procedures.

Please send this list to coordinating center once ready to close the site.

TO VERIFIED	CHECK
MASTER BINDER	
o Ensure that all Essential Study Documents and the study-related correspondence are in the Regulatory Master Binder;	
o Ensure that there are any outstanding required signatures;	
Note (if any):	
PHARMACY	
Ensure that all Essential Study Documents related to study medication dispensing and storage are in the Regulatory Master Binder;	
Ensure that there remaining study medications, if any, are recorder and appropriately stored.	
Note (if any):	
FINANCE	
o Ensure that all financial matters are in good standing (example: all site payments have been processed as agreed in the study contract);	
Note (if any):	
PARTICIPANT FILES	
o Ensure that all adverse events have been properly reported and dealt with (refer to 2R2 **SOP09** Adverse Event report & Management);	
o Ensure that all Active TB cases have been properly reported and dealt with as per **SOP08** "Active TB reporting");	
o Ensure that all Death have been properly reported and dealt with as per 2R2 **SOP07** "Follow-up post treatment");	

o Ensure that all participant files have been closed as per **SOP17** "Closing participant files";	
o Ensure that all PK sub-study sample were all sent to the coordinating center (for Canadian sites) or to the PK lab of prof. Rovina Ruslami, Bandung, Indonesia (in Vietnam sites), as per **SOP24** "shipping of PK samples";	
o Verify that all data queries have been appropriately resolved or addressed;	
o Check that all issues from previous monitoring, auditing, or inspection visits have been resolved and were documented;	
Note (if any):	

ANONYMIZING THE PARTICIPANT FILES	
o Ensure that all participant files were anonymized – participant file must not contain no directly identifiable information, such as name, initials, home address, or any Informed Consent Form. Documents must be identified with the study participant number (i.e. for source documents, the name must have been removed and the study participant number added);	
Note (if any):	

ARCHIVING	
o Ensure archiving arrangement for at least one copy of the Essential Study Documents (master binder) and participant files for a minimum of 15 year after completion of the entire study as calculated by the coordinating centre;	
o A site's plan for archiving must meet all applicable regulations and standards – including Good Clinical Practice;	
o Ensure that all participant identification form and consent/assent form are separate from the participant files and stored in a double locked room or in a specific storage place;	
o Ensure to print the Screening log and the List of participant identification codes for children/adults and stored in the same place as the consent form (double locked);	
o Storage should guarantee safety against disasters (e.g.: fire, floods etc) and confidentiality of the information contained in the participant file (i.e. it must be under lock);	
o Data must be retrievable in such a fashion that all information regarding each individual participant in a study is attributable to that participant specifically;	
o The site investigator must make sure that the persons in charge of the archive understand that participant files must not be destroyed - the coordinating centre will advise each site when they can have destroyed all the study documentation;	
o The plan must detail the transfer of responsibility for record retention in the event the investigator dies, retires, or for any other reason, must withdraw from assuming their record retention role;	
Note (if any):	

ETHIC	
o Notify the research ethics board overseeing the study site close-out using their procedures	
Note (if any):	

Plan for annual renewal of REB approval (if applicable at this site), until all analyses possible on the data collected are completed:
A)- People in charge of asking for annual REB's approval:

1. **Name:**_____

email address: _____

tel Number: _____

2. **Name:**_____

email address: _____

tel Number: _____

b) Place where the approvals will be stored once site is closed and master binder already archived:

STORAGE CONTACT information

Specific place of storage of all Study documents: _____

Hospital/storage company name: _____

Address:

Local (if applicable):

1st Person responsible of the study once in storage/Person to be contacted if the coordinating center need information regarding participants:

Full name: Phone number: Email: **2nd Person responsible of the study once in storage/Person to be contacted if the coordinating center need information regarding participants:** Full name: Phone number: Email:	