Research Ethics Boards – Continuing Review

25.5.509.1

PROCEDURE

Procedures are a series of required steps to complete a task, activity or action

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Purpose:	• To provide Island Health a description of the policy and notice requirements for annual (interval) renewals and related continuing review prior to the expiration of the Research Ethics Board (REB) approval period. It should be read together with standard operating procedure (SOP) 508 Ongoing Research Ethics Board Review Activities which articulates the Boards' responsibilities, policies and processes for conducting on-going review (continuous oversight) of approved projects. • This SOP will also outline the process to be followed by REB Office Personnel to track and monitor continuing review submissions. The SOP will delineate the options of the REB in the event that the Principal Investigator (Investigator) fails to comply with the requirement to notify the REB, on at least an annual basis, of the status of the approved study.
Context:	Island Health offers programs and services on the unceded and traditional territories of the Coast Salish, Nuu-chah-nulth, and Kwakwaka'wakw Peoples. As a signatory to the 2015 Declaration of Commitment to Cultural Safety and Cultural Humility, Island Health is committed to addressing the ongoing impacts of colonialism and Indigenous-specific racism in order to provide a culturally safe, inclusive, healthy and respectful environment. The organization is committed to strengthening diversity, equity and inclusion to enable excellence in health and care for everyone, everywhere, every time. Through these commitments, Island Health strives to deliver the highest possible standard of care and to promote safe workplaces.

Scope:	• **Audience:**
	  ○ All REB Chairs
	  ○ All REB Members
	  ○ All REB Office Personnel
	• **Environment:**
	  ○ Research Environment
	• **Indications**: This Standard Operating Procedure (SOP) applies to all research submitted to the Island Health's REBs.
	• **Exceptions**: None.

Outcomes:	• Procedures for the continuing review of research that is overseen by the REBs and the criteria for continued REB approval.

1.0 Responsibility

- 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/or the assigned REB reviewer are responsible for conducting an in-depth review of all submitted materials for their assigned research studies.
- If required, all other REB members are responsible for reviewing the submitted materials for each research application in enough depth to be prepared to discuss the research meaningfully at a Full Board meeting.

2.0 Procedure

- The REBs conduct continuing review of approved research involving human participants at intervals appropriate to the degree of risk to which participants are exposed, but not less than once per year. The Island Health REBs make the determination concerning the duration of the approval period and the interval by which continuing review must occur at the time of initial review and approval.

2.1 Continuing Review by the Full Board

- The Researcher is required to submit an application 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.
- 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 closure of the research has been acknowledged by the REB.
- The REB requires continuing review progress reports on an annual basis unless they designate otherwise.
- 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; and
    - The REB believes that more frequent review is required.
- 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 prior to the date of the subsequent REB meeting), regardless of the type of review they may undergo.
- To assist the Researchers in submitting on time, courtesy reminders prior to the expiry date will be generated as outlined below:
    - The research will be reviewed before the one-year anniversary date of the previous REB approval even though the research activity may not have begun until sometime after the REB approval;
    - Investigators or qualified designees are required to submit an Annual Renewal Application form and other materials as outlined on the form. The application form should normally be submitted at least six weeks before the study approval period ends;
- Renewal notices will be sent out to the researchers by REB Office Personnel at least six weeks in advance of the REB meeting that falls immediately prior to expiry of the approval, and again at least three weeks in advance of the REB meeting if no renewal application has been received. This allows for the renewal to be added to the Full Board agenda, if required, once assessed.The responsible REB Office Personnel reviews the application for completeness, and requests any clarifications, missing documents, or other information from the Researcher, as applicable.
- The REB may request verification from sources other than the Investigator that no material changes have occurred since previous REB 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 REB deems appropriate.

- 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.
- Only one primary reviewer will be assigned to the submission at the Full Board.
- A summary report of the continuing review applications assigned to the REB meeting may be attached to the REB meeting agenda.
- For research that meets the criteria for Full Board review, the REB 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.
- 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 clearly 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.
- The REB Chair or designate can put a request forward for continuing review by the Full Board at any time.
- Annual renewals will be reviewed by the Full Board if required by the study Sponsor, Funding Agency, or Regulatory Agency.

2.2 Continuing Review by Delegated Review Procedures

- When the research received initial approval via delegated review it may undergo delegated review at the time of continuing review.
- 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 conditions for delegated review criteria are met.
- 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.
- If required, the responsible REB Office Personnel will forward the application to the appropriate REB reviewer.
- 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.
- If, 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.

2.3 REB Determinations

- Continuing review must be substantive and meaningful, the rigour of which shall be in accordance with a proporationate approach to ethics assessment. In order 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;
  - 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 (DSMB) 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;
  - Any complaints from research participants have been followed-up appropriately.
- 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.
- Island Health's REBs have the authority to determine which research activities require verification from sources other than the Researcher. This may be during the conduct of the research project in the course of an on-going review as described in SOP 508 Ongoing Research Ethics Board Review Activities, or at the time of annual (interval) renewal.
- The criteria that the Boards will use to determine if such a third party verification is required shall include, but not be limited to:
  - If information provided by the Investigator is internally inconsistent or inconsistent with other information known to the REB, and the inconsistency cannot be satisfactorily resolved by communications with the Investigator;
  - If the Board has reasons to doubt the veracity of the information provided by the Investigator;
  - If the Investigator has a history of serious or continuing non-compliance with continuing review requirements in the past three years; or
  - If the Board has other reasons in which it believes that verification from sources other than the Investigator that no material changes have occurred since prior REB review is required.

- If the Board determines that external verification is required, it will direct REB staff to obtain verification from sources other than the Investigator that no material changes have occurred since prior REB review and to report back at a future convened meeting.

2.4 Required Information and Documentation

- The following information and documentation is required to be included with continuing review submissions:
  - An assessment of whether the annual renewal qualifies for delegated review based upon the delegated review criteria for the applicable REB;
  - Whether or not the study involves enrollment of human participants;
  - Whether or not the study is currently open to enrollment, or will be open in the future for enrollment. If so, the consent and/or assent form(s) must be current;
  - The number of participants enrolled at institutions covered by the REB approval certificate;
  - The enrollment goal;
  - The number of participants who discontinued their participation; and a summary of the reasons for the withdrawals if known;
  - A summary of the progress of the study including any summary reports;
  - A summary of the impact of all unanticipated problems, including serious and unexpected adverse events either observed throughout the study period or submitted to the Principal Investigator by the Sponsor for other sites in multicenter trials;
  - Whether there are any outstanding actions that the REB has requested the Investigator to take with regard to an unanticipated problem, serous adverse events (SAE) or safety letter, and if so, an explanation of same;
  - A summary of recent findings and new information, including changes in the Investigator's situation or qualifications;
  - Based on the information provided, an opinion on whether any changes should be made to the protocol or the consent form;
  - A summary of any monitoring that took place, including any reports from any third party observations of the research carried out under U.S. Federal Regulations;
  - Any changes in conflict of interest since the last approval;
  - A summary of any complaints about the research from participants or others since the last REB Review,
  - If the study has expired, and the renewal is being completed with the permission of the REB Chair or qualified Office Personnel, a written explanation for the late renewal and confirmation by the Investigator that NO study related actions took place during the time over which there was no valid ethics approval; and
  - Additional comments and information or documents, including reports from Data Safety Monitoring Boards (DSMBs) or Data Monitoring Committee (DMC)s that are available.

2.5 Continuing Review Applications Not Received By The Expiry Date

- Approvals shall expire on the anniversary date of their original approval at a Full Board meeting, or the date they were approved pursuant to the delegated review process.
- If an application for continuing review is not submitted by the expiry date, a warning or suspension notice will be issued to the Researcher by REB Office Personnel. When suspended, the Researcher must suspend 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.

- No research-related activities may occur after the approval expiration date unless the Principal Investigator contacts the REB and a determination is made that it is in the best interest of individuals to continue during the lapse in REB approval.
- 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.
- The Researcher must document the reasons for the lapse and identify the steps taken to prevent future lapses.
- If the REB approval lapses and the Researcher wants to continue with the research, 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 Coordinator in consultation with the relevant REB Chair or the Manager, Research Ethics & Compliance is fully authorized to do one or more of the following as deemed appropriate:
    - Hold the review or approval of current or future submissions by the Principal Investigator or their Department until the status of the expired study has been addressed;
    - Notify the funding agency, industry sponsor or the appropriate regulatory authority of the expiry of the ethics approval for the study;
    - Notify Research Finance personnel to advise them that the study is no longer approved and that no further funds from the account should be released; and
    - Terminate the study in the online database system.

2.6 U.S. Federally Funded Research

- 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).**

2.7 Training

- Review of the SOP 509.1 Research Ethics Boards – Continuing Review

2.8 Compliance Monitoring

- The Island Health Manager, Research Ethics & Compliance or their delegate is responsible for ongoing monitoring of Island Health operations to verify compliance with this SOP.
- The Island Health Manager, Research Ethics & Compliance or their delegate is responsible for communicating any changes to this SOP to all relevant personnel.
- Deviations from this SOP will be addressed through corrective and preventative action implementation.

3.0 Definitions

- **Research Ethics Board Chair**: is responsible for ensuring that the REB review process conforms to the requirements of this Policy.
- **Research Ethics Office Personnel:** Current employees of Island Health that make up the supporting structure for administration of Research Ethics Board(s).
- **Research Ethics Board EB Members:** Current members of the Research Ethics Boards according to the roster.
- **Full Research Ethics Board (REB) review:** the level of Research Ethics Board (REB) review assigned to above minimal risk research studies. Conducted by the full membership of the REB, it is the default requirement for the ethics review of research involving human participants.
- **Researcher:** the leader of a research team who is responsible for the conduct of the research, and for the actions of any member of the research team. (Also known as "Qualified Investigator").
- **Prinicpal Investigator (Investigator):** is responsible for ensuring that the consent process is followed. This person is also responsible for the actions of any member of the research team involved in the consent process.
- **Continuing research ethics review** (also referred to as "continuing review"): any review of ongoing research conducted by a Research Ethics Board (REB) occurring after the date of initial REB approval and continuing throughout the life of the project to ensure that all stages of a research project are ethically acceptable in accordance with the principles in the Policy.
- **Non-compliance**: failure to follow applicable guidelines and regulations governing human participant research; failure to follow the protocol approved by the Research Ethics Board (REB), or failure to follow stipulations imposed by the REB as a condition of approval.
- **Protocol deviation**: the term protocol deviation is not well defined by regulations or guidelines, but deviations are identified as any unplanned or unforeseen change to a Research Ethics Board (REB) approved protocol or protocol procedures. Deviations are different from amendments in that they generally apply to a single occurrence or participant and are not intended at the time to modify the entire protocol.

4.0 Related Island Health Policy Documents

- Continuing Review – Research Ethics Board Process for Expired Studies
- Ongoing Research Ethics Board Review Activities

5.0 References

- Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada. (2022). Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2022). (Chapter 2, Article 2.8).
- Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada. (2022). Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2022). (Chapter 6, Article 6.14).
- Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada. (2022). Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2022). (Chapter 2, Article 2.9).
- Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada. (2022). Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2022). (Chapter 6, Article 6.12).

- Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research, 45 C.F.R. § 46.110b(2) (2023).
- Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research, 21 C.F.R. § 56.110 (2023).
- International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline – Guidelines for Good Clinical Practice E6(R2).(2016). (3.1.4).
- IRB Review of Research, 45 C.F.R. § 46.109e (2023).
- IRB Review of Research, 21 C.F. R. § 56.109f (2023).
- Office for Human Research Protections (2010). Continuing Review Guidance.

6.0 Resources

- Network of Networks (N2), SOP 405.003 Continuing Review
- University of British Columbia, SOP 405: *Continuing Review*
- Refer to The Glossary – Research Ethics

7.0 Summary of Changes

Version	Effective Date	Change Description
1.0	01 SEP 2013	New procedure
2.0	12 JAN 2024	Name changed from Annual Renewals to Continuing Review. Control number revised to SOP 509.1 to differentiate between 'SOP 509.2 Continuing Review – Research Ethics Board Process for Expired Studies' that addresses process for expired studies. Issuing Authority changed from Research & Capacity Building to Vice President Quality, Research & Chief Nursing & Allied Health Officer.