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| <b>SOP Title</b>      | <b>Continuing Review</b> |
| <b>Number.Version</b> | N406.003                 |
| <b>Effective Date</b> | 02/27/2025               |

## Approvals

| <b>Name and Title of Signatories</b>                         | <b>Signature</b>   | <b>Date<br/>mm/dd/yyyy</b> |
|--|--|----------------------------|
| Erika Basile<br>Director, Research Ethics and Compliance     |  | Mar 3, 2025                |
| Dr. Isha DeCoito<br>Chair, Non-Medical Research Ethics Board |  | Mar 4, 2025                |

## 1. PURPOSE

This Standard Operating Procedure (SOP) describes the procedures for the continuing review of research that has been approved by the NMREB and is overseen by the Non-Medical Research Ethics Board (NMREB) and the criteria for continued NMREB review.

## 2. GENERAL POLICY STATEMENT

Research involving human participants is subject to continuing review from the date of the initial NMREB approval throughout the life of the study. The Research Ethics Board must establish procedures for conducting the continuing review of approved research studies, at intervals appropriate to the degree of risk, but not less than once a year. For multi-year research studies, a Continuing Ethics Review (CER) Form must be submitted on an annual basis. For studies lasting less than one year, a Study Closure Form must be submitted. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn.

## 3. RESPONSIBILITY

This SOP is applicable to the Office of Human Research Ethics (OHRE), NMREB Chair, Vice-Chair(s) and NMREB members.

The NMREB Chair, Vice- Chair(s) and assigned NMREB members are responsible for conducting an in-depth review of all progress reports for their assigned research projects. For research studies requiring review at a convened NMREB meeting, appropriate documentation for the review will be available to all NMREB members

## 4. DEFINITIONS

See Glossary of Terms

## 5. SPECIFIC POLICIES AND PROCEDURES.

### 5.1. Continuing Review by the Full Board

5.1.1. Investigators are required to submit an application for continuing review using the CER Form at a frequency determined by the NMREB at the time of initial approval but not less than once per year;

5.1.2. The OHRE must review the CER form, at a minimum, once per year until all data have been collected, contact with study participants has concluded and a Study Closure Form has been acknowledged by the OHRE;

5.1.3. The OHRE 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 study,
- The degree of uncertainty regarding the risks involved,
- The vulnerability of the participant population,
- The experience of the Investigators in conducting research,
- The NMREBs previous history with the investigators,
- The projected rate of enrollment; and estimated study closure date,
- Whether the research study involves novel interventions;

5.1.4. It is the Investigator's responsibility to submit the CER form on time. To assist the Investigators, the OHRE staff will send a courtesy reminder at different time points prior to the expiry date. Should an Investigator fail to submit the CER form despite the reminder/follow-up notifications, a notice that NMREB approval has expired will be issued and the study will be suspended. If the CER form is still not submitted within 2 weeks of the study expiry date the NMREB may close the file and Investigators will be required to submit a new study. If the CER form is submitted after the expiry date but before file closure this will result in a lapse in NMREB approval. The OHRE may also elect to pursue investigations for serious or continuing non-compliance.

5.1.5. Once the CER form is submitted, the Ethics Officer (EO)/Ethics Coordinator (EC) reviews the application for completeness and may request any clarifications, or missing documents or information, if applicable.

5.1.6. The NMREB may request verification from sources other than the investigator that no material changes have occurred since previous NMREB review. For example,

- Based on the results of a previous 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 NMREB deems appropriate;

5.1.7. The EO will assign the application to the agenda of the next applicable NMREB meeting;

5.1.8. The NMREB will discuss the research study and make a decision regarding the continued approval of the research as well as any additional determinations regarding the conduct of the research study, if applicable.

## **5.2. Continuing Review by Delegated Review**

5.2.1. Research that was previously reviewed by delegated review procedures may be reviewed at the time of continuing review using delegated review procedures. However, if the NMREB Chair, or designee, determines that the risks are now more than minimal, the NMREB Chair, or designee, will refer the study for Full Board review at a convened NMREB meeting. The NMREB will discuss the research at a convened meeting and will make a decision regarding the continued approval of the research as well as any other additional determinations regarding the conduct of the research, as applicable;

- 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 when there are minimal risk changes;
- 5.2.3. The EO/EC reviews the continuing review application for completeness, including verification of the currently approved Letter(s) of Information, and may request any clarifications, or missing documents or information, if applicable;
- 5.2.4. The EO/EC distributes the renewal progress reports to the NMREB Chair, or designee, for review;
- 5.2.5. The NMREB Chair, or designee, will make a decision regarding the continued approval of the research study.

### 5.3. NMREB Determinations

5.3.1. For continuation of approval to be issued, the NMREB must determine that:

- There have been no material changes to the study protocol or Letter(s) of Information/Consent that have not been previously submitted and approved,
- There is no conflict of interest or new information that has emerged that might adversely affect the safety or well-being of study participants,
- Risks to research participants are minimized and reasonable in relation to the anticipated benefits,
- Letter(s) of Information continue to be compliant with applicable guidelines, regulations and policies;

5.3.2. The NMREB may also make additional determinations, including:

- Requiring changes to the Letter(s) of Information,
- Requiring changes for the continuing review interval (based on risks),
- Imposing special precautions (e.g., frequency of monitoring, the requirement, for interim reports or duration of approval period),
- Lifting or relaxing special precautions,
- Requiring modifications to the research,
- Suspending or terminating NMREB approval;

### 5.4. Continuing Ethics Review not Received by the Expiry of the Continuing Ethics Review Period

- 5.4.1. If the CER form for continuing review is not submitted by the expiry date, a warning or suspension notice will be issued to the Investigator. When suspended, the Investigator must suspend all study related activities as specified by the NMREB. The responsible NMREB Office Personnel will follow-up with the Investigator to ensure that the application for continuing review is submitted as soon as possible;
- 5.4.2. In the event of a lapse in approval, it is the Investigator's responsibility to promptly notify the OHRE if there are safety related needs that require study participants to continue to receive study related treatments/procedures. The NMREB Chair or designee will review the request as quickly as possible and discuss the proposed continued activities with the Investigator;
- 5.4.3. The Investigator must document the reasons for the lapse and identify the steps taken to prevent future lapses. These activities will be documented and filed;

5.4.4. If the NMREB approval lapses and the Investigator wants to continue with the research, the NMREB will complete the review of the research as soon as possible and the Investigator may resume the suspended activities once approval of the research has been issued. The lapse in approval will be documented.

5.4.5. If the CER form is still not submitted within 2 weeks of the study expiry date the NMREB may close the file and Investigators will be placed on Hold and unable to submit any new applications or amendments until the file is back in good standing. The Ethics Officer will review the CER form and assign the form to the next Full Board meeting for review. The Board must vote to re-open the study or not. If the CER form is submitted after the expiry date but before file closure this will result in a lapse in NMREB approval. The OHRE may also elect to pursue investigations for serious or continuing non-compliance.

**6. References**

- 6.1. Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans 2022 (TCPS2); Article 2.8 and 6.12;
- 6.2. US Office for Human Research Protections (OHRP) Code of Federal Regulations (CFR) Title 45 Part 46.109, 46.111, 46.113, 46.115;
- 6.3. OHRP Guidance on Continuing Review.

**7. SOP HISTORY**

| <b>SOP Number.Version</b> | <b>Key Changes</b>  | <b>Effective Date<br/>mm/dd/yyyy</b> |
|---------------------------|---|--------------------------------------|
| N406.001                  | Original  | 07/07/2016                           |
| N406.002                  | Administrative revisions  | 05/11/2018                           |
| N406.003                  | Updated NMREB Chair, Administrative changes,<br>Updating information regarding Board Voted Closures | 02/27/2025                           |