# RESEARCH ETHICS BOARD
# STANDARD OPERATING PROCEDURES

## 1.0 PURPOSE:

The Research Ethics Board (REB) of St. Joseph's Health Centre (SJHC) ensures that all human subjects research involving physicians, staff (including staff acting as investigators outside the institution) students (i.e. research within the institution or using institutional resources), or patients is conducted in accordance with the Tri-Council Policy Statement: Ethical Conduct for Research involving Human Subjects (TCPS), Part C Division 5 of the Food and Drug Regulations of Health Canada; Good Clinical Practice Guidelines (Health Canada GCP), International Conference on Harmonization Guidelines (ICH Guidelines), The Common Rule (45 CFR 46), Personal Health Information Protection Act (PHIPA) and the Personal Information Protection and Electronic Document Act (PIPEDA). The REB follows the ethical decision making framework (termed YODA) when conducting reviews of study documents.

## 2.0 REB ORGANIZATION AND ADMINISTRATION:

### 2.1 Accountability

In order for the REB to perform its functions properly it must exist, operate and be regarded by others as an independent body. It must also be responsible and accountable to others[1].

The REB through the office of the Chair of the REB, reports and is accountable to Senior Management and the Board of Directors, through the Chief Executive Officer, and the Medical Advisory Committee (MAC) of St. Joseph's Health Centre. The REB is delegated by the Board of Directors through the MAC.

While the REB is a subcommittee of the MAC, in accordance with current standards outlined in the Tri-Council Policy, the REB is an administratively independent body within the St. Joseph's Health Centre and operates at arm's

[1] Tri-Council Policy Statement Article 1.1 & 1.2

length from administrative, programmatic and research structures within St. Joseph's Health Centre[1].

2.2 Authority

All human subjects research carried out at St. Joseph's Health Centre or under its auspices must be reviewed and approved, or deemed exempt to review, before the involvement of humans in research.

The REB's authority includes, but is not limited to, the authority to approve, reject, propose modifications to, monitor, suspend and/or terminate any proposed or ongoing research activities involving human subjects that is conducted within, or by members of, the institution. The REB retains the authority to suspend, or terminate any research that is not being conducted according to the requirements of the REB, or any research that is associated with unexpected serious harm to human subjects.

St. Joseph's Health Centre retains the authority to deny the implementation of REB approved research protocols for reasons other than research ethics (such reasons may be administrative, programmatic, philosophical, or resource based in nature). However, neither the board of directors, MAC, or other administrative bodies at St. Joseph's Health Centre may override a decision of the REB to reject a research project.

2.3 Membership

As set forth in Health Canada Food and Drug Regulations Part C Division 5, The REB consists of at least five voting members, including both men and women of whom:

1. two members whose primary experience and expertise are in a scientific discipline, who have broad experience in the methods and areas of research to be approved and one of whom is from a medical discipline or, if the clinical trial is in respect of a drug to be used fro dental purposes only, is from a medical or dental discipline
2. one member knowledgeable in ethics
3. one member knowledgeable in Canadian laws relevant to the biomedical research to be approved
4. one member whose primary experience and expertise are in a non-scientific discipline

5. one member who is from the community or is a representative of an organization interested in the areas of research to be approved and who is not affiliated with the sponsor or the site where the clinical trial is to be conducted

Approvals of clinical trials must be made by a quorum of members that meet the required representation as outlined above[2].

The REB Chair, at his or her discretion and in consultation with the board, may nominate additional members to the board[3].

A membership list will be updated for all new members. All previous membership lists will be kept on file[4].

## 2.4 Confidentiality

Upon appointment to the REB, or attendance of an REB meeting, members (voting or otherwise), consultants or guests will sign St. Joseph's Health Centre confidentiality and Security Agreement – Form SE10-1-2.

Staff of St. Joseph's Health Centre who previously signed a confidentiality agreement will not have to re-sign upon joining the REB.

## 2.5 Conflict of Interest

During research studies, all parties (REB members, Investigators, Sponsors, Coordinators) are responsible for disclosing any actual, perceived or potential conflict of interest to the REB before the trial is approved, or as soon as the conflict of interest arises.

No member will participate in the REB's initial or continuing approval of a research project in which the member has a conflicting interest unless to provide information to the REB[5].

## 2.6 Training of REB Members

[2] Health Canada Food and Drug Regulations – Division 5 Section C.05.012
[3] Tri-Council Policy Statement Article 1.3
[4] Guidance for Industry: Good Clinical Practice 3.2.1
[5] Tri-Council Policy Statement Article 1.12

Upon appointment, new REB members will be given an REB Handbook containing Health Canada Food & Drugs Act and Regulations – Part C, Division 5, Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans and Good Clinical Practice Consolidated Guideline (Health Canada) to review. This handbook also contains general information about St. Joseph's Health Centre REB and its forms and guidelines.

All members will be required to read the most current version of the St. Joseph's Health Centre Research Ethics Board Standard Operating Procedures and sign a reading attestation when the document is read. All members will also be required to complete the TCPS tutorial (or new versions) and provide a certificate of completion to the REB office.

## 2.7 Meeting Frequency

The REB meets no less than ten (10) times per year from September to July. The board may also meet at the discretion of the Chair. Ordinarily, the REB does not meet in August.

During the period between scheduled REB meetings, any material that requires immediate attention will be brought to the Chair for review. In some circumstances additional REB members may also be asked to review this material.

## 2.8 REB Meeting Minutes

Minutes will be recorded at each REB meeting and will be in sufficient detail to show attendance at the meetings, actions taken by the REB, the basis for requiring changes in or disapproving research and a written summary of the discussion of issues and their resolution[6].

## 2.9 REB Payment

Clinical trials sponsored by industry are charged initial and periodic fees for REB review. This fee is applicable regardless if a protocol is approved by the REB. The Sponsor will be invoiced by the REB Coordinator following the submission of an application to the REB. The REB may delay the review of any study

[6] Guidance for Industry: Good Clinical Practice 3.1.2

documents until outstanding REB invoices have been paid to the Research Ethics Board (Not Research Department). Please refer to REB Fees at St. Joseph's Health Centre Form for more guidance.

2.10 Signing Authority

Only the REB Chair, or Acting Chair, has the authority to sign letters that summarize the decision made by the Research Ethics Board.

The REB Coordinator has the authority to sign all letters that confirm or clarify decisions made by the Research Ethics Board. The REB Coordinator also has the authority to sign administrative documents such as reminder letters and notifications.

2.11 REB Records

Records, such as membership, qualifications of members, procedures for the conduct of reviews for approval of biomedical research and communication with Qualified Investigators should be retained for 25 years. Other essential documents that are not unique to the REB, such as records of drug reactions and review documents should be retained for a period of at least 3 years after completion of the trial as per GCP Guidelines[7].

## 3.0 REB REVIEW AND APPROVAL PROCESS:

3.1 REB Application

An application must be submitted for all research involving human subjects. No study related contact will be made with human subjects until the St. Joseph's Health Centre REB has granted ethics approval.

Although all research involving human subjects requires REB review and approval, quality assurance studies, performance reviews or testing that proceeds within normal educational requirements are not, as a general rule, subject to REB review and approval[8]. However, studies that contain an element of research in addition to assessment may require ethics approval. Any questions

[7] Health Canada Food and Drug Regulations – Division 5 Section C.05.012
[8] Tri-Council Policy Statement Article 1.1

about whether a proposed research activity is governed by, or exempt from REB review should be directed to the REB[8].

When conducting chart reviews, researchers do not obtain informed consent from the group of patients being studied and therefore privacy legislation and guidelines apply. For this reason, the researcher must clearly demonstrate to the satisfaction of the REB that privacy and confidentiality of target populations will be maintained. The researcher must sign a Confidentiality Agreement in the application form accepting full responsibility for protection of information that has been collected by the research or a delegate on his/her behalf.

Every application for REB review must contain either the St. Joseph's Health Centre Human Subjects Research Application Form or the St. Joseph's Health Centre Chart Review Application Form, and any of the following materials relevant to the research project[9]:

- Study Protocol
- Informed Consent Forms or Assent Forms
- All recruitment materials (posters, advertisements, letters to participants etc.)
- Questionnaires, interview scripts, phone scripts
- Fact or information sheets
- Investigator Brochure
- Data collection form
- Study budget
- Focus group guides
- Documentation of approvals from any other reviewing bodies
- Documentation of training in research ethics
- Any other tools that will be used in the conduct of the study
- Health Canada No Objection Letter
- Current curriculum vitae for the Principal Investigator and all Co-Investigators

The REB may request further information and materials as it deems necessary in order to evaluate an application.

An On-Site Lead will be designated for all research projects conducted at St. Joseph's Health Centre. This lead is responsible for overseeing all study related activities that occur at SJHC. The site lead is also responsible for designating a

[9] Guidance for Industry: Good Clinical Practice 3.1.2

replacement should they be unavailable for an extended period of time during the study when there will be patient interactions. The REB should be notified if the On-Site Lead has been re-assigned or is no longer associated with the study.

3.2 Submission Deadlines

Applications for review must be submitted no later than the last business day of the month immediately preceding the REB meeting at which the researcher wishes to have the application **reviewed (in some cases the deadline may be earlier)**. Applications are added to the agenda on a first come, first served basis. If the agenda is full, the REB may defer consideration of an application until the next scheduled meeting.

3.3 REB Review

The REB adopts a proportionate approach to review based on the principle that the more invasive the research, the greater the care will be taken in assessing the research[10]. There are two types of REB review available at SJHC.

1) Full Board Review
2) Expedited Review

As a general rule, all research studies undergo full board review unless otherwise identified by the REB Chair as meeting criteria for expedited approval.

Some research projects may receive expedited review at the discretion of the Chair or his/her designee. Some categories of research that may be eligible for expedited review include research protocols that involve no more than minimal risk, annual renewals of approved projects in which there has been little or no change in the ongoing research, research involving review of patient records by hospital personnel or affirmations that conditions laid down by the REB as a condition of approval have been met[11].

When the Chair authorizes an expedited review, such approvals will be reported to the full REB, permitting the REB to maintain surveillance over the decisions made on its behalf.

A study protocol may be sent out for external review; in that instance, consent form the PI will be sought for the external review.

[10] Tri-Council Policy Statement Article 1.6
[11] Tri Council Policy Statement Article 1.6

## 3.4 REB Determinations

Studies may receive:

a) Approval - In the case of approval with no changes, the research may proceed once the principal investigator receives written documentation of the REB approval. Unless otherwise indicated by the REB, the approval period for research without changes is one year from the date full approval was granted.

b) Conditional Approval – The REB may determine that a study may be approved with minor changes or clarifications. Minor changes include, but are not limited to, changes that do not involve potential for increased risk or decreased benefit to human subjects.

   A Conditional Approval may be required to be returned to the full ethics board or to the Chair to ensure that all conditions have been met.

c) Request for Resubmission – The submission is incomplete or there may be serious concerns with the study plan. The REB may request the researcher to re-work his or her application and resubmit it.

d) Approval Denied – Approval has been denied and the study may not proceed. If the REB decides to deny approval, it shall be in written notification with a statement of reasons for its decision.

e) Suspension or Termination of Study – The REB Chair or the Board itself may suspend a study at any time if it is determined that the study requires further review or evaluation. This may be due to an adverse event, non-compliance or other risks to human subjects. If a project is suspended, research (including all contact with human subjects other than ensuring subject safety) must immediately cease. Though the Chair may suspend a study, pending REB review, only the convened REB may terminate a study. If a study is suspended or terminated, the Chair (in the instance of a suspension) or the REB (in the instance of a termination) shall provide the principal investigator written notification that includes a statement of reasons for the decision.

f) Deferred – the REB Chair or the Board may defer a decision on any type of REB submission if necessary (for ex. an appropriate primary reviewer is not available).

3.5 Appeals and Requests for Reconsideration

Researchers have the right to request reconsideration of REB decisions made regarding a researcher project. Every effort will be made to resolve a disagreement between the researcher and the REB through deliberation, consultation or advice. The onus is on researchers to justify the grounds on which they request reconsideration by the REB.

In the event that researchers and the REB cannot reach agreement through reconsideration, an ad hoc appeal committee that reflects a range of expertise and knowledge similar to the REB, must be established by the same authority that established the REB. Members of the REB whose decision is under appeal shall not serve on that appeal committee.

The appeal committee will have the authority to review negative decisions made by an REB. The onus is on researchers to justify the grounds on which they request an appeal. The appeal committee shall function impartially and provide reasoned and appropriately documented opinions and decisions. Both the researcher and the REB representative shall be granted the opportunity to address the appeal committee, but neither shall be present when the appeal committee deliberates and makes a decision. Appeal committee decisions on behalf of the institution shall be final and will be communicated in writing to the researcher.[12]

Requests for reconsideration and appeals should be made in writing within 30 days of the REB's decision, include all relevant documentation detailing the grounds for reconsideration or appeal and the desired remedy. Any requests for reconsideration or appeal will be directed to the REB Chair (through the REB coordinator) who will determine whether there is sufficient basis for the case to be heard by the REB or appeal committee.[13]

[12] TCPS 2
[13] Guidelines and Practices Manual for Research Involving Human Subjects, University of Toronto, Version 1.0.

## 4.0 CONTINUING REB COMMUNICATION AND REVIEW:

### 4.1 Modifications of Approved Protocols

A modification is a deviation from, an amendment of, or a change to a research protocol. Prior REB approval and review is required before investigators may modify research protocols, except when necessary to eliminate immediate hazards to research subjects or when the change involves only logistical or administrative aspects of the trial (e.g. change of monitor, address, telephone number).

Proposed changes to a previously approved project must be submitted as an amendment to that project along with the reasons therefore and any and all supporting documentation. Proposed changes to a previously approved project may, depending on the Chair's assessment of the associated risk, receive expedited or full review.

Any deviation from the approved research protocol, consent form or study addenda should be reported to the REB using the SJHC Protocol Deviation Report no later than 7 days after their discovery. Any protocol exceptions (inclusion/exclusion waivers) that do not affect patient safety or the integrity/outcome of the study should be reported within 2 months from time of occurrence. Please refer to the Research Ethics Board Instructions for Reporting Protocol Deviations, Violations and Waivers for further guidance.

### 4.2 Safety Reporting

Investigators must promptly report to the REB:

- Deviations, from, or changes to, the protocol that serve to eliminate immediate hazards to the trial subjects
- Changes that increase the risk to subjects and/or significantly affect the conduct of the trial
- Any new information that may adversely affect the safety of the subjects or the conduct of the trial
- All adverse events

An adverse event is an unexpected or normally avoidable event that negatively affects, or would reasonably be expected to have the potential for negatively affecting the patient's heath and/or overall well-being, and which event occurred

in the course of research and/or health care treatment and is not due directly to the natural course of the patient's illness or underlying condition.

If an SJHC subject experiences a serious adverse event or if the principal investigator or local study lead become aware of any new information that may adversely affect the safety of the subjects or the conduct of the trial, the principal investigator or local study lead must notify the REB within 48 hours (or within two working days). If an external subject experiences an adverse event the principal investigator must notify the REB within 10 working days.

Any and all such reports must contain the following information:

- REB Study number
- Title of protocol
- Name of principal investigator
- Subject identifier (study number/reference of subject)
- Date and location of the event
- Description of the event (nature of injury or other adverse occurrence, assessment of severity and assessment of event's relationship to the study)
- Handling of/response to the event
- Any proposed changes in the protocol or the consent form as a result of the event
- To whom else the event has been reported
- Signature of the principal investigator

The REB may ask the Principal Investigator to provide additional information.

For further information regarding one's responsibilities with regards to adverse events which occur at SJHC please see SJHC policy Communication of Adverse Events to Patients and Substitute Decision Makers, Policy #SJ-04-01-19 and for institutional responsibilities regarding the reporting of critical incidents please see SJHC policy Management of Critical Patient Related Incidents #SJ03-03-06 and Incident Report #SJ03-02-01.

4.3 Annual Renewal

Research Ethics Board approval is for a maximum of one year from the original date of approval. Generally, the approval period for studies is one year, but in some cases, the REB may give its approval for a shorter period of time[14].

Research that will continue beyond the expiration date of REB approval is required to submit an Annual Renewal Form with all applicable documents. This form should be provided to the REB no later than one month prior to the anniversary of the study approval date, with due regard for the next date on which the REB is scheduled to meet.

The application for renewal/continuing review must include a progress report in which the principal investigator provides sufficient information for it to determine whether the research ought to be continued/renewed[15].

A study lapses if its approval period expires prior to a renewal of its approval by the REB. If a study lapses, all research-related activities must halt, except where and insofar as doing so would jeopardize the welfare of human subjects. If the principal investigator fails to submit materials for continuing review/renewal within one month of the expiration date, then the lapsed study will be classified as inactive.

4.4 Completion of Study

Study closures refer to the completion of recruitment and all follow-up components of a study. In some cases, specific external reporting requirements may require annual renewal even after a study has closed [16].

The REB must be notified when a study is closed and a Final Report Form must be submitted with all applicable information completed.

4.5 Monitoring

The REB conducts continuing review of research covered by this policy, at intervals that are and in a manner that is appropriate to the degree of risk. The REB does this in order for it both to protect human subjects and to maintain the

[14] Guidance for Industry: Good Clinical Practice 3.1.4
[15] Guidance for Industry: Good Clinical Practice 4.10.1
[16] Guidance for Industry: Good Clinical Practice 4.12

scientific and ethical integrity of the research that is covered by this policy. Monitoring may include, but is not limited to the following[17]:

- Reviewing periodic reports
- Reviewing final reports at the completion of a study
- Providing on-site audit and/or observation of ongoing research projects
- Observing or having a third party observe the consent process
- Reviewing consent forms
- Reviewing documents e.g. patient charts
- Reviewing records pertaining to the production and maintenance of data
- Identifying unapproved activities e.g. unauthorized research

[17] Tri- Council Policy Statement Article 1.13