RR0400—CONTINUING REVIEW

1.0 PURPOSE

To provide direction for the continuing ethics review of research involving human participants by the Interior Health (IH) Research Ethics Board (REB).

2.0 DEFINITIONS

TERM	DEFINITION
Amendment	A written description of a modification or change(s) to the previously approved research study. Amendments include any changes to the protocol or related research documents.
Continuing Ethics Review	Any review of ongoing research conducted by the 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 of the Tri-Council Policy Statement.
Minor Change	Any change that would not materially affect an assessment of the risks and benefits of the research or the integrity of the data, and does not substantially change the specific aims or design of the study.
Protocol Deviations	The term protocol deviation is not well defined by regulations or guidelines, but deviations are identified as any unplanned or unforeseen change to a 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.
Renewal	A request for renewal of ethical approval for a project that continues on past the term of initial approval.
Unanticipated Issues	Issues that occur during the conduct of research; may increase the level of risk to participants or have other ethical implications that may affect participants' welfare; and were not anticipated by the Researcher in the research proposal submitted for research ethics review.

3.0 POLICY

3.1 The REB 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. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn.

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

3.2.1 The nature of any risks posed by the research;

3.2.2 The degree of uncertainty regarding the risks involved;

3.2.3 The vulnerability of the participant population;

3.2.4 The projected rate of enrolment and estimated research closure date;

3.2.5 Whether the research involves novel interventions;

3.2.6 The REB believes that more frequent review is required.

3.3 Continuing review activities include the following:

3.3.1 Amendments;

3.3.2 Minor changes;

3.3.3 Unanticipated issues[1];

3.3.4 Protocol deviations;

3.3.5 Safety and serious adverse events[2];

3.3.6 Renewals[3]; or

3.3.7 Closure.

3.4 The REB will use a proportionate approach with continuing review activities so that the level of review is commensurate with the level of risk. The REB reserves the right to provide full Board review for any continuing review activity that poses greater than minimal risk to research participants.

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

3.5.1 There have been no material changes to the research or to the informed consent form that have not been previously submitted and approved;

3.5.2 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;

3.5.3 Risks to research participants are minimized and reasonable in relation to the anticipated benefits;

3.5.4 Selection of research participants is equitable;

[1] REB policy RA0900 Research Ethics Board Reporting
[2] REB policy RR0900 Safety and Serious Adverse Events Reporting
[3] REB policy RR0500 Renewals

3.5.5 Informed consent processes continue to be appropriate and documented;

3.5.6 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;

3.5.7 Any complaints from research participants have been followed up appropriately.

3.6 The REB may also make additional determinations, including:

3.6.1 Request changes to the informed consent form(s);

3.6.2 Request changes for the continuing review interval (based on risks);

3.6.3 Impose special precautions (e.g. frequency of monitoring, requirement of interim reports or change in duration of approval period);

3.6.4 Require modifications to the research.

3.7 The REB has the authority to observe or have a third party observe, the consent process of research it has approved, and to verify that the project is being conducted as required by the REB and within IH and site specific policies and procedures as appropriate.

3.8 The REB will consider the following criteria to determine if a site visit is required:

3.8.1 The research involves vulnerable populations or high risk procedures;

3.8.2 The researcher has a history of serious or continuing non-compliance related to continuing review in the past three years;

3.8.3 The REB has reason to doubt the veracity of the information provided by the researcher;

3.8.4 The information provided by the researcher is inconsistent with other information known to the REB and the inconsistency cannot be resolved through communication with the researcher;

3.8.5 A regulatory audit report indicates issues of concern with compliance to TCPS2;

3.8.6 Any other reason where the REB believes verification is required.

3.9 The REB may request verification from sources other than the researcher that no material changes have occurred since previous REB review. Those sources may include but are not limited to:

3.9.1 Interior Health;

3.9.2 The researcher's supervisor;

3.9.3 Health Canada or FDA Inspection reports;

3.9.4 Media reports;

3.9.5 Internet sites for research (Health Canada, OHRP, FDA);

3.9.6 Participant complaints;

3.9.7 Research staff informants;

3.9.8 Site visit reports.

3.10 The REB has the authority to suspend or terminate approval for any project that is not being conducted in accordance with REB policies and/or is not in compliance with applicable regulations and/or has been associated with unexpected serious harm to participants per policy *RR1200 Suspensions and Terminations of Research Ethics Board Approval*.

3.11 The researcher will submit any new information generated through the course of the research that might affect the rights, safety and well-being of research participants. Such information may include:

3.11.1 Modifications or changes to the previously approved research;

3.11.2 Reports of unanticipated problems involving risks to participants or others;

3.11.3 Reports of any changes significantly affecting the conduct of the research or increasing the risk to participants;

3.11.4 Deviations to the previously approved research;

3.11.5 Reports of privacy breaches;

3.11.6 Summary of any audits and inspections;

3.11.7 Any other new information that may adversely affect the safety of participants or the conduct of the research.

3.12 The researcher is responsible to submit appropriate documentation for all continuing review activities in a timely manner, including any Certificates of Approval from another REB for the same activity. At minimum, the researcher will provide an annual status report.

3.13 The researcher should submit all revised documents in tracked changes mode. All revised documents must be dated and version noted.

3.14 The researcher will not implement any amendment or change to a protocol or project without prior approval of the REB; **except** in a serious event where immediate action is required to eliminate harm to participants.

3.15 The researcher will report any unanticipated issue or protocol deviation that may increase the level of risk to participants, or has other ethical implications that may affect participants' welfare within 14 days. Serious events, where there is potential or real harm to participants will be reported to the IH REB at the earliest opportunity and no later than 7 days from the time of the event (TCPS2, 2010, Article 6.15).

3.16 For protocol deviations and unanticipated issues the researcher should include the following information in the report of the event:

3.16.1 A description and explanation of the event;

3.16.2 The researcher's opinion regarding the causality;

3.16.3 The action taken in response to the event;

3.16.4 The outcome of the event;

3.16.5 Any change in the risk or the possibility of risk for participants;

3.16.6 The researcher's opinion regarding the implications for continuation of the project;

3.16.7 The researcher's opinion regarding the need for any changes to the protocol, research procedures or consent documents.

4.0 PROCEDURES

4.1 Research Ethics Office (REO)

4.1.1 Receives all continuing review activities and determines the level of risk. Reviews and approves minimal risk activities for delegated review as delegated by the Chair.

4.1.2 Adds activities requiring full Board review to the agenda for the next scheduled REB meeting.

4.1.3 Adds all continuing review applications and related documents to the project file.

4.1.4 Maintains Tracking Tools on all continuing review activities and reports these to the REB at the next scheduled meeting.

4.1.5 Issues Certificate of Approval to the researcher for all continuing review activities that have been approved by full Board review, by the Chair, or by a qualified delegated reviewer.

- Certificate of Approval (Amendment) is issued for the remainder of the current term.
- Certificate of Approval (Renewal) is issued for one year or for the length of term approved by the Board.

4.2 REB

4.2.1 Reviews, makes recommendations for changes to the project if required, and approves all continuing review activities that require full Board review.

4.2.2 Primary reviewers for above minimal risk studies will be consulted on continuing review activities for those projects as required.

4.2.3 Makes a recommendation regarding approval and the length of the term of approval.

4.3 REB Chair

4.3.1 Reviews continuing review activities of indeterminate risk status and makes a determination regarding whether the activity qualifies for delegated review. If significant ethical concerns are identified, forwards the activity for full Board review at the next scheduled REB meeting.

4.3.2 If a delegated or full Board review results in recommendations for change, the Chair or delegate will communicate the recommendations to the researcher in a Report of Review.

4.3.3 Reports serious events posing immediate potential or real harm to participants to the Scientific Director of Research, who will then report to the Vice President responsible for research for consideration of referral to the IH Board;

5.0 REFERENCES

- Canadian Association of Research Ethics Boards and N2 Network of Networks. (2016). Standard Operating Procedure 404.002: *Ongoing REB Review Activities.*
- Canadian Association of Research Ethics Boards and N2 Network of Networks. (2016). Standard Operating Procedure 405.002: *Continuing Review.*
- Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, December 2014.
- Fraser Health Authority. (2014). Research and Evaluation Policy: *The Ethical Conduct of Research and Other Studies Involving Human Subjects*.
- Health Canada, Food and Drug Regulations, Part C, Division 5, *Drugs for Clinical Trials Involving Human Subjects*, (Schedule 1024), June 20, 2001.
- Interior Health. (2018). Research Policy Manual: *RR0500 Annual Renewals.*
- Interior Health. (2018). Research Policy Manual: *RR0900 Safety and Serious Adverse Events Reporting.*
- Interior Health. (2018). Research Policy Manual: *RR1200 Suspensions and Terminations of REB Approval.*
- International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), ICH Harmonized Guideline, Integrated Addendum to ICH E6(R1); *Guideline for Good Clinical Practice*, E6(R2), November 9, 2016.
- Island Health Authority. (2013). Research Ethics Standard Operating Procedure 504: *Managing Protocol Waivers and Deviations by Research Ethics Board,* version 3.

- Island Health Authority. (2013). Research Ethics Standard Operating Procedure 508: *Amendments and Ongoing Review,* version 1.
- Island Health Authority. (2013). Research Ethics Standard Operating Procedure 510: *Study Completion,* version 1.
- Office of Human Research Protections. (2010). *Guidance on IRB Continuing Review of Research.*
- UBC Office of Research Ethics. (2011). Standard Operating Procedure 405: *Ongoing Review and Reporting*.
- UBC Office of Research Ethics. (2013). Standard Operating Procedure 406a: *Annual Renewal Processes*.
- UBC Office of Research Ethics. (2013). Standard Operating Procedure 407: *Study Completion*.
- US Department of Health and Human Services, Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects (45CFR46).
- US Food and Drug Administration Code of Federal Regulations, Title 21, Volume 1:
  - Part 50, Protection of Human Subjects, (21CFR50).
  - Part 56, Institutional Review Boards, (21CFR56).

**This policy replaces the following policies which are no longer active:
IH REB Policy: *RE0100 Amendments* approved March 6, 2008
IH REB Policy: *RE0600 Continuing Review* approved December 6, 2007