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THE UNIVERSITY OF BRITISH COLUMBIA

SOP 405

TITLE	**405: Continuing Review**
SCOPE	All research submitted to the University of British Columbia's Research Ethics Boards
RESPONSIBILITIES	The Vice-President, Research & Innovation, delegated to the Director, Office of Research Ethics, all Research Ethics Board (REB) Chairs and members and all REB Office Personnel
APPROVAL AUTHORITY	The Vice-President, Research & Innovation
EFFECTIVE DATE	May 2018
Supersedes documents dated	August 2013, May 2011, March 2010, April 2009; July 2003

1.0 PURPOSE

The purpose of this standard operating procedure (SOP) is to describe the policy and notice requirements for annual (interval) renewals and related continuing review prior to the expiration of the REB approval period. It should be read together with SOP 404 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 fails to comply with the requirement to notify the REB, on at least an annual basis, of the status of the approved study.

2.0 DEFINITIONS

See the Glossary of Terms.

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 projects.

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.

4.0 PROCEDURE

The REBs conduct continuing review of approved research taking place within their jurisdiction at intervals appropriate to the degree of risk to which participants are exposed, but not less than once per year[1]. The UBC 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].

4.1 Continuing Review by the Full Board

4.1.1 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;

4.1.2 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 closure of the research has been acknowledged by the REB;

4.1.3 The REB requires continuing review progress reports on an annual basis unless they designate otherwise;

4.1.4 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;

4.1.5 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), regardless of the type of review they may undergo;

4.1.6 To assist the Researchers in submitting on time, courtesy reminders prior to the expiry date will be generated as outlined in Administrative SOP 405a;

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

4.1.8 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;

4.1.9 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;

4.1.10 Only one primary reviewer will be assigned to the submission at the Full Board,

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

4.1.12 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.

4.1.13 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[3]:

- 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;

4.1.14 The REB Chair or designate can put a request forward for continuing review by the Full Board at any time;

4.1.15 Annual renewals will be reviewed by the Full Board if required by the study Sponsor, Funding Agency, or Regulatory Agency,

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 may also 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 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;

4.2.4 The responsible REB Office Personnel will forward the application to the appropriate REB 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 REB Determinations

4.3.1 Continuing review must be substantive and meaningful, the rigour of which shall be in accordance with a proportionate approach to ethics assessment[4]. 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 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;

4.3.2 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;

4.3.3 UBC'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 on-going review as described in SOP 404, or at the time of annual (interval) renewal;

4.3.4 The criteria that the Boards will use to determine if such 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 two 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;

4.3.5 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;

4.4 Required Information and Documentation

4.4.1 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 multi-centre trials,
- Whether there are any outstanding actions that the REB has requested the Investigator to take with regard to an unanticipated problem, 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 Manager pursuant to Administrative SOP 405a, 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,

- Additional comments and information or documents, including reports from DSMBs or DMCs that are available.

4.5 Continuing Review Applications not Received by the Expiry Date

4.5.1 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;

4.5.2 If an application for continuing review is not submitted with all required information by the expiry date, a warning or suspension notice will be issued to the Researcher. 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;

4.5.3 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;

4.5.4 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;

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

4.5.6 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;

4.5.7 The REB Manager in consultation with the relevant REB Chair or the Director, Office of Research Ethics 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 his/her 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 financial accounts personnel to advise them that the study is no longer approved and that no further funds from the account should be released,
- Terminate the study in the RISe system.

4.6 U.S. Federally Funded Research

4.6.1 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

1. *UBC Policy 89*, section 3.1:
http://universitycounsel.ubc.ca/files/2012/06/policy89.pdf

2. *The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, Article 2.8:
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter2-chapitre2/#toc02-1a
The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, Article 6.14:
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter6-chapitre6/#ch6_en_a6.14
International Conference on Harmonization – Good Clinical Practice (ICH-GCP 3.1.4):
http://ichgcp.net/3-institutional-review-boardindependent-ethics-committee-irbiec
U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.109(e)):
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.109
U.S. Department of Health and Human Services – Title 21 Code of Federal Regulations Part 56 (21 CFR 56.109(f)):
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=56.109

3. *U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.110(b)(2)):*
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.110
U.S. Department of Health and Human Services – Title 21 Code of Federal Regulations Part 56 (21 CFR 56.110(b)(2)):
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=56.110
Office for Human Research Protections, Continuing Review Guidance:
https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-continuing-review-2010/index.html

4. *The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, Article 2.9:
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter2-chapitre2/#ch2_en_a2.9
The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, Article 6.12:
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter6-chapitre6/#ch6_en_a6.12