[Section 1]

ETHICS REVIEW

This section outlines the standards and procedures to be used by Research Ethics Boards (REBs) for ethics review.

A. Research Requiring Ethics Review

Article 1.1

(a) All research that involves living human subjects requires review and approval by an REB in accordance with this Policy Statement, before the research is started, except as stipulated below.

(b) Research involving human remains, cadavers, tissues, biological fluids, embryos or foetuses shall also be reviewed by the REB.

(c) Research about a living individual involved in the public arena, or about an artist, based exclusively on publicly available information, documents, records, works, performances, archival materials or third-party interviews, is not required to undergo ethics review. Such research only requires ethics review if the subject is approached directly for interviews or for access to private papers, and then only to ensure that such approaches are conducted according to professional protocols and to Article 2.3 of this Policy.

(d) Quality assurance studies, performance reviews or testing within normal educational requirements should also not be subject to REB review.

Canada adheres to a model of ethics review that has emerged in the international community in recent decades. The model generally involves the application of national norms by multidisciplinary, independent local REBs for reviewing the ethical standards of research projects developed within their institutions.

The REB is established to help ensure that ethical principles are applied to research involving human subjects. The REB, therefore, has both educational and review roles. The REB serves the research community as a consultative body and thus contributes to education in research ethics; it also has responsibility for independent, multidisciplinary review of the ethics of research to determine whether the research should be permitted to start or to continue.

Article 1.1(a) includes the basic elements that determine whether research involving human subjects should undergo ethics review by an REB before the research begins. First, the undertaking must involve “research,” which involves a systematic investigation to establish facts, principles or generalizable knowledge. This concept of research parallels those employed in other research ethics norms in Canada and abroad. Secondly, the research must involve humans as “research subjects,” for which the potential scope is evidently very wide and requires further elaboration.

For example, REB review is generally not required for research involving public policy issues, the writing of modern history, or literary or artistic criticism, even though all of these might well involve human subjects. Research for a critical biography about someone deceased should not require REB review because the term “research subjects” refers to living individuals. Article 1.1 (c) indicates that research about a living individual, particularly one in public life, or criticism of a living artist based exclusively on published or publicly available works, performances, archival materials, or information derived from third-party interviews, is also usually not required to undergo ethics review, because such research involves no interaction with the person who is the subject of the public records. Where the research involves interaction with an individual in public life or an artist as a research subject by way of a request for an interview or for access to private papers, the ethics review should focus only on whether these requests will be made in accordance with appropriate ethical and professional standards. Similarly, REBs should ensure that interviews with third parties are conducted according to a professional interview protocol and to Article 2.1 of this Policy, and that the potential interviewees be fully informed about publication of the interview and their identity. REBs should not require such third-party interviews to be controlled in any way by the primary focus of the research.

Nothing in this Policy should be interpreted to mean that research subjects have the right to veto a project, though they do, of course, have the right to refuse to cooperate with the researcher(s).

Article 1.1(d) indicates that studies related directly to assessing the performance of an organization or its employees or students, within the mandate of the organization or according to the terms and conditions of employment or training, should also not be subject to REB review. However, performance reviews or studies that contain an element of research in addition to assessment may need ethics review.

The opinion of the REB should be sought whenever there is any doubt about the applicability of this Policy to a particular research project. Appendix 1 indicates areas of research in which the REB should at least be consulted.

B. Research Ethics Boards (REBs)

B1. Authority of the REB

Article 1.2 **The institution in which research involving human subjects is carried out shall mandate the REB to approve, reject, propose modifications to, or terminate any proposed or ongoing research involving human subjects that is conducted within, or by members of, the institution, using the considerations set forth in this Policy as the minimum standard.**

The authority of the REB should be delegated through the institution’s normal process of governance. In defining the REB’s mandate and authority, the institution must make clear the jurisdiction of the REB and its relationship to other relevant bodies or authorities. Institutions must ensure that REBs have the appropriate financial and administrative independence to fulfil their primary duties.

Institutions must respect the authority delegated to the REB. The institution may not override negative REB decisions reached on grounds of ethics without a formal appeal mechanism as set out below. Institutions may refuse to allow certain research within its jurisdiction, even though the REB has found it ethically acceptable.

Each institution is accountable for the research carried out in its own jurisdiction or under its auspices. An institution can authorize its REB(s) to accept the review of other REBs constituted under the Tri-Council Policy Statement if it so wishes. This might involve specific agreements between institutions for sharing the work.

B2. Membership of the REB

Article 1.3 **The REB shall consist of at least five members, including both men and women, of whom:**

(a) At least two members have broad expertise in the methods or in the areas of research that are covered by the REB;

(b) At least one member is knowledgeable in ethics;

(c) For biomedical research, at least one member is knowledgeable in the relevant law; this is advisable but not mandatory for other areas of research; and

(d) At least one member has no affiliation with the institution, but is recruited from the community served by the institution.

These basic membership requirements are designed to ensure the expertise, multidisciplinarity and independence essential to competent research ethics review by REBs. The concept of independence implies that members of the REB under Article 1.3(a-c) should contain a majority of those whose main responsibilities are in research or teaching. The institution may need to exceed these minimum requirements in order to ensure an adequate and thorough review. The Agencies consider it essential that effective community representation be maintained. Thus, as the size of an REB increases beyond the minimum of five members, the number of community representatives should also increase.

The majority of members of an REB should have both the training and the expertise to make sound judgements on the ethics of research proposals involving human subjects. The terms of REB appointments should be arranged to balance the need to maintain continuity with the need to ensure diversity of opinion and the opportunity to spread knowledge and experience gained from REB membership throughout the institution and community.

Because the REB should reflect the ethical values of this Policy in the context of the society within which it operates, its membership should be broad enough to reflect that society. The members of the REB therefore play different but complementary roles. Article 1.3(a) indicates that general expertise in the relevant sciences or research disciplines is essential. Article 1.3(b) requires a member knowledgeable in ethics, so as to alert the REB to potential ethics issues and options.

The role of the member knowledgeable in the applicable law is to alert REBs to legal issues and their implications, not to provide formal legal opinions nor to serve as legal counsel for the REB. An understanding of relevant legal issues and contexts is advisable for all REBs, although for non-biomedical research such insights may be sought from someone who sits on the REB only for specific research projects. The institution's legal counsel should not be a member of the REB.

The community member requirement of Article 1.3(d) is essential to help broaden the perspective and value base of the REB beyond the institution, and thus advances dialogue with, and accountability to, local communities.

REBs should husband their resources and expertise prudently. For example, in the event that the REB is reviewing a project that requires particular community or research subject representation, or a project that requires specific expertise not available from its regular members, the REB Chair should nominate appropriate *ad hoc* members for the duration of the review. Should this occur regularly, the membership of the REB should be modified.

Institutions should consider the nomination of substitute REB members so that Boards are not paralysed by illness or other unforeseen eventualities. The use of substitute members should not, however, alter the membership structure as outlined in Article 1.3.

B3. Number of REBs Within an Institution and Relationships Among REBs

Article 1.4

(a) REBs shall be established by the highest levels of the institution, and cover as broad a range of research as is consistent with manageable workloads. Departmental REBs normally are not acceptable (except as discussed below for review of undergraduate research within course requirements). A multiplicity of REBs with small workloads within the same institution should be avoided.

(b) Large institutions may find it necessary to create more than one REB, usually to cover different areas of research. The jurisdiction of each REB should be clearly defined by the normal processes of governance within the institution, and a mechanism should be established to coordinate the practices of all REBs within the institution.

(c) Small institutions may wish to explore regional cooperation or alliances, including the sharing of REBs.

When an institution has more than one REB, it should define their jurisdictions. Researchers should apply to the designated REB and not seek review by another REB, whether inside or outside the institution. REBs within an institution should have the authority to transfer research proposals among themselves to ensure review by an REB with the appropriate expertise. Furthermore, when more than one REB is established by an institution, lines of communication should be open between the REBs in order to keep each aware of the research under review and of the decisions made.

As a special exception to Article 1.4(a), an institution may decide that ethics review of research that is carried out by undergraduate students as part of their course work may be delegated to a departmental-level process that complies with this Policy Statement. The institution should set out criteria for determining which categories of research proposal are suitable for consideration through this means, and establish procedures, such as who is responsible for implementing and overseeing the approval mechanisms. As with other levels of review, proper accountability demands

appropriate record keeping. Departmental-level review should not be used for research in which an undergraduate student is carrying out research that is part of a faculty member's own research program. Such research should be reviewed by the regular institutional REB procedures.

C. Analysis, Balance and Distribution of Harms and Benefits

C1. Minimal Risk

The standard of minimal risk is commonly defined as follows: if potential subjects can reasonably be expected to regard the probability and magnitude of possible harms implied by participation in the research to be no greater than those encountered by the subject in those aspects of his or her everyday life that relate to the research, then the research can be regarded as within the range of minimal risk. Above the threshold of minimal risk, the research warrants a higher degree of scrutiny and greater provision for the protection of the interests of prospective subjects. There is a similar threshold regarding undue or excessive offers of benefit. As an offer of payment in relation to research participation exceeds the normal range of benefits open to the research subject, it is increasingly likely to amount to an undue incentive for participation (see Section 2B).

This concept of minimal risk raises special issues in clinical research, especially clinical trials, in which patients suffering from disease participate in research on interventions undertaken for purposes of therapy. In such research, the procedures to which the subject is exposed may be either directly required for the therapy that the patient is undergoing for illness, or they may be undertaken because extra actions (for example, more X-rays, blood samples, colonoscopies) are needed for proper analysis of the therapy. Hence, risks in clinical trials can be described as either therapeutic or non-therapeutic.

In some areas of treatment (for example, surgery, chemotherapy or radiation therapy), the treatments themselves are known to pose considerable risks of harm. Such therapeutic risks may be regarded as within the range of minimal risks for patient-subjects, since they are inherent in the treatment that the patient will be undergoing as a part of his or her current everyday life. Adherence to the principle of clinical equipoise[1] (see Section 7) requires that the fundamental ethical consideration in the decision to expose patients to experimental procedures derives from the premise that the interventions being tested are not different in terms of the anticipated balance between their harms and benefits. Hence, the idea that considerable anticipated therapeutic risks might also be within the range of minimal risks extends to the therapies in the trial.

This consideration does not apply to non-therapeutic risks, which arise from actions that go beyond the needs of the subject as a patient, and that are incurred only for the needs of the research. REBs should be sensitive to this distinction for all research projects. They should recognize the need to minimize harms, and to ensure that these harms are proportionate to the benefits that might be expected from the knowledge gained from the study. For projects that involve both therapeutic and non-therapeutic risks, the risks that are required for therapy as opposed to research need to be delineated.

C2. Scholarly Review as Part of Ethics Review

Article 1.5

(a) The REB shall satisfy itself that the design of a research project that poses more than minimal risk is capable of addressing the questions being asked in the research.

(b) The extent of the review for scholarly standards that is required for biomedical research that does not involve more than minimal risk will vary according to the research being carried out.

(c) Research in the humanities and the social sciences that poses, at most, minimal risk shall not normally be required by the REB to be peer reviewed.

(d) Certain types of research, particularly in the social sciences and the humanities, may legitimately have a negative effect on public figures in politics, business, labour, the arts or other walks of life, or on organizations. Such research should not be blocked through the use of harms-benefits analysis or because of the potentially negative nature of the findings. The safeguard for those in the public arena is through public debate and discourse and, *in extremis*, through action in the courts for libel.

Traditions for scholarly and ethical review undertaken vary between disciplines. The following mechanisms are among those that should be considered by the REB. The REB may:

- Conclude that the proposed research has already passed appropriate peer review, for example by a funding agency;
- Establish an *ad hoc* independent external peer review;
- Establish a permanent peer review committee reporting directly to the REB;
- Assume complete responsibility for the scholarly merit, which would require that it have the necessary scholarly expertise in the discipline to carry out peer review of the research in question.

REBs should normally avoid duplicating previous professional peer-review assessments unless there is a good and defined reason to do so. However, they may request the researcher to provide them with the full documentation of those reviews.

In evaluating the merit and the scholarly standards of a research proposal, the REB should be concerned with a global assessment of the degree to which the research might further the understanding of a phenomenon, and not be driven by factors such as personal biases or preferences. REBs should not reject research proposals because they are controversial, challenge mainstream thought, or offend powerful or vocal interest groups. The primary tests to be used by REBs should be ethical probity and high scientific and scholarly standards.

Article 1.5(d) reflects the tradition in the humanities and the social sciences for researchers to publish their results and then debate with their readers and reviewers the merits of what they have written. In the context of harms and benefits to research subjects, prior to starting the research the risks of censorship of ideas through peer review do not seem justified. Nothing in this section, however, shall be interpreted to mean that other relevant parts of this Policy—such as the need for REB review, interview protocols, free and informed consent and privacy—are not applicable to their research.

D. Review Procedures

D1. A Proportionate Approach to Ethics Assessment

Article 1.6 **The REB should adopt a proportionate approach based on the general principle that the more invasive the research, the greater should be the care in assessing the research.**

The concept of proportionate review gives practical expression to the general principle that, especially in the context of limited resources, the more potentially invasive or harmful is the proposed and ongoing research, the greater should be the care in its review. While all research must be reviewed adequately, proportionate review is intended to reserve most intensive scrutiny, and correspondingly more protection, for the most ethically challenging research.

Potential harms are usually understood in relation to risks, which are defined in terms of the magnitude of a harm and the probability of its occurrence. Both potential harms and benefits may span the spectrum from minimal through significant to substantial. A proportionate approach to ethics review thus starts with an assessment, primarily from the viewpoint of the potential subjects, of the character, magnitude and probability of potential harms inherent in the research. The concept of minimum risk provides a foundation for proportionate review.

In practice, proportionate review implies different levels of REB review for different research proposals. The following approach to proportionate review is offered for the consideration of research institutions and universities. It envisages three levels of review, each linked to the other through formal authorization by the institution, as well as by accountability through the REB to the institution's authorities. The three levels proposed are:

- Full REB review;
- Expedited REB review by an individual or subgroup of the REB; and
- Departmental-level review of undergraduate projects carried out within formal course requirements.

Full review by an REB should be the default requirement for all research involving human subjects unless the institution decides to authorize expedited review based primarily on the harms that are expected to arise from the research. For example, the institution may decide that categories of research that are confidently expected to involve minimal risk may be approved by the chair or another designated member or a subcommittee of the REB. Examples of such categories of expedited REB review might 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.

The possibility of departmental level review for projects that are carried out by undergraduate students as part of their course work has been discussed above (see Section 1, B3).

An institution that decides to authorize expedited REB review mechanisms, either within the REB structure or through departments (see Section 1, B.3), must require that such approvals be reported in appropriate ways to the full REB, permitting the REB to maintain surveillance over the decisions made on its behalf. Principles of accountability require that, regardless of the review strategy, the REB continue to be responsible for the ethics of all research involving human subjects that is carried out within the institution.

D2. Meetings and Attendance

Article 1.7 **REBs shall meet regularly to discharge their responsibilities.**

Face-to-face meetings are essential for adequate discussion of research proposals and for the collective education of the REB. A schedule of when the REB will sit to review research proposals should be communicated to researchers so that the research can be planned in an orderly way. REBs should also hold general meetings, retreats and educational workshops in which members can (1) take advantage of educational opportunities that may benefit the overall operation of the REB, (2) discuss any general issues arising out of the REB's activities or (3) revise policies.

Regular attendance by REB members at meetings is important, and frequent unexplained absences should be construed as a notice of resignation. Institutions should also establish quorum rules for REBs. When there is less than full attendance, decisions requiring full review should be adopted only if the members attending the meeting possess the range of background and expertise stipulated in Article 1.3.

REBs and researchers may request informal meetings with each other prior to the formal review process, in order to expedite and facilitate the review process. Such informal meetings cannot, however, substitute for the formal review process.

D3. Record Keeping

Article 1.8 **Minutes of all REB meetings shall be prepared and maintained by the REB. The minutes shall clearly document the REB's decisions and any dissents, and the reasons for them. In order to assist internal and external audits or research monitoring, and to facilitate reconsideration or appeals, the minutes must be accessible to authorized representatives of the institution, researchers and funding agencies.**

Article 1.8 indicates the need for REBs to act, and be seen to be acting, fairly and reasonably. To ensure accurate and fair administration and integrity of the research process, the maintenance of satisfactory records and documentation is essential. Failure to do so may expose researchers and institutions to legal liability.

D4. Decision Making

Article 1.9 **REBs shall meet face-to-face to review proposed research that is not delegated to expedited review. REB review shall be based upon fully detailed research proposals or, where applicable, progress reports. The REB shall function impartially, provide a fair hearing to those involved and provide reasoned and appropriately documented opinions and decisions. The REB shall accommodate reasonable requests from researchers to participate in discussions about their proposals, but those researchers may not be present when the REB is making its decision. When an REB is considering a negative decision, it shall provide the researcher with all the reasons for doing so and give the researcher an opportunity to reply before making a final decision.**

Especially in complex research proposals, the formal REB decision on whether to allow the research will often be preceded by extensive discussion (1) of ethical concerns and (2) of possible means of improving such aspects as the research design or the information to be provided in the process of free and informed consent. Participation by the researcher in such discussions is often very helpful to both REBs and researchers. Such discussions may result in a deferral of the REB's decision until the researcher has considered the discussions and possibly modified the proposal. Such discussions are an essential part of the educational role of the REB.

The REB must reach a decision on whether to allow the proposed research. Article 1.9 outlines the duty of REBs to function impartially and to provide reasoned and well-documented decisions. In the event that a minority within the REB membership considers a research project unethical, even though it is acceptable to a majority of members, an effort should be made to reach consensus. Consultation with the researcher, external advice, and/or further reflection by the REB may be helpful. If disagreement persists, a decision should be made under the procedural rules mandated by the institution. In such instances, the position of those disagreeing may be communicated to the researcher. The Chair should monitor the REB's decisions for consistency, ensure that these decisions are recorded properly, and ensure that researchers are given written communication of the REB's decisions (with reasons for negative decisions) as soon as possible.

D5. Reconsideration

Article 1.10 **Researchers have the right to request, and REBs have an obligation to provide, reconsideration of decisions affecting a research project.**

Article 1.10, together with Article 1.9, obligates REBs to be guided by principles of natural and procedural justice in their decision making. Such principles include providing a reasonable opportunity to be heard, an explanation of the reasons for opinions or decisions, and the opportunity for rebuttal, fair and impartial judgement, and reasoned and written grounds for the decisions.

D6. Appeals

Article 1.11

(a) In cases when researchers and REBs cannot reach agreement through discussion and reconsideration, an institution should permit review of an REB decision by an appeal board, provided that the board's membership and procedures meet the requirements of this Policy. No *ad hoc* appeal boards are permitted.

(b) Small institutions may wish to explore regional cooperation or alliances, including the sharing of appeal boards. If two institutions decide to use each other's REB as an appeal board, a formal letter of agreement is required.

(c) The Agencies will not entertain any appeals of REB decisions.

E. Conflicts of Interest

Article 1.12 **If an REB is reviewing research in which a member of the REB has a personal interest in the research under review (e.g., as a researcher or as an entrepreneur), conflict of interest principles require that the member not be present when the REB is discussing or making its decision. The REB member may disclose and explain the conflict of interest and offer evidence to the REB, provided the conflict is fully explained to the REB, and the proposer of the research has the right to hear the evidence and to offer a rebuttal.**

Matters pertaining to possible conflict of interest by the proposers of research projects are included in Section 4 of this Policy.

F. Review Procedures for Ongoing Research

Article 1.13

(a) Ongoing research shall be subject to continuing ethics review. The rigour of the review should be in accordance with a proportionate approach to ethics assessment.

(b) As part of each research proposal submitted for REB review, the researcher shall propose to the REB the continuing review process deemed appropriate for that project.

(c) Normally, continuing review should consist of at least the submission of a succinct annual status report to the REB. The REB shall be promptly notified when the project concludes.

Beyond scrutinizing reports, the REB itself should not normally carry out the continuing ethics review, except in specific cases where the REB believes that it is best suited to intervene. For research posing significant risks, the REB should receive reports on the progress of the research project at intervals to be predetermined. These reports should include an assessment of how closely the researcher and the research team have complied with the ethical safeguards initially proposed.

In accordance with the principle of proportionate review, research that exposes subjects to minimal risk or less requires only a minimal review process. The continuing review of research exceeding the threshold of minimal risk that is referred to in Article 1.13(b), in addition to annual review (Article 1.13(c)) might include:

- Formal review of the process of free and informed consent;
- Establishment of a safety monitoring committee;
- Periodic review by a third party of the documents generated by the study;
- Review of reports of adverse events;
- Review of patients' charts; or
- A random audit of the process of free and informed consent.

Other models of a continuing ethics review may be designed by researchers and REBs to fit particular circumstances.

The process of a continuing ethics review should be understood as a collective responsibility, to be carried out with a common interest in maintaining the highest ethical and scientific standards. Research institutions should strive to educate researchers on the process of a continuing ethics review through workshops, seminars and other educational opportunities.

G. Review of Multicentred Research

Principles of institutional accountability require each local REB to be responsible for the ethical acceptability of research undertaken within its institution. However, in multicentred research, when several REBs consider the same proposal from the perspectives of their respective institutions, they may reach different conclusions on one or more aspects of the proposed research. To facilitate coordination of ethics review, when submitting a proposal for multicentred research, the researcher may wish to distinguish between core elements of the research—which cannot be altered without invalidating the pooling of data from the participating institutions—and those elements that can be altered to comply with local requirements without invalidating the research project.

REBs may also wish to coordinate their review of multicentred projects, and to communicate any concerns that they may have with other REBs reviewing the same project. The needed communication would be facilitated if the researcher provides information on the institutional REBs that will consider the project.

H. Review of Research in Other Jurisdictions or Countries

Article 1.14 **Research to be performed outside the jurisdiction or country of the institution that employs the researcher shall undergo prospective ethics review both (a) by the REB within the researcher's institution; and (b) by the REB, where such exists, with the legal responsibility and equivalent ethical and procedural safeguards in the country or jurisdiction where the research is to be done.**

An institution is responsible for the ethical conduct of research undertaken by its faculty, staff or students regardless of the location where the research is conducted. Thus, review of research by that institution's REB is required in addition to review by any agency having jurisdiction over the site of the research.

Rules pertaining to research abroad should be created and interpreted in the spirit of the Helsinki Accords and subsequent documents that encourage the free movement of researchers across national boundaries. REBs should, therefore, not veto research about authoritarian or dictatorial countries on the grounds that the regime or its agents have not given approval for the research project or have expressed a dislike of the researchers. They should, however, legitimately concern themselves about the safety of research subjects and indeed of the researchers, and the security of research materials.

University research should be open. It is thus unethical for researchers to engage in covert activities for intelligence, police or military purposes under the guise of university research. REBs must disallow any such research.

Researchers should normally provide copies of publications or other research reports to the institution, normally the host institution, that is best suited to act as a repository and disseminator of the results. This may not be necessary in countries when the results are readily available in print or electronically. However, such reporting is particularly important in countries where Western publications are unavailable or prohibitively expensive. If feasible, and so long as the human rights of the research subjects and the ethical rights set out in this Policy are not compromised, a copy of the field material ought to be provided as well, with due regard to commitments concerning anonymity and confidentiality of research subjects. These latter safeguards are especially important in countries with authoritarian regimes.

Furthermore, researchers should ensure that the benefits of their research are available in the host country. Benefits may, for example, take the form of information-sharing, training for local personnel both in the host country and in Canada, or health care or similar services. However, since researchers are not aid agencies, REBs should not try to force them to undertake aid work.

Endnotes

[1] "At the start of the trial, there must be a state of clinical equipoise regarding the merits of the regimens to be tested, and the trial must be designed in such a way as to make it reasonable to expect that, if it is successfully conducted, clinical equipoise will be disturbed." Freedman, B., "Equipoise and the Ethics of Clinical Research", *New England Journal of Medicine.* 1987, 317.3: 141–145.