# JOINT BRIDGEPOINT HEALTH- WEST PARK HEALTHCARE CENTRE – TORONTO CENTRAL COMMUNITY CARE ACCESS CENTRE (CCAC) - TORONTO GRACE HEALTH CENTRE RESEARCH ETHICS BOARD RESEARCH ETHICS BOARD (JREB)
# Operating Procedures

**What Activity Requires Review by the REB**

**Types of Reviews**

**Protocol Review Process**

I. Initiating the review process
II. The review process
IIa. Full review process by the REB
IIb. Expedited review process
III. The decision process
IV. Conflict of Interest
V. Appeal Process
VI. Rejected Protocols and Appeals
VIII. Subject Confidentiality, Privacy, Recruitment and Surrogate Consent

**Ongoing Ethical and Scientific Validity and Ethical Conduct**

## What Activity Requires Review by the REB

All research involving human subjects conducted under the authority of Bridgepoint Health, West Park Healthcare Centre, Toronto Central Community Care Access Centre (CCAC) or the Toronto Grace Health Centre (hereafter called the Partnering Institutions) requires approval by the Joint Bridgepoint Health, West Park Healthcare Centre, Toronto Central Community Care Access Centre (CCAC) and Toronto Grace Health Centre Research Ethics Board (JREB) prior to the initiation of a research project. Included within the jurisdiction of the JREB are staff of the Partnering Institutions who are carrying out research as a member of these institutions regardless of whether this research is being carried out within or outside of these institutions. Additionally, the JREB has similar authority over investigators from other institutions who may wish to carry out research on the premises of either institution noted above or with patients under the care of these institutions.

The definition of research is outlined in the Tri-Council Policy. In summary, human research is considered to include any of the following: if the researcher

- will administer a drug, take a blood sample, do a test or perform any procedure, clinical, therapeutic, or otherwise, upon the person of himself/herself or someone else, for research rather than treatment
- will ask people information whether by telephone, letter, survey, questionnaire or interview
- will review information from patient charts (even their own patients' charts) for research rather than clinical purposes
- will use material derived from people (tissue samples, blood, DNA)
- will be using non-public records (e.g. not the telephone book) which contain identifying information about anyone either directly or indirectly
- will use information previously gathered about anyone, even if anonymized (secondary data analysis)
- will be observing anyone's responses or behaviour, either directly or indirectly

In the event that an investigator cannot determine whether an intended investigation constitutes research (for instance, quality assurance studies do not constitute research), the investigator should approach the Chair of the JREB or the Secretariat of the JREB for such a determination. Providing such consultation on ethics matters is part of the responsibility of the JREB.

## Type of Reviews

In accordance with the Tri-Council Policy Statement, the JREB conducts a proportionate review of research protocols. The default review process is the full REB review process where the REB considers the science and ethics associated with a research protocol in a face-to-face meeting. The discussion of such REB meetings are captured in minutes and the consensus opinion of the JREB are forwarded in writing to the principal investigator.

Some research protocols will qualify, based on a decision made by the JREB Chair, for an expedited review as is outlined in the proportionate review process of the Tri-Council Policy. Several types of research protocols usually qualify for expedited review:

- protocols involving of minimal risk or protocols where there are minimal incremental risks over standard procedures
- minimal risk protocols where data are collected non-invasively such as questionnaires or direct/indirect observation
- protocols primarily using previously collected data such as chart reviews, data base information such as that used in epidemiological studies
- protocols primarily using previously collected tissue or other samples
- protocols that may be involve greater than minimal risk but have previously been reviewed by acceptable peer-review panels or other appropriately constituted (in compliance with Tri-Council Policy) and acceptable REBs

In the case of previously reviewed and approved protocols, the protocol may only be expedited if all relevant documentation accompanies the application. Documentation regarding the correspondence between the investigator and the REB (or peer-review agency) must be submitted with the application so that the review process can be adequately adjudicated. It is insufficient simply to submit a letter of approval. Without such supporting material, protocols will not be reviewed by the full REB.

## Protocol Review Process

### I. Initiating the Review Process

Investigators should complete the appropriate Application Form (JREB General Application Form or Application Form for Access to Retrospective Data) depending on the nature of the research. All applications require the appropriate administrative approval prior to being submitted to the JREB. The JREB accepts the Department/Division Head signature as Institutional acceptance of the application. The Department/Division Head signature will be interpreted as an approval by the institution that the application is acceptable to the institution based on institutional (mission), departmental, and programmatic goals, feasible in terms of the resource expenditure and availability of resources, and that the Investigators are qualified (in terms of professional standing and experience) to carry out the proposed research.

Prior to being submitted to the JREB, Partnering Institution submitting the research application will conduct a preliminary review of the application and study protocol to determine that the quality of the submission is acceptable for review by the JREB. In addition, Partnering Institutional will conduct an analysis of the impact of this research on their facility. This study impact will examine the resources required for the study and will require the support of the appropriate departments within the organizations. Contact the JREB Secretariat for appropriate forms for each institution.

Completed application forms and inquiries should be directed to the Secretariat for the JREB. The Secretariat of the JREB is the organizing body for the JREB and will be responsible for the receipt of all applications and the maintenance of all records for the JREB. The Secretariat will be resourced appropriately by the Partnering Institutions with each Partnering Institution providing the physical site and staffing of the Secretariat on a rotational basis. For the current two (2) year period (2010-2012 inclusive), the Secretariat will be located at Toronto Central CCAC. All applications should be sent to the Secretariat, c/o Ms. Ruby Paner, 82 Buttonwood Avenue, Toronto ON, M6M 2E6, (416) 243-3600 x4333, Ruby.Paner@westpark.org

Applications will not be considered until all relevant information for the review are complete. A complete application includes the application form, protocol, consent form(s) (as necessary), all supplemental material (e.g., questionnaires and other assessment tools), the most recent investigators brochure for clinical trials, the allocated budget and any other relevant correspondence. In addition, other supplemental material necessary for the decision process should be provided before the review. Such supplemental material may include advertisements for recruitment, preclinical information from animal studies depending on the Phase of the clinical trial, and any correspondence from other sources that might be pertinent to the review (such as the details from any other scientific or ethical reviews that have been carried out by other review committees or Boards).

Meetings are held at least bi-monthly or more frequently depending on the volume of protocols that require full review by the REB. All applications must arrive at the Secretariat three (3) weeks in advance of the JREB meeting in order to be considered. In general the investigator will receive an initial response from the JREB within 2 weeks of the meeting for a full review. Please see Appendices for the application forms and guidelines for the completion of consent forms.

## II. The Review Process

### a) Full Review Process by the REB

Reviews will generally involve internal review though external review may be sought at the discretion of the JREB if specific expertise not available on the JREB is required. If either the Chair of the JREB, the internal appraisers of the submitted protocol, or member of the JREB at large feel that the protocol cannot be adequately reviewed by the JREB, external reviewers are sought. In the application form, investigators are asked to provide names of potential external reviewers for their protocol. These potential reviewers, or others, may be selected by the JREB to serve as external reviewers.

The JREB internal reviewers will present the protocol to the JREB at the JREB meetings where all members can meet face-to-face. All JREB members are provided with the application form and the Consent Form for all studies but access to the entire protocol for the discussion. The investigator may be invited to attend. Alternatively, the investigator may request attendance at an JREB meeting though the investigator will be asked to withdraw during deliberations. Following the JREB meeting, any requested modifications are communicated in writing to the investigator as official JREB correspondence. All official communication with investigators comes through the Secretariat of the JREB who coordinates the activities of the JREB.

During the review process and discussion, the following issues are considered:

Scientific

- background and study rationale
- objectives
- importance of study
- research design
- methodology
- appropriate inclusion/exclusion criteria
- sample size justification
- statistical analysis
- overall scientific merit and validity

Ethical Considerations

- risk-benefit assessment
- the treatment of research subjects with dignity and respect
- method of recruitment (to assess perceived coercion, conflict of interest, privacy)
- method of obtaining consent
- justification for substitute consent if necessary
- funding, budget and sponsor insurance
- consent form and patient information

Decisions will be made by consensus; only in exceptional circumstances will decisions be made by majority vote. A decision can be approval, a request for minor or major points of clarification or modification, or rejection (as submitted). Typically, a request for modification is made to the investigator. The JREB usually delegates the responsibility for reviewing the responses to such requests for modification to the Chair of the JREB and directs the Chair to issue approval for the protocol if the investigator has satisfactorily responded to the concerns of the JREB. If the response from the investigator is not satisfactory, the Chair will request further modifications or information to ensure that the concerns of the JREB have been adequately addressed. Alternatively, the JREB may request that the response from the investigator be considered by the full JREB. Typically such a request would be required if significant modification to the protocol were deemed necessary. Approval is not granted until the investigator satisfies the JREB.

On behalf of the full REB, the Chair of the JREB is delegated the authority to review and approve amendments and monitor reports of serious adverse events for all approved protocols. All actions of the Chair of the JREB will be reported to the full JREB at the next available opportunity.

Refer to Review Process Timeline outlined in Appendix A

### b) Expedited Review Process

Consistent with the Tri-Council Policy Statement, research protocols receive a proportionate review. While the default remains a full JREB meeting review, some research protocols involving minimal incremental risk or those that have had previous ethical review may qualify for an expedited review process. The Chair of the JREB is mandated on behalf of the full JREB to determine which research protocols qualify for expedited review and to review, modify and approve such expedited protocols. An expedited review will result in either:

- approval
- request for modification
- a full review by the committee (with the attendant requirement for documentation)
- rejection

Protocols that are likely to qualify for an expedited review include:

- protocols that involve only minimal risk or minimal incremental risk over standard procedures
- chart reviews, use of secondary data sources, and use of tissue or other samples

Expedited reviews will be carried out by the Chair or delegate, will be reported at the next JREB meeting and will be reflected in the minutes of that meeting. Any JREB member may request that an expedited protocol receive consideration from the full JREB with appropriate discussion. By reporting to the full JREB expedited protocols and allowing these protocols to be challenged by any member, the full JREB fulfills its obligation to maintain surveillance over all research at the partnering institutions.

In addition to submitted protocols that qualify for expedited review, on behalf of the full JREB, the Chair of the JREB is delegated the authority to review and approve amendments and monitor reports of serious adverse events. All such actions of the Chair of the JREB will be reported to the full JREB at the next available opportunity.

Refer to Review Process Timeline outlined in Appendix B

## III. The Decision Process

Decisions will be made by consensus; only in exceptional circumstances will decisions be made by majority vote. All documentation and communication will be through the JREB Chair and Sceretariat to investigators. Decisions by the JREB will be communicated to the investigator by the JREB based on the documentation and deliberations at the JREB meeting.

Submissions to the JREB may receive approval, approval pending revision and clarification, deferral in order obtain further information or consultation, or rejection (as submitted). If a submission is rejected, the JREB will provide the investigator with a detailed list of the

deficiencies so that any resubmission will meet the standards needed for an appropriate JREB review.

As the JREB has an obligation to monitor studies that have been approved, the approval of any study will remain in force for a 12 month period (unless otherwise stipulated). The investigator must seek a renewed approval for a further 12 months prior to the expiration of the current approval. The investigator cannot continue with the study after the 12 month (or stipulated) period without applying for a renewal of the JREB approval.

## IV. Conflict of Interest

Investigators must disclose any real or apparent conflict of interest with regard to the proposal. JREB members must disclose any real or apparent conflict of interest regarding a proposal under review. Members may not be present for any JREB discussion regarding a proposal in which they have any vested interest and may not participate in the decision process regarding such a proposal. Finally, the Partnering Institutions must disclose and real or apparent conflict of interest (e.g. investment in a Sponsor of a study).

## V. Appeal Process

In the event that the JREB rejects a submission, an appeal of the JREB decision may be made to a standing Appeal Committee of the Toronto Academic Health Sciences Committee. The Appeal Committee will decide whether or not to hear the appeal. If the Appeal Committee decides to hear the appeal, it will review the JREB process by which the JREB reached its decision. The Appeal Committee may dismiss the appeal or may direct the JREB to reconsider its decision based on their findings of the Appeal Committee. The Appeal Committee will provide the JREB and the person appealing with a written decision documenting the reasons for its decision.

The Appeal Committee will be composed of the current Chairs of the Hospital REBs (University Health Network, Hospital for Sick Children, Sunnybrook Health Sciences Center, Bloorview MacMillan Rehabilitation Centre, the Center for Addictions and Mental Health, St. Michael's Hospital, Toronto Rehab, Mount Sinai Hospital, and the Baycrest Centre for Geriatric Care). This committee will also include a lay person from the community and a member knowledgeable in relevant law. Additional scientific experts in the area of study or ethics experts in the area of contention will be added to the Appeal Committee as deemed necessary by the committee.

This Appeal process is intended to satisfy the appeal mechanism mandated under the Tri-Council Policy Statement.

## VI. Rejected Protocols and the Authority of the JREB and Institutions

The Chief Executive Officers (CEOs) of the Partnering Institutions delegated the authority to determine ethical acceptability of research projects to the JREB. If the investigator is unable to modify a protocol to make it satisfactory to the JREB, the protocol will be rejected by the JREB and the research may not be initiated at Bridgepoint Health, West Park Healthcare Centre or the

Toronto Central CCAC. Neither the CEO, other executives, nor the Board of Governors (Trustees) may overturn a negative decision (rejection) by the JREB but may disallow a project approved by the JREB for other administrative, philosophical or resource-based issues.

## VII. Subject Confidentiality, Privacy, Recruitment and Surrogate Consent

Some of the most common concerns of JREB in regard to reviewing research protocols are the methods of subject recruitment and the methods of obtaining consent.

Regarding subject recruitment, the JREB pays special attention to issues of inappropriate or perceived coercion of subjects to participate, conflict of interest for research staff enrolling subjects, and issues of patients' rights to privacy. Therefore we ask that investigators carefully consider and explicitly state in their protocols: who will be enrolling subjects; what is their relationship to the subject; and whether the recruiter may have real, subtle or even the appearance of other motivators to recruit subjects.

Ensuring **confidentiality**, while necessary, may not be sufficient to justify the use of patient information. Patient **privacy** must also be ensured as the preservation of privacy is generally considered fundamental to respect for human dignity. For example, the process of identifying potential research subjects may seem to violate patients' sense of privacy of privileged information regarding their health status and/or health records even if the researchers claim to keep the information confidential. As a further example, investigators often request that the REB grant permission for the investigator and the study sponsors to obtain information by reviewing medical charts. To protect such information, the REB requests specifically the information to be obtained from such charts so that only relevant information is gathered from the patients' confidential and private medical charts.

Generally, referral to a study is best initiated by medical care personnel to whom the patient has already entrusted their **private and confidential** medical information. **Recruitment** and **Consent**, on the other hand, is best obtained by persons not involved in the care and treatment of the patient.

All issues regarding privacy and confidentiality will be compliant with the following legislation/guidelines as applicable:

- ICH Good Clinical Practice (GCP)
- Department of Health and Human Services (DHHS) and FDA laws and requirements (US)
- Tri-Council Policy on Privacy and Confidentiality (Canadian National Code)
- PIPEDA (Canadian Federal Privacy Legislation)
- PHIPA (Ontario Privacy Legislation)

Regarding the subject information and consent form, the JREB has drafted guidelines to help investigators compose their information and consent forms.

**Surrogate consent** is appropriate when **all** of the following criteria are met:

- the research protocol has scientific merit
- it would not be feasible to carry out the research relying only on subjects who are capable to give free and informed consent
- any imposition on the individual subject does not expose the subject to more than minimal risk without the potential for direct benefit
- the research is limited to the investigation of those conditions or aspects of behaviour which are directly related to the identifying characteristic of the group
- the researchers describe how the surrogate consent will be obtained and how the best interests of the subjects will be protected
- the researchers must demonstrate that they will ascertain the wishes of the subject and respect the "dissent" of the incompetent subject

**Ongoing Ethical and Scientific Validity and Ethical Conduct**

It is a requirement that research involving human subjects be continually reevaluated with respect to ongoing ethical and scientific validity. It is the responsibility of the investigator to ensure that their research projects remain valid with respect to changes in the ethical or scientific context of the study. The REB will request that investigator report immediately on any significant deviations in the protocol or any significant new information that might alter the risk/benefit ration. In addition, all protocols require annual review to assess any relevant changes that may affect the ongoing validity of the study. This will include a request to summarize adverse event reports with an opinion regarding their impact on the ongoing safety of the study. Further, the annual review will assess the progress of the study to ensure that the study remain sufficiently feasible and viable to warrant subject participation. The Annual Review Form will function as a reporting mechanism for investigators of the ongoing ethical conduct of their research.

Should the ethical conduct associated with any specific study be questioned, the REB will investigate any allegations. The REB has the authority to withdraw their previous approval and suspend the study if circumstances warrant.