TITLE	**405: Continuing Review**
SCOPE	All health research submitted to the Health Research Ethics Board (HREB) operating under the direct authority of the Health Research Ethics Authority (HREA)
APPROVAL AUTHORITY	Ethics Director
EFFECTIVE DATE	April 2024

1.0 PURPOSE

This standard operating procedure (SOP) describes the procedures for the continuing review of research that is overseen by the HREB, and the criteria for continued HREB approval.

2.0 DEFINITIONS

See the Glossary of Terms.

3.0 RESPONSIBILITIES

HREB members and Research Ethics Office (REO) Personnel are responsible for ensuring that the requirements of this SOP are met.

The HREB Chairperson or designee and the assigned HREB reviewer are responsible for conducting an in-depth review of all submitted materials for their assigned research projects.

All other HREB members are responsible for reviewing the submitted materials for each research application and be prepared to discuss the research at a Full Board meeting.

4.0 PROCEDURE

The HREB will conduct continuing review of approved research taking place within its jurisdiction at intervals appropriate to the degree of risk to which participants are exposed, but not less than once per year. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn.

4.1 Continuing Review by the Full Board

4.1.1 The Researcher is required to submit an Event for continuing review of research at a frequency to be determined by the HREB and which will be defined at the time of the initial approval of the research, or as otherwise revised.

4.1.2 At a minimum, the HREB requires that an application for continuing review (i.e. annual renewal) be submitted once per year until all of the data has been collected, all contact with research participants has concluded and the closure of the research has been acknowledged by the HREB.

4.1.3 The HREB 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; and
- the HREB believes that more frequent review is required.

4.1.4 Continuing review applications are due by the deadline for the applicable HREB meeting (i.e., the expiry date must be on or after the HREB meeting date and prior to the date of the subsequent HREB meeting), regardless of the type of review they will undergo.

4.1.5 To assist the Researchers in submitting on time, courtesy reminders prior to the expiry date will be generated.

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

4.1.7 The HREB may request verification from sources other than the investigator that no material changes have occurred since previous HREB 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; and
- any other situation that the HREB deems appropriate.

4.1.8 The responsible REO Personnel will assign the application to the agenda of the next applicable HREB meeting, as per submission deadlines, if the research meets the criteria for Full Board review.

4.1.9 Only one primary reviewer will be assigned to the submission at the Full Board.

4.1.10 A summary report of the continuing review applications assigned to the HREB meeting will be attached to the HREB meeting agenda.

4.1.11 For research that meets the criteria for Full Board review, the HREB will discuss the research at a Full Board 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.

4.1.12 Continuing review of studies funded by the U.S. Federal Government or regulated by the U.S. Food and Drug Administration must be reviewed by the Full Board unless they meet the

following criteria:

- the research is (i) permanently closed to the enrollment of new participants; (ii) all participants have completed all research-related interventions; and (iii) the research remains active only for long-term follow up of participants; OR
- where no participants have been enrolled and no additional risks have been identified; OR
- where the remaining research activities are limited to data analysis.

4.2 Continuing Review by Delegated Review Procedures

4.2.1 When the research received initial approval via delegated review it may undergo delegated review at the time of continuing review.

4.2.2 Research that was previously reviewed by the Full Board will be reviewed at the time of continuing review using delegated review procedures if the conditions for delegated review criteria are met.

4.2.3 The responsible REO 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.

4.2.4 The responsible REO Personnel will forward the application to the appropriate HREB reviewer.

4.2.5 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.

4.2.6 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.

4.3 HREB Determinations

4.3.1 In order to grant a continuation of the approval of the research the HREB 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;
- 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;
- where applicable, the reports of Data Safety Monitoring Boards and Sponsor-generated Safety Reports are favourable for continuation of the study;
- there is no new literature/information which might affect the willingness of study participants to participate; and
- any complaints from research participants have been followed-up appropriately.

4.3.2 The HREB 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; and
- suspend or cancel the research project.

4.4 Continuing Review Applications not Received by the Expiry Date

4.4.1 Approvals shall expire on the anniversary date of their original approval pursuant to a Full Board meeting or the delegated review process.

4.4.2 If an application for continuing review is not submitted with all required information by the expiry date, a suspension notice will be issued to the Researcher. When suspended, the Researcher must suspend all research activities as specified by the HREB. The responsible REO Personnel will follow-up with the Researcher to ensure that the application for continuing review is submitted as soon as possible.

4.4.3 No research-related activities are permitted to occur after the approval expiration date unless the Researcher contacts the HREB and a determination is made that it is in the best interest of individuals to continue during the lapse in HREB approval.

4.4.4 In the event of a lapse in approval, the Researcher is responsible for notifying the HREB if there is a need to continue research-related medical treatment of current research participants for their safety and well-being. The Researcher will provide as much detail as possible about the proposed continued activities. The HREB Chairperson or designee will review the request as quickly as possible and discuss the proposed continued activities with the Researcher.

4.4.5 In the event of a lapse in approval, the Researcher must submit a letter outlining the reason(s) for the lapse and identify the steps taken to prevent future lapses. This letter will be stored in the study file.

4.4.6 If the HREB approval lapses and the Researcher wants to continue with the research, the HREB 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 date for subsequent approvals shall continue to be the anniversary date of the original approval, unless otherwise stated in the approval letter.

4.5 U.S. Federally Funded Research

4.5.1 Studies that are funded or supported by the U.S. federal government are considered open and subject to annual review requirements until a research project no longer involves human subjects, as defined by the Office of Human Research Protections (OHRP). OHRP considers a research project to no longer involve human subjects when investigators have finished obtaining data through interaction or intervention with subjects or obtaining identifiable private information about the subjects which includes the using, studying, or analyzing identifiable private information (including identifiable tissue).

5.0 REFERENCES

The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, Chapters 2 and 6: Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2022) (ethics.gc.ca)

International Conference on Harmonization – Good Clinical Practice (ICH-GCP 3.1.4): ICH GCP - 3. INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE (IRB/IEC) - ICH GCP

U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46): Electronic Code of Federal Regulations (eCFR)

U.S. Department of Health and Human Services – Title 21 Code of Federal Regulations Part 56 (21 CFR 56): Electronic Code of Federal Regulations (eCFR)

Office for Human Research Protections, Continuing Review Guidance: Continuing Review Guidance (2010) | HHS.gov

Health Research Ethics Authority Act: An act to establish a health research ethics authority for the province. (2011). Retrieved from: SNL2006 CHAPTER H-1.2 - HEALTH RESEARCH ETHICS AUTHORITY ACT (assembly.nl.ca)