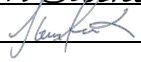
Title	Continuing Review
SOP Code	405.004
Effective Date	15-May-2023

Site Approvals

Name and Title (typed or printed)	Signature	Date MM/DD/YYYY
Meera Sidhu, Research Ethics Manager		02/13/2024
Steven Smith, Deputy VP Research		02/13/2024

1.0 PURPOSE

This standard operating procedure (SOP) describes the procedures for the continuing review of research overseen by the Research Ethics Board (REB) and the criteria for continued REB approval.

2.0 SCOPE

This SOP pertains to REBs that review human participant research in compliance with applicable regulations and guidelines.

3.0 RESPONSIBILITIES

All REB members and REB Office Personnel are responsible for ensuring that the requirements of this SOP are met.

The REB Chair or designee and the assigned REB reviewer are responsible for conducting an in-depth review of all submitted materials for their assigned research **ethics applications.** ~~**projects.**~~

All other REB members are responsible for reviewing the submitted materials for each research **ethics** application in enough depth to be prepared to discuss the research meaningfully at a Full Board meeting.

4.0 DEFINITIONS

See Glossary of Terms.

5.0 PROCEDURE

REBs must establish procedures for conducting the continuing review of approved research involving human participants at intervals appropriate to the degree of risk, but not less than once a year. A periodic review of research activities is necessary to determine whether approval should be continued or withdrawn.

5.1 Continuing Review by the Full Board

5.1.1 The Researcher is required to apply for continuing review of research at a frequency to be determined by the REB and which will be defined at the time of the initial approval of the research or as otherwise ~~**revised**~~ **advised by the REO.**

In Clinical Trials Ontario (CTO), submission of a Provincial Continuing Review (PCR) and a Centre Continuing Review (CCR), typically, the Provincial Applicant (PA) will submit a PCR and CCR. The overall status of the PCR should be inclusive and reflective of all CCRs. PCRs and CCRs will have the same expiry date.

In TRAQ, a renewal form is submitted. All queries in the renewal must be answered to completion.

With respect to HSREB and GREB, in consideration with the Chair and the Research Ethics Manager, the REB/Research Ethics Coordinators may ask for a new application or an amendment to be submitted for previously approved applications, particularly in the case where the application has had multiple amendments, including sub-studies. The renewal will be processed and approved but additional documentation/submission may be required within a specified amount of time.

5.1.2 At a minimum, the REB requires that an application for continuing review be submitted once per year until all of the data has been collected, all contact with research participants has concluded, and the REB has acknowledged the closure of the research.

If an application is being renewed through TRAQ, the expiry date of the application will reflect the last approved expiry date provided the event was submitted within 60 days prior to the existing expiry date. However, if a renewal is received after termination of the study in the system, so long as the renewal is received within 30 days of termination, the study will reflect the new expiry date (date of approval of the study renewal post termination). For studies reviewed at Full Board meetings, the renewal date will be the date of the meeting (i.e., when approval is granted).

In the CTO system, the expiry date will be the date of approval. This may change from year to year. The REO will take every effort to minimize the change in expiry date.

5.1.3 The REB may determine that the research requires continuing review more frequently than once per year by considering the following:

- The nature of any risks posed by the research,
- The degree of uncertainty regarding the risks involved,
- The vulnerability of the participant population,
- The projected rate of enrolment and estimated research closure date,
- Whether the research involves novel interventions,
- The REB believes that more frequent review is required.

A renewal may be submitted to the Full Board for review if the status of the research ethics application is:

- **Activated/open to enrollment: participants have been enrolled, but none are currently receiving study treatment/intervention**
- **Activated/open to enrollment with one or more study participant(s) receiving study treatment/intervention**
- **Activated/open to enrollment with current participants in follow-up only**
- **Permanently closed to enrolment, one or more study participant(s) receiving treatment/intervention**

The renewal status and risk level, Health Canada and FDA regulated status will be considered when determining the proportionate review level.

5.1.4 Continuing review applications are due by the deadline for the applicable REB meeting (i.e., the expiry date must be on or after the REB meeting date

and before the date of the subsequent REB meeting), regardless of the type of review they may undergo.

5.1.5 To assist the Researchers in submitting on time, a courtesy reminder(s) before the expiry date may be generated.

5.1.6 The responsible REB Office Personnel reviews the application for completeness and requests any clarifications, missing documents or other information from the Researcher, as applicable.

5.1.7 The REB may request verification from sources other than the investigator that no material changes have occurred since the previous REB review. For example:

- Based on the results of a prior audit or inspection (internal or external),
- Suspected non-compliance,
- Studies involving vulnerable populations,
- Studies involving a potentially high risk to participants,
- Suspected or reported protocol deviations,
- Participant or Research Staff complaints,
- Any other situation that the REB deems appropriate;

5.1.8 The responsible REB Office Personnel will assign the application to the agenda of the next REB meeting if the research meets the criteria for Full Board review;

In CTO, all CCRs will be reviewed via a delegated review before the Full Board meeting date. However, the PCRs will be reviewed via Full Board (if the criteria for a full board review are met). The expiry date of the PCR and all CCRs will reflect the board meeting date.

In TRAQ, all renewals will be reviewed either through a delegated review method or, if the criteria for a Full Board review are met, via a Full Board review method. The expiry date will be reflective of the date it was approved.

5.1.9 A summary report of the continuing review applications assigned to the REB meeting may be attached to the meeting agenda.

5.1.10 For research that meets the criteria for Full Board review, the REB will discuss the research at a Full Board meeting. It will decide on the continued approval of the research, as well as any other additional determinations regarding the conduct of the research, as applicable.

5.1.11 **The REB will communicate with the researcher about the decision of continuation by the REB or delegate re: the PCR, CCR or Renewal that has been approved via a Full Board review through a letter in the system and/or through the audit trail in the CTO system.**

5.2 Continuing Review by Delegated Review Procedures

5.2.1 When the research receives initial approval via delegated review, it may undergo delegated review at the time of continuing review.

5.2.2 Research that was previously reviewed by the Full Board may also be reviewed at the time of continuing review using delegated review procedures if the **appropriate** conditions are met;

• Continuing review of research that is more than minimal risk for which enrolment is closed permanently and all research-related interventions for all participants are complete and the only remaining research activities are post-intervention activities or follow-up of participants.

OR

• Where the remaining research activities are limited to data analysis.

OR

• Where no participants have been enrolled and no additional risks have been identified.

OR

• Continuing review of research that is more than minimal risk when there has been little or no modification of the research; and when there has been no increase in risk to or other ethical implications for participants since the initial review by the full REB; if permissible under all applicable governing regulations.

A renewal will be sent to delegated review if the status of the study is:

- **Not yet activated,**
- **Activated, but no participants enrolled to date,**
- **Permanently closed to enrolment, no participants are receiving treatment/intervention, and all study participants are in long term follow up or data collection continues,**
- **Study completed (i.e., no further involvement of study participants and no further data collection).**

5.2.3 The responsible REB Office Personnel reviews the continuing review application for completeness, including verification of the currently approved informed consent form(s), and requests any clarifications, missing documents or other information as applicable.

5.2.4 The responsible REB Office Personnel will forward the application to the appropriate REB reviewer **or qualified REB Office Personnel**.

5.2.5 The reviewer may request additional information or clarification, as necessary, and will make a decision regarding the continued approval of the research and the continued conduct of the research.

5.2.6 Upon reviewing an application that was sent for delegated review, if the reviewer determines that the risks are now greater than minimal, the reviewer will refer the application for review by the Full Board.

5.2.7 **The REB will communicate with the researcher about the decision of continuation by the REB or delegate re: the CCR or Renewal that has been approved via a Delegated review through communication in the TRAQ system and/or through the audit trail in the CTO system.**

5.3 REB Determinations

5.3.1 To grant a continuation of the approval of the research the REB must determine that:

- There have been no material changes to the research or to the informed consent form that have not been previously submitted and approved, **these should be submitted to the REB as they**

occur via a provincial amendment (PAM) in CTO or an amendment in TRAQ.

- There is no new conflict of interest or new information that has emerged that might adversely affect the safety or the well-being of research participants,
- Risks to research participants are minimized and reasonable in relation to the anticipated benefits,
- Selection of research participants is equitable,
- Informed consent processes continue to be appropriate and documented,
- Adequate provisions are in place for monitoring and data protection to ensure the safety and privacy of participants and confidentiality and integrity of the data,
- Any complaints from research participants have been followed up appropriately.

5.3.2 The REB may also make additional determinations, including:

- Request changes to the informed consent form(s),
- Request changes for the continuing review interval (based on risks),
- Impose special precautions (e.g., frequency of monitoring, the requirement for interim reports or duration of approval period),
- Require modifications to the research,
- Suspend or terminate REB approval.

5.4 Continuing Review Applications not Received by the Expiry Date

5.4.1 ~~**If an application for continuing review is not submitted by the expiry date, a warning or suspension notice will be issued to the Researcher. a termination notice will be issued. When suspended, terminated the Researcher must suspend stop all research activities as specified by the REB. The responsible REB Office Personnel will follow-up with the Researcher to ensure that the application for continuing review is submitted as soon as possible;**~~

If an application for continuing review is not submitted by the expiry date, **a termination notice will be issued.** When **terminated,** the Researcher must **stop** all research activities as specified by the REB.

In CTO, if a PCR is not received by the expiry date, the PCR and all related CCRs will be terminated.

In CTO, if a PCR is received by the expiry date any centres whose CCR was submitted by the expiry date will receive approval to continue but any outstanding CCRs will result in that particular centre being terminated.

In TRAQ, if a renewal is not submitted by the renewal expiry date, the study will be terminated.

If a renewal application is submitted within 30 days following termination, the application may be re-opened, and renewal accepted with the lapse of ethics approval documented. The researcher will have to provide a reason for the late submission of the application and describe steps to take so this does not occur again.

If a renewal is not submitted at the end of 30 days and the researcher wishes to re-open the study, a new application is required to be submitted to the REB.

NOTE: in the TRAQ system, researchers are given 2 renewal reminders (4 weeks prior to the renewal date and 2 weeks prior to the renewal date).

5.4.2 In the event of a lapse in approval, the Researcher is responsible for notifying the REB if there is a need to continue research-related medical treatment of current research participants for their safety and well-being. The Researcher should provide as much detail as possible about the proposed continued activities. The REB Chair or designee will review the request as quickly as possible and discuss the proposed continued activities with the Researcher; **In the event of ethical approval lapse, all research-related activities must cease until REB approval is re-established.**

5.4.3 The Researcher must document the reasons for the lapse and identify the steps taken to prevent future lapses.

5.4.4 Suppose the REB approval lapses and the Researcher wants to continue with the research. In that case, the REB will complete the review of the research as soon as possible and the Researcher may resume the suspended activities once approval of the research has been issued. The lapse in approval will be documented.

The REB Office Personnel may close a new application that has been sitting in the system 'untouched' or not responded to by the study team/applicant after six (6) months.

The REB Office Personnel may close an event or amendment that has been sitting in the system 'untouched' or not responded to by the study team/applicant after three (3) months.

If an application contains documents (i.e., an informed consent form, other participant facing documents), that are five (5) years or older, the REB Office Personnel will request updated documents to be submitted to the REB Office Personnel/REB for re-review.

The REB Office Personnel may request that studies approved as "umbrella studies" or those not containing information in the electronic application system be re-submitted as a new initial application and subjected to a new REB review.

6.0 REFERENCES

See References.

7.0 REVISION HISTORY

SOP Code	Effective Date	Summary of Changes
SOP405.001	15-Sept-2014	Original version
SOP405.002	08-Mar-2016	No revisions needed
SOP405.003	08-Oct-2019	No revisions needed
SOP405.004	15-May-2023	No revisions needed
SOP405.004	1-Dec-2023	Queen's Specific Revisions/Clarifications added to the N2 SOPs with modifications in bolded text
SOP405.004	13-Feb-2024	Queen's Specific Clarifications added to the N2 SOPs re: renewal dates in bolded text.