TRI-COUNCIL POLICY STATEMENT

Ethical Conduct for Research Involving Humans

Medical Research Council of Canada
Natural Sciences and Engineering Research Council of Canada
Social Sciences and Humanities Research Council of Canada

Canada

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August, 1998

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INTRODUCTION

This *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* describes the policies of the Medical Research Council (MRC), the Natural Sciences and Engineering Research Council (NSERC), and the Social Sciences and Humanities Research Council (SSHRC). The document replaces SSHRC's *Ethics Guidelines for Research with Human Subjects*, MRC's *Guidelines on Research Involving Humans*, and MRC's *Guidelines for Research on Somatic Cell Gene Therapy in Humans.*

The Councils will consider funding (or continued funding) only to individuals and institutions which certify compliance with this policy regarding research involving human subjects.

This joint policy expresses to the continuing commitment by the three Councils to the people of Canada, to promote the ethical conduct of research involving human subjects. This commitment was first expressed in the publication of guidelines in the late 1970s. Work on the joint Policy was started by formation of the Tri-Council Working Group in 1994. The Councils published three documents prepared by the Working Group: an Issues Paper in November 1994, a Discussion Draft in May 1996, and its Final Report (*Code of Ethical Conduct for Research Involving Humans*) in July 1997. Each of these documents stimulated extensive discussion in the academic community. The present *Policy Statement* was prepared by the Councils by revision of the Working Group's Final Report in the light of consultations between mid-1997 and May 1998.

The Councils believe that this policy statement will benefit research through addressing the paramount need for the highest ethical standards. The key is sensitive and thoughtful implementation of the spirit and requirements of the document. Nonetheless, the Councils recognize that considerations around the ethical conduct of research involving human subjects are complex and continually evolving. We therefore welcome comment and discussion, and commit to regular updates of this document.

GOALS OF THE POLICY

This *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* describes standards and procedures for governing research involving human subjects.

A. Mandate of the Councils

The people of Canada, through Acts of Parliament[1] have created and funded the MRC, NSERC and SSHRC, to promote, assist and undertake research in the domains indicated by their names. In discharging our mandates, the Councils wish to promote research that is conducted according to the highest ethical standards. The Councils have therefore adopted this policy as our standard of ethical conduct for research involving human subjects. As a condition of funding, we require, as a minimum, that researchers and their institutions apply the ethical principles and the articles of this policy.

B. Goals and Rationale of the Policy

The interests of the Councils in promoting ethical research, combined with the evolving needs of the research community, have led us to define a common policy of ethical conduct for research involving human subjects. This policy seeks to respond to, and address, several needs:

1. The Policy addresses the interdependent duties to research subjects[2], that are shared by researchers, institutions and Research Ethics Boards (REBs).

2. By addressing common issues and needs, the Policy seeks to articulate ethical norms that transcend disciplinary boundaries. The fundamental ethical issues and principles in research involving human subjects are common across the social sciences and humanities, the natural sciences and engineering, and the health sciences. They reflect shared fundamental values that are expressed in the duties, rights, and norms of those involved in research. Research subjects reasonably expect that their rights shall be equally recognized and respected, regardless of the researcher's discipline. Similarly, Canadian society legitimately expects that the benefits and harms of research shall be fairly distributed.

3. The Policy seeks to harmonize the ethics review process. The Councils expect that REBs will benefit from common procedures within a shared ethical framework. This will also benefit those projects involving researchers from different disciplines or institutions. The Councils hope that the Policy will serve as an educational resource.

4. The effective working of ethics review — across the range of disciplines conducting research involving human subjects — requires a reasonable flexibility in the implementation of common principles. The Policy therefore seeks to avoid imposing one disciplinary perspective on others, while expressing the shared principles and wisdom of researchers in diverse fields. It is designed to help both researchers and REBs, as a matter of sound ethical reasoning, to scrutinize the contexts and accommodate the needs of specialized research disciplines.

5. The Policy updates some norms, while seeking to encourage continued reflection and thoughtful consensus around more contentious ethical issues. The Policy does not offer definitive answers to such ethical questions. Rather it seeks (a) to outline guiding principles and basic standards and (b) to identify major issues, and points of debate and consensus, which are essential to the development and implementation of coherent policies for research ethics.

Endnotes

[1] See, *Medical Research Council Act*, Rev. Stats. Can., 1985, c. M-4; *Natural Science & Engineering Research Council Act*, Rev. Stat. Can., 1985, c. N-21; *Social Sciences & Humanities Research Council Act*, Rev. Stats. Can., 1985, c. S-12.

[2] During preparation of this Policy Statement, there was extensive discussion of the optimal term to describe those on, or about whom, the research is carried out. This discussion focused on the terms "participant" and "subject." Though research subjects may participate actively in research, so also do many others, including the researchers, their staff, administrators in the institutions, and funding sponsors and members of research ethics boards. Research subjects are unique amongst the many participants because it is they who bear the risks of the research. The Councils have therefore chosen to retain the word "subject" because of its relative unambiguity in this context, and because the prime focus of the Policy Statement is on those who bear the risks of research.

CONTEXT OF AN ETHICS FRAMEWORK

Norms for the ethics of research involving human subjects are developed and refined within an ever-evolving societal context, elements of which include the need for research and the research community, moral imperatives and ethical principles, and the law.

A. The Need for Research

Research involving human subjects is premised on a fundamental moral commitment to advancing human welfare, knowledge and understanding, and to examining cultural dynamics. Researchers, universities, governments and private institutions undertake or fund research involving human subjects for many reasons, for example: to alleviate human suffering, to validate social or scientific theories, to dispel ignorance, to analyze policy, and to understand human behaviour and the evolving human condition. Research involving human subjects imparts at least three general categories of benefits:

- The basic desire for new knowledge and understanding is the driving force for research.
- The quest to advance knowledge sometimes benefits research subjects. Subjects may benefit from improved treatments for illnesses; the discovery of information concerning one's welfare; the identification of historical, written, oral or cultural traditions; or the satisfaction of contributing to society through research.
- As well, research benefits particular groups and society as a whole. Thus, insights into political behaviour may produce better policy; information about the incidence of disease may improve public health; sociological data about lifestyles may yield social reform; and disciplines based on, for example, texts, dance, theatre or oral history, continue to illuminate past and present realities.

B. A Moral Imperative: Respect for Human Dignity

An ethic of research involving human subjects should include two essential components: (1) the selection and achievement of morally acceptable ends, and (2) the morally acceptable means to those ends.

The first component is directed at defining acceptable ends in terms of the benefits of research for subjects, for associated groups, and for the advancement of knowledge. The second component is directed at ethically appropriate means of conducting research. For example, even in the most promising of research initiatives, the Tri-Council Policy Statement objects to tricking a person into participating by promising false benefits. Part of our core moral objection would concern using another human solely as a means toward even legitimate ends.

The objection provides moral insight that proves pertinent to human research in several ways: First, it translates into the familiar moral imperative of respect for human dignity. It is unacceptable to treat persons solely as means (mere objects or things), because doing so fails to respect their intrinsic human dignity and thus impoverishes all of humanity. Second, it translates into the requirement that the welfare and integrity of the individual remain paramount in human research.[1] Thus, the moral imperative of respect for human dignity translates into a number of important correlative ethical principles in research ethics. These are elaborated in C. below.

C. Guiding Ethical Principles

The approach taken in this framework is to guide and evoke thoughtful actions based on principles. The principles that follow are based on the guidelines of the Councils over the last decades,[2] on more recent statements by other Canadian agencies,[3] and on statements from the international community.[4] The principles have been widely adopted by diverse research disciplines. As such, they express common standards, values and aspirations of the research community.

Respect for Human Dignity: The cardinal principle of modern research ethics, as discussed above, is respect for human dignity. This principle aspires to protecting the multiple and interdependent interests of the person — from bodily to psychological to cultural integrity. This principle forms the basis of the ethical obligations in research that are listed below.

In certain situations, conflicts may arise from application of these principles in isolation from one other. Researchers and REBs must carefully weigh all the principles and circumstances involved to reach a reasoned and defensible conclusion.

Respect for Free and Informed Consent:[5] Individuals are generally presumed to have the capacity and right to make free and informed decisions. Respect for persons thus means respecting the exercise of individual consent. In practical terms within the ethics review process, the principle of respect for persons translates into the dialogue, process, rights, duties and requirements for free and informed consent by the research subject.

Respect for Vulnerable Persons: Respect for human dignity entails high ethical obligations towards vulnerable persons — to those whose diminished competence and/or decision-making capacity make them vulnerable. Children, institutionalized persons or others who are vulnerable are entitled, on grounds of human dignity, caring, solidarity and fairness, to special protection against abuse, exploitation or discrimination. Ethical obligations to vulnerable individuals in the research enterprise will often translate into special procedures to protect their interests.

Respect for Privacy and Confidentiality: Respect for human dignity also implies the principles of respect for privacy and confidentiality. In many cultures, privacy and confidentiality are considered fundamental to human dignity. Thus, standards of privacy and confidentiality protect the access, control and dissemination of personal information. In doing so, such standards help to protect mental or psychological integrity. They are thus consonant with values underlying privacy, confidentiality and anonymity respected.

Respect for Justice and Inclusiveness: Justice connotes fairness and equity. Procedural justice requires that the ethics review process have fair methods, standards and procedures for reviewing research protocols, and that the process be effectively independent. Justice also concerns the distribution of benefits and burdens of research. On the one hand, distributive justice means that no segment of the population should be unfairly burdened with the harms of research. It thus imposes particular obligations toward individuals who are vulnerable and unable to protect their own interests in order to ensure that they are not exploited for the advancement of knowledge. History has many chapters of such exploitation. On the other hand, distributive justice also imposes duties neither to neglect nor discriminate against individuals and groups who may benefit from advances in research.

Balancing Harms and Benefits: The analysis, balance and distribution of harms and benefits are critical to the ethics of human research. Modern research ethics, for instance, require a favourable harms-benefit balance — that is, that the foreseeable harms should not outweigh anticipated benefits. Harms-benefits analysis thus affects the welfare and rights of research subjects, the informed assumption of harms and benefits, and the ethical justifications for competing research paths. Because research involves advancing the frontiers of knowledge, its undertaking often involves uncertainty about the precise magnitude and kind of benefits or harms that attend proposed research. These realities and the principle of respect for human dignity impose ethical obligations on the prerequisites, scientific validity, design and conduct of research. These concerns are particularly evident in biomedical and health research; in research they need to be tempered in areas such as political science, economics or modern history (including biographies), areas in which research may ethically result in the harming of the reputations of organizations or individuals in public life.

Minimizing Harm: A principle directly related to harms-benefits analysis is non-maleficence, or the duty to avoid, prevent or minimize harms to others. Research subjects must not be subjected to unnecessary risks of harm, and their participation in research must be essential to achieving scientifically and societally important aims that cannot be realized without the participation of human subjects. In addition, it should be kept in mind that the principle of minimizing harm requires that the research involve the smallest number of human subjects and the smallest number of tests on these subjects that will ensure scientifically valid data.

Maximizing Benefit: Another principle related to the harms and benefits of research is beneficence. The principle of beneficence imposes a duty to benefit others and, in research ethics, a duty to maximize net benefits. The principle has particular relevance for researchers in professions such as social work, education, health care and applied psychology. As noted earlier, human research is intended to produce benefits for subjects themselves, for other individuals or society as a whole, or for the advancement of knowledge. In most research, the primary benefits produced are for society and for the advancement of knowledge.

D. A Subject-Centred Perspective

Research subjects contribute enormously to the progress and promise of research in advancing the human condition. In many areas of research, subjects are participants in the development of a research project and collaboration between them and the researcher in such circumstances is vital and requires nurturing. Such collaboration entails an active involvement by research subjects, and ensures both that their interests are central to the project or study, and that they will not be treated simply as objects. Especially in certain areas of the humanities and social sciences this collaborative approach is essential, and the research could not be conducted in any other way. For example, a study on how a theatrical company developed its approach to a particular play would be difficult without the participation of the theatre company in question. Nevertheless, some research will require a more formal separation between subject and researcher because of the nature of the research design.

A subject-centred approach should, however, also recognize that researchers and research subjects may not always see the harms and benefits of a research project in the same way. Indeed, individual subjects within the same study may respond very differently to the information provided in the free and informed consent process. Hence, researchers and REBs must strive to understand the views of the potential or actual research subjects.

In this context, researchers should take into account that potential subjects who are asked to participate in research by, for example, their caregiver, teacher or supervisor may be overly influenced by such factors as trust in the researcher or the hope for other goals, more than by assessment of the pros and cons of participation in the research. A patient may hope for a cure from an experimental drug, an employee for better working conditions, a student for better marks. This places extra demands on the researcher for accuracy, candour, objectivity and sensitivity in informing potential subjects about proposed research.

However, researchers and REB should also be aware that some research may be deliberately and legitimately opposed to the interests of the research subjects. This is particularly true of research in the social sciences and the humanities that may be critical of public personalities or organizations. Such research should, of course, be carried out according to professional standards, but it should not be blocked through the use of harms/benefits analysis or because it may not involve collaboration with the research subjects.

E. Academic Freedoms and Responsibilities

Researchers enjoy, and should continue to enjoy, important freedoms and privileges. To secure the maximum benefits from research, society needs to ensure that researchers have certain freedoms. It is for this reason that researchers and their academic institutions uphold the principles of academic freedom[6] and the independence of the higher education research community. These freedoms include freedom of inquiry and the right to disseminate the results thereof, freedom to challenge conventional thought, freedom from institutional censorship, and the privilege of conducting research on human subjects with public monies, trust and support. However, researchers and institutions also recognize that with freedom comes responsibility, including the responsibility to ensure that research involving human subjects meets high scientific and ethical standards. The researcher's commitment to the advancement of knowledge also implies duties of honest and thoughtful inquiry, rigorous analysis, and accountability for the use of professional standards. Thus, peer review of research proposals, the findings and their interpretation contribute to accountability, both to colleagues and to society.

Review of the ethics of research helps ensure a more general accountability to society. Accountability, moreover, requires that the whole process should always be open to critical assessment and debate.[7]

F. Ethics and Law

The law affects and regulates the standards and conduct of research involving human subjects in a variety of ways, such as privacy, confidentiality, intellectual property, competence, and in many other areas. Human rights legislation prohibits discrimination on a variety of grounds. In addition, most documents on research ethics prohibit discrimination and recognize equal treatment as fundamental. REBs should also respect the spirit of the Canadian Charter of Rights and Freedoms, particularly the sections dealing with life, liberty and the security of the person as well as those involving equality and discrimination.

This legal context for research involving human subjects is constantly evolving and varies from jurisdiction to jurisdiction. For this reason, researchers, institutions and REBs should have recourse to expertise to identify legal issues in the ethics review process.

However, legal and ethical approaches to issues may lead to different conclusions. The law tends to compel obedience to behavioural norms. Ethics aim to promote high standards of behaviour through an awareness of values, which may develop with practice and which may have to accommodate choice and liability to err. Further, though ethical approaches cannot preempt the application of the law, they may well affect its future development or deal with situations beyond the scope of the law.

G. Putting Principles into Practice

For meaningful and effective application, the foregoing ethical principles must operate neither in the abstract, nor in isolation from one another. Ethical principles are sometimes criticized as being applied in formulaic ways. To avoid this, they should be applied in the context of the nature of the research and of the ethical norms and practices of the relevant research discipline. Good ethical reasoning requires thought, insight and sensitivity to context, which in turn helps to refine the roles and application of norms that govern relationships. Thus, because principles are designed to guide ethical reflection and conduct, they admit flexibility and exceptions. To preserve the values, purpose and protection that they attempt to advance, the onus for demonstrating a reasonable exception to a principle should fall on those claiming the exception.

National norms in research ethics should not be developed in a vacuum. REBs should be aware that there are a variety of philosophical approaches to ethical problems and that debate between various schools of thought both informs ethical decisions and ensures an evolving context for ethical approaches. Some approaches are traditional, but others, such as feminist analysis, are centred on context, relationships of power and allocations of privilege that perpetuate disadvantage and inequality. Hence, the approach may help to correct the systemic exclusion of some groups from research.

Often, more than one principle will apply to a specific case. This is due in part to the diversity of research and in part to the range of fundamental values upon which the research ethics enterprise is founded. If the application of principles yields conflicts, then such conflicts properly demand probing ethical reflection and difficult value choices. Such choices and conflicts are inherent in the ethics review process. In their best uses, principles serve as short-hand reminders of more complex and context-specific moral reflection.

REBs should recognize that certain types of research — particularly biographies, artistic criticism or public policy research — may legitimately have a negative effect on organizations or on public figures in, for example, politics, the arts or business. Such research does not require the consent of the subject, and the research should not be blocked merely on the grounds of harms/benefits analysis because of the potentially negative nature of the findings.

Beyond a keen appreciation for context, effective guiding principles also depend on procedures and policies for their implementation. Indeed, modern research ethics are premised on a dynamic relation between ethical principles and procedures. This relationship is implemented through a mechanism that has emerged in many countries over the last decades and which consists of the articulation of national norms that are applied through prospective ethics review of research projects. Typically, the review is undertaken in local research institutions by independent, multidisciplinary ethics committees that apply substantive and procedural norms. This Policy is consistent with this model.

Endnotes

[1] Social Sciences and Humanities Research Council of Canada, *Ethics Guidelines for Research Involving Human Subjects*. Ottawa, 1977, p. 1. UNESCO. Universal Declaration on the Human Genome & Human Rights. Paris: 1997, article 10.

[2] Medical Research Council of Canada, Guidelines for Research Involving Human Subjects, 1987. Ottawa, 1988; Social Sciences and Humanities Research Council, Ethics in Human Experimentation. Ottawa, 1978.

[3] See, e.g., National Research Council of Canada, *Ethical Guidelines for Research*. Ottawa, 1993; Canada. Royal Commission on New Reproductive Technologies. *Proceed with Care: Final Report of the Royal Commission on New Reproductive Technologies*. Ottawa: Minister of Government Services Canada, 1993; vol. 1: 53-66.

[4] See, e.g., The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Washington, DC: 1979; Council for International Organizations of Medical Sciences. International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva, 1993. UNESCO. Ethical Guidelines for International Comparative Social Science Research in the Framework of M.O.S.T. (Management of Social Transformation). Paris, 1994. The Research Council of Norway, Guidelines for Research Ethics in the Social Sciences, Law and the Humanities. Oslo, 1994.

[5] During preparation of this Policy Statement, there was extensive discussion of the optimal way to refer to the decision made by the potential research subject on whether to participate in the research. The frequently used phrase "obtain informed consent" was rejected early in the discussion because "obtain" implies that getting the consent is the goal, whereas ethically the goal must be to enable the potential subject to choose freely, and with full information, on whether to agree to participate in the research. Though earlier drafts used both "choice" and "consent," it was often difficult to be certain which was the most appropriate in the various contexts. Hence, a brief means of expressing this concept was sought.

"Free and informed consent" was decided upon for a number of reasons: it states the requirement for voluntariness and information; it was felt to include the idea that consent is the act of deciding, perhaps as a result of balancing a number of choices; it retains the traditional word "consent"; and the phrase has unambiguous meaning in the law.

[6] For a definition of academic freedom, see Chapter VI of the Recommendation concerning the Status of Higher-Education Teaching Personnel, UNESCO, Paris, 1997. For responsibilities, see Section VII — Duties and Responsibilities of Higher Education Teaching Personnel and Section V — Institutional Rights, Duties and Responsibilities. Canada spoke in favour of, and voted for, this statement when it was adopted by the General Conference of UNESCO in 1997. For further definitions of academic freedom, see Canadian Association of University Teachers, Policy Statement on Academic Freedom, Ottawa, 1977; Association of Universities and Colleges of Canada, Statement on Academic Freedom and Institutional Autonomy, Ottawa, 1988.

[7] UNESCO, Recommendation on the Status of Higher-Education Teaching Personnel, Paris, 1997 which deals with the rights and responsibilities of faculty. Also to the CAUT Policy Statement on Academic Freedom and to that of the AUCC.

[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 public 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 which 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.

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 Articles 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 Councils 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 such procedural issues as to who will be responsible for implementing and overseeing the approval mechanisms. As with other levels of review, proper account-

ability 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 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 which poses, at most, minimal risks 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 sub-group 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 & 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 can not, 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 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 free and informed consent process. 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 can not reach agreement through discussion and reconsideration, an institution should permit review of an REB decision by an appeal board, provided that the board is within the same institution and its membership and procedures meet the requirements of this Policy. No *ad hoc* appeal boards are permitted.

(b) The Councils 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 free and informed consent process,
- 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 free and informed consent process.

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 Multi-Centred Research

Principles of institutional accountability require each local REB to be responsible for the ethical acceptability of research undertaken within its institution. However, in multi-centred 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 multi-centred 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 multi-centred 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 which 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, which 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, 317.3 (1987): 141-145.

[Section 2]

FREE AND INFORMED CONSENT

A. Requirement for Free and Informed Consent

Article 2.1

(a) Research governed by this Policy (see Article 1.1) may begin only if (1) prospective subjects, or authorized third parties, have been given the opportunity to give free and informed consent about participation, and (2) their free and informed consent has been given and is maintained throughout their participation in the research. Articles 2.1(c), 2.3 and 2.8 provide exceptions to Article 2.1(a).

(b) Evidence of free and informed consent by the subject or authorized third party should ordinarily be obtained in writing. Where written consent is culturally unacceptable, or where there are good reasons for not recording consent in writing, the procedures used to seek free and informed consent shall be documented.

(c) The REB may approve a consent procedure[1] which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent, provided that the REB finds and documents that:

- **i. The research involves no more than minimal risk to the subjects;**
- **ii. The waiver or alteration is unlikely to adversely affect the rights and welfare of the subjects;**
- **iii. The research could not practicably be carried out without the waiver alteration;**
- **iv. Whenever possible and appropriate, the subjects will be provided with additional pertinent information after participation; and**
- **v. The waivered or altered consent does not involve a therapeutic intervention.**

(d) In studies including randomization and blinding in clinical trials, neither the research subjects nor those responsible for their care know which treatment the subjects are receiving before the project commences. Such research is not regarded as a waiver or alteration of the requirements for consent if subjects are informed of the probability of being randomly assigned to one arm of the study or another.

Free and informed consent lies at the heart of ethical research involving human subjects. It encompasses a process that begins with the initial contact and carries through to the end of the involvement of research subjects in the project. As used in this Policy, the process of free and informed consent refers to the dialogue, information sharing and general process through which prospective subjects choose to participate in research involving themselves.

Article 2.1(a) states the requirement in both ethics and law: to protect and promote human dignity. Ethical research involving humans requires free and informed consent. As elaborated more fully below, free and informed consent is exercised by an authorized third party for those who lack legal competence.

Article 2.1(b) states the preference for written evidence of free and informed consent. The Article acknowledges that written consent is not always appropriate. For most people in our society, a signed statement is the normal evidence of consent. However, for some groups or individuals, a verbal agreement, perhaps with a handshake, is evidence of trust, and a request for a signature may imply distrust. Nonetheless, in most cases a written statement of the information conveyed in the consent process, signed or not, should be left with the subject. In some types of research, oral consent may be preferable. In others, written consent is mandatory. Where oral consent is appropriate, the researcher may wish to make a contemporaneous journal entry of the event and circumstances. These and like elements may sometimes need to be refined in concert with the REB, which plays an essential educational and consultative role in the process of seeking free and informed consent. When in doubt about an issue involving free and informed consent, researchers should consult their REB.

The requirement for free and informed consent should not disqualify research subjects who are not proficient in the language used by the researchers from the opportunity to participate in potential research. Such individuals may give consent providing that one or more of the following are observed to the extent deemed necessary by the REB, in the context of a proportionate approach to the harms envisaged in the research and the consent processes that are to be used:

- An intermediary not involved in the research study, who is competent in the language used by the researchers as well as that chosen by the research subject, is involved in the consent process.
- The intermediary has translated the consent document or approved an existing translation of the information relevant to the prospective subject.
- The intermediary has assisted the research subject in the discussion of the research study.
- The research subject has acknowledged in his or her own language, that he or she understands the research study, the nature and extent of his or her participation, including the risks involved, and freely gives consent (see exception in Article 2.1(c)).

Consent is not required from organizations such as corporations or governments for research about their institutions. However, individuals who are approached to participate in a research project about their organization have the right to give free and informed consent. In particular, they should be fully informed about the views of the organization's authorities, if these are known, and of the possible consequences of participation. In this context, researchers should pay special attention to confidentiality. Private corporations and organizations have the right as institutions to refuse to cooperate with researchers or to deny them access to their private records if they so wish, and may have rules governing the conduct of their employees. However, such organizations need not be approached for consent, and REBs should not require such an approach. Nor should institutions be given the right to veto research projects.

Under Article 2.1(c), the REB should exercise judgement on whether the needs for research justify limited and/or temporary exception to the general requirements for full disclosure of information relevant for a research subject's meaningful exercise of free and informed consent. In such cases, subjects may be given only partial information or may be temporarily led to believe that the

research has some other purpose because full disclosure would be likely to colour the responses of the subjects and thus invalidate the research. For example, social science research that critically probes the inner workings of publicly accountable institutions might never be conducted without limited recourse to partial disclosure. Also, some research in psychology seeks to learn about human responses to situations that have been created experimentally. Such research can only be carried out if the subjects do not know in advance the true purpose of the research. In some research, therefore, subjects may be told in advance about the task that they will be asked to perform, yet given additional information, perhaps as part of the consent process or as part of the manipulated experimental conditions, that provides subjects with a different perspective on some aspect of the task or experiment and/or its purpose. Another scenario, in questionnaire research, embeds questions that are central to the researcher's hypothesis within distracter questions, decreasing the likelihood that subjects will adapt their responses to their perceptions of the true objective of the research. For such techniques to fall within the exception to the general requirement of full disclosure for free and informed consent, the research must meet the requirements of Article 2.1(c).

The debriefing referred to in Article 2.1(c)(iv) should be proportionate to the sensitivity of the issue. Often debriefing can be quite simple and straightforward. In sensitive cases, researchers should provide, in addition to candid disclosure, a full explanation as to why subjects were temporarily led to believe that the research or some aspect of it had a different purpose, or received less than full disclosure. They should give details about the importance of the research, the necessity of having to resort to partial disclosure, and their concern about the welfare of the subject. They should seek to remove any misconceptions that may have arisen, and to reestablish any trust which might have been lost, assuring the research subject during debriefing that these research procedures were neither arbitrary nor capricious, but necessary for scientifically valid findings. Debriefing is an important mechanism in maintaining the subject's trust in the research community.

Immediate, full debriefing of all persons who have contributed data may not be feasible in all cases. In studies with data collection over a longer term, debriefing may have to be deferred until the end of the project. In some cases, for example in research involving children, it may be more appropriate to debrief the parents, guardians or authorized third parties rather than the subjects themselves. In other cases, it may be more appropriate to debrief the entire family or community. It may sometimes be appropriate to modify the debriefing to be sensitive to the subject's needs and feelings.

In studies in which a waiver of informed consent has been allowed, it may still be practicable for subjects to exercise their consent at the conclusion of the study, following debriefing. In cases where a subject expresses concerns about a study, the researcher may give the subject the option of removing his or her data from the project. This approach should be used only when the elimination of the subject's data will not compromise the validity of the research design, and hence diminish the ethical value of participation by other subjects.

When subjects express significant concern about being temporarily misled or the use of partial disclosure in the research, the researcher should report those concerns to the REB.

B. Voluntariness

Article 2.2 **Free and informed consent must be voluntarily given, without manipulation, undue influence or coercion.**

The element of voluntariness has important implications. Consent must be freely given and may be withdrawn at any time. Undue influence may take the form of inducement, deprivation or the exercise of control, or authority over prospective subjects.

Voluntariness is especially relevant in research involving restricted or dependent subjects, and is absent if consent is secured by the order of authorities or as a result of coercion or manipulation. The influence of power relationships on voluntary choice should be judged according to the particular context of prospective subjects. For example, the voluntariness of prisoners, members of organizations with authoritarian structures (such as the military, police, some religious groups or street gangs), or of employees or students may be restricted because their institutional context implies undue pressure. Care should be exercised in developing relationships between researchers and authorities, so as not to compromise either the free and informed consent or the privacy and confidentiality of subjects.

Conversely, situations may arise in which an organization, such as a corporation, a government, a political party or a criminal organization that may have been approached about a research project, may wish to prevent the research; however, individuals over whom the organization has some authority may be willing to participate. Researchers and REBs should not prevent such research, but should ensure that potential subjects are fully informed of the views of the organization's authorities and the possible consequences of participation, and pay special attention to confidentiality.

REBs should also pay particular attention to the elements of trust and dependency, for example, within doctor/patient or professor/student relationships, as these can constitute undue influence on the patient to participate in research projects, especially those involving residents in long-term care facilities or psychiatric institutions.

Researchers should avoid being put in a position of becoming informants for authorities or leaders of organizations. The offer of benefits in some contexts may amount to undue inducement, and thus negate the voluntary aspect of the consent of subjects who may perceive such offers as a way to gain favour or improve their situation.

C. Naturalistic Observation

Article 2.3 **REB review is normally required for research involving naturalistic observation. However, research involving observation of participants in, for example, political rallies, demonstrations or public meetings should not require REB review since it can be expected that the participants are seeking public visibility.**

Naturalistic observation is used to study behaviour in a natural environment. Because knowledge of the research can be expected to influence behaviour, naturalistic observation generally implies that the subjects do not know that they are being observed, and hence can not have given their free and informed consent. Due to the need for respect for privacy, even in public places, naturalistic observation raises concerns of the privacy and dignity of those being observed. These concerns are accentuated if, for example, the research records permit identification of the subjects, or if the research environment is staged.

In considering research involving naturalistic observation, researchers and REBs should pay close attention to the ethical implications of such factors as: the nature of the activities to be observed; the environment in which the activities are to be observed (in particular, whether it is to be staged for the purposes of the research); and the means of recording the observations (in particular, if the records will allow subsequent identification of the subjects). Naturalistic observation that does not allow for the identification of the subjects, and that is not staged, should normally be regarded as of minimal risk.

Researchers and REBs should also be aware that, in some jurisdictions, publication of identifying information — for example a photograph taken in a public place but focusing on a private individual who was not expecting this action — may be interpreted in a civil suit as an invasion of privacy.

D. Informing Potential Subjects

D1. General Conditions

Article 2.4 **Researchers shall provide, to prospective subjects or authorized third parties, full and frank disclosure of all information relevant to free and informed consent. Throughout the free and informed consent process, the researcher must ensure that prospective subjects are given adequate opportunities to discuss and contemplate their participation. Subject to the exception in Article 2.1(c), at the commencement of the free and informed consent process, researchers or their qualified designated representatives shall provide prospective subjects with the following:**

(a) Information that the individual is being invited to participate in a research project;

(b) A comprehensible statement of the research purpose, the identity of the researcher, the expected duration and nature of participation, and a description of research procedures;

(c) A comprehensible description of reasonably foreseeable harms and benefits that may arise from research participation, as well as the likely consequences of non-action, particularly in research related to treatment, or where invasive methodologies are involved, or where there is a potential for physical or psychological harm;

(d) An assurance that prospective subjects are free not to participate, have the right to withdraw at any time without prejudice to pre-existing entitlements, and will be given continuing and meaningful opportunities for deciding whether or not to continue to participate; and

(e) The possibility of commercialization of research findings, and the presence of any apparent or actual or potential conflict of interest on the part of researchers, their institutions or sponsors.

Under the normal process of obtaining written consent, the prospective subject should be given a copy of the consent form and any relevant written information. The consent of the participants shall not be conditional upon, or include any statement to the effect that, by consenting, subjects waive any legal rights.

In light of (b) and (c), REBs may require researchers to provide prospective subjects with additional information, such as that detailed in Table 1 on the following page.

Article 2.4 indicates the requirement to give prospective subjects the information they need to give free and informed consent on whether to be involved in the research project. In a research team, the principal researcher is ultimately responsible for the actions of those acting with delegated authority.

Research subjects, whether inside or outside Canada, may have cultural values different from those of the researcher. Thus, as Articles 2.4(a-c) indicate, researchers must clearly explain the nature and goals of the research and other essential information, in a manner appropriate for the prospective subjects' cultural settings. With some cross-cultural research projects, it may not be possible to offer an adequate translation of the researcher's understanding to prospective subjects. REBs should proceed cautiously in such cases and require stringent protection for the interests of subjects, such as appointing an individual to act in an independent advocacy role. On the other hand, REBs should not assume an unnecessarily protective role which suggests that those who do not share the culture of the researchers, particularly those in foreign countries, are incapable of making rational decisions in their own interest.

Articles 2.2 and 2.4(d) help to ensure that a prospective subject's choice to participate is voluntary. Pre-existing entitlements to care, education and other services shall not be prejudiced by the decision on whether to participate. Accordingly, a physician should ensure that continued clinical care is not linked to research participation, and teachers should not recruit prospective subjects from their classes, or students under their supervision, without REB approval. Nothing in this Section should be interpreted as meaning that normal classroom assessments of course work require REB approval. Article 2.4(d) also requires that researchers specifically ascertain continuing consent from subjects on the basis of new information.

TABLE 1

Additional information that may be required for some projects

1. An assurance that new information will be provided to the subjects in a timely manner whenever such information is relevant to a subject's decision to continue or withdraw from participation;

2. The identity of the qualified designated representative who can explain scientific or scholarly aspects of the research;

3. Information on the appropriate resources outside the research team to contact regarding possible ethical issues in the research;

4. An indication as to who will have access to information collected on the identity of subjects, descriptions of how confidentiality will be protected, and anticipated uses of data;

5. An explanation of the responsibilities of the subject;

6. Information on the circumstances under which the researcher may terminate the subject's participation in the research;

7. Information on any costs, payments, reimbursement for expenses or compensation for injury;

8. In the case of randomised trials, the probability of assignment to each option;

9. For research on biomedical procedures, including health care interventions; information about (a) foregoing alternative procedures that might be advantageous to the subject, (b) which aspects of the research involve the use of procedures that are not generally recognized or accepted; and, (c) particularly in trials of therapeutic interventions, the care provided if the potential subject decides not to consent to participation in the study;

10. The ways in which the research results will be published, and how the subjects will be informed of the results of the research.

Article 2.4(e) reminds researchers of relevant ethical duties that govern potential or actual conflicts of interest, as they relate to the free and informed consent of subjects. To preserve and not abuse the trust on which many professional relations reside, researchers should separate their role as researcher from their roles as therapists, caregivers, teachers, advisors, consultants, supervisors, students or employers and the like. If a researcher is acting in dual roles, this fact must always be disclosed to the subject. Researchers should disassociate their role as researcher from other roles, in the recruitment process and throughout the project. Conflict of interest matters are further elaborated below in Section 4.

Table 1 also indicates other information that researchers may be required to provide in some areas of research for the purpose of obtaining free and informed consent. Item 2 refers to the qualified designated representative who is usually someone on the research team. When the research poses more than minimal risk, it may be advisable to have a person who is independent of the research team in this role. Item 3 acknowledges that some institutions may decide either to name an ombudsman for research subjects, or designate, with the agreement of the researcher, a resource person to handle queries, receive complaints, and transmit them to the REB. Item 7 is intended to prevent the development of a payment structure for research participation that might place undue pressure on research subjects either to join or remain within a research project. It does not imply that subjects should be paid for their participation in research. In research projects where subjects will be compensated, REBs should be sensitive to the possibility of undue inducement for participation, such as payments that would lead subjects to undertake actions that they would not ordinarily accept. REBs should pay attention to issues such as the economic circumstances of those in the pool of prospective subjects, and to the magnitude and probability of harms.

Item 10 of the Table indicates that subjects have the right to know whether they will be identified directly or indirectly in publications resulting from the research.

Rushing the free and informed consent process or treating it as a perfunctory routine violates the principle of respect for persons, and may cause difficulty for potential subjects. The time required for the free and informed consent process can be expected to depend on such factors as the magnitude and probability of harms, the setting where the information is given (e.g., hospital or home) and the subject's situation (e.g., level of anxiety, maturity or seriousness of disease).

In some circumstances, witnessing the signatures on the consent form may be felt to be appropriate. In law, the role of a witness is only to attest that the person actually signed the form; a witness is not responsible for certifying such factors as the signature being obtained under defined conditions or that the signers were competent. However, a court might subsequently seek the opinions of the witness on such issues.

E. Competence

Competence refers to the ability of prospective subjects to give informed consent in accord with their own fundamental values. It involves the ability to understand the information presented, to appreciate the potential consequences of a decision, and to provide free and informed consent. This ability may vary according to the choice being made, the circumstances surrounding the decision, or the time in question. Competence to participate in research, then, is not an all-or-nothing condition. It does not require prospective subjects to have the capacity to make every kind of decision. It requires that they be competent to make an informed decision about participation in particular research. Competence is neither a global condition nor a static one; it may be temporary or permanent.

The law on competence varies between jurisdictions. Researchers must comply with all applicable legislative requirements.

Ethical considerations around research involving those who are not competent to give a free and informed consent on their own behalf must seek to balance (1) the vulnerability that arises from their incompetence with (2) the injustice that would arise from their exclusion from the benefits of research.

As indicated in the Ethical Framework in Part 1 above, the principle of respect for human dignity entails high ethical obligations to the vulnerable populations. Such obligations often translate into special procedures to promote and protect their interests and dignity. The Articles that follow detail the special procedures for research involving individuals with diminished decision-making capacity.

Article 2.5 **Subject to applicable legal requirements, individuals who are not legally competent shall only be asked to become research subjects when:**

(a) the research question can only be addressed using individuals within the identified group(s); and

(b) free and informed consent will be sought from their authorized representative(s); and

(c) the research does not expose them to more than minimal risks without the potential for direct benefits for them.

Article 2.5(a) expresses the general requirement to restrict research involving incompetent subjects to questions that can not be addressed with competent subjects. It also expresses the general moral preference for involving competent rather than incompetent research subjects, and the need to avoid selecting prospective subjects merely because of convenience. Article 2.5(b) provides a means of protecting their interests and dignity through the free and informed consent of authorized representatives (see also Articles 2.6 and 2.7), who are acting in the interests of the potential subjects and are not influenced by conflict of interest. Article 2.5(c) restricts the extent to which their authorized representatives can consent on their behalf.

Sound ethical reasoning and the subject-centred perspective require attention to context. In this instance, the notion of harm applied to children should be understood differently from harm in adults. Harm induced in children may have longer-term consequences to their growth and development. Furthermore, harms and benefits for children with chronic disabilities and terminal illnesses require special consideration. Every researcher working with child subjects must consider the possibility of their suffering pain, anxiety or injury, and must develop and implement suitable precautions and ameliorating measures. Cumulative physical, moral, psychological and social consequences (relevant to pain, anxiety and injury) should be reviewed by REBs when assessing the probability, magnitude and character of any harmful impact the research may have on the child.

Article 2.6 **For research involving incompetent individuals, the REB shall ensure that, as a minimum, the following conditions are met:**

(a) **The researcher shall show how the free and informed consent will be sought from the authorized third party, and how the subjects' best interests will be protected.**

(b) **The authorized third party may not be the researcher or any other member of the research team.**

(c) **The continued free and informed consent of an appropriately authorized third party will be required to continue the participation of a legally incompetent subject in research, so long as the subject remains incompetent.**

(d) **When a subject who was entered into a research project through third-party authorization becomes competent during the project, his or her informed consent shall be sought as a condition of continuing participation.**

Article 2.6 outlines other safeguards to protect the dignity, interests and integrity of those who lack competence to give their free and informed consent to participation in research. The Article details various considerations relevant to the use of third-party authorization. Beyond the legal requirements for obtaining free and informed consent from authorized third parties, family members and friends may provide information about the interests and previous wishes of prospective subjects. In some cases, the REB will have to determine from whom the free and informed consent should be sought.

Article 2.7 **Where free and informed consent has been obtained from an authorized third party, and in those circumstances where the legally incompetent individual understands the nature and consequences of the research, the researcher shall seek to ascertain the wishes of the individual concerning participation. The potential subject's dissent will preclude his or her participation.**

Many individuals who are not legally competent are still able to express their wishes in a meaningful way, even if such expression may not fulfil the requirements for free and informed consent. Prospective subjects may thus be capable of verbally or physically assenting to, or dissenting from, participation in research. Those who may be capable of assent or dissent include: (a) those whose competence is in the process of development, such as children whose capacity for judgement and self-direction is maturing; (b) those who once were capable of making an informed decision about

informed consent, but whose competence is now considerably, but not completely, diminished, such as individuals with early Alzheimer's disease; and (c) those whose competence remains only partially developed, such as those suffering from permanent cognitive impairment.

F. Research in Emergency Health Situations

Article 2.8

Subject to all applicable legislative and regulatory requirements, research involving emergency health situations shall be conducted only if it addresses the emergency needs of individuals involved, and then only in accordance with criteria established in advance of such research by the REB. The REB may allow research that involves health emergencies to be carried out without the free and informed consent of the subject or of his or her authorized third party if ALL of the following apply:

(a) A serious threat to the prospective subject requires immediate intervention; and

(b) Either no standard efficacious care exists or the research offers a real possibility of direct benefit to the subject in comparison with standard care; and

(c) Either the risk of harm is not greater than that involved in standard efficacious care, or it is clearly justified by the direct benefits to the subject; and

(d) The prospective subject is unconscious or lacks capacity to understand risks, methods and purposes of the research; and

(e) Third-party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so; and

(f) No relevant prior directive by the subject is known to exist.

When a previously incapacitated subject regains capacity, or when an authorized third party is found, free and informed consent shall be sought promptly for continuation in the project and for subsequent examinations or tests related to the study.

For purposes of studying potential improvement in the treatment of life-threatening conditions, Article 2.8 outlines an exception, in addition to that in Article 2.1(c), to the general obligation of obtaining the free and informed consent from those participating in research.

The exception is intended for a limited class of health research: that which takes place in emergency situations where obtaining free and informed consent from the subjects is not possible due to loss of consciousness or competence, and free and informed consent from an authorized third party is not possible due to the urgent time constraints for effective intervention. Seeking consent in advance is often impossible due to the unforeseeable nature of the causes of the medical emergency. However, individuals and those in comparable future situations should not be denied potential benefits of research because of the inability to consent.

Researchers must justify to the REB recourse to the provisions of this exception. The underlying assumption of Article 2.8 is that direct research benefits to the subject could not be secured without foregoing the free and informed consent of the subject or of his or her authorized third party. Article 2.8 indicates that research in emergency medicine must be reviewed by the REB, be restricted to the emergency needs of the subjects, and be conducted under criteria designated by the REB. Article 2.8 outlines the minimal conditions necessary for the REB to authorize a research without free and informed consent.

It is unethical to expose subjects to any additional risk of harm without their free and informed consent if standard efficacious care exists, unless it can clearly be shown that there is a realistic possibility of significantly improving the subject's condition. Accordingly, Articles 2.8 (b) and (c) indicate that researchers and REBs must assess the potential risk of harms and benefits of proposed research against existing standard efficacious care. Together, Articles 2.8(b) and (c) require that the therapeutic aspects of the trial satisfy the requirements of clinical equipoise. To respect the autonomy of the research subject, Article 2.8(e) requires researchers to undertake diligent efforts to contact family members or authorized third parties, if reasonably feasible, and to document such efforts for the benefit of both the subject and for the monitoring or continuing review functions of the REB. The Article also requires that research subjects who become competent be promptly afforded the opportunity to give free and informed consent concerning continued participation. Concern for the patient's well-being is paramount and should be informed by ethical and professional judgement.

Because their incapacity to exercise free and informed consent makes them vulnerable, prospective subjects for emergency research are owed special ethical obligations and protection commensurate with the harms involved. Their interests, rights, and welfare should be protected by additional safeguards which should include, where feasible and appropriate, one or more of the following:

- Additional scientific, medical or REB consultation;
- Procedures to identify potential subjects in advance to obtain free and informed consent prior to the occurrence of the emergency situation;
- Consultation with former and potential subjects;
- Special monitoring procedures to be followed by safety and monitoring boards; and
- Careful review by the REB of the relative harms and benefits of participation.

Endnotes

[1] Article 2.1(c) was adapted from *Protection of Human Subjects*, U.S. Dept. of Health & Human Services, Title 45; *Code of Federal Regulations, Part 46.116(d).*

[Section 3]

PRIVACY AND CONFIDENTIALITY

Dignity and autonomy of human subjects is the ethical basis of respect for the privacy of research subjects. Privacy is a fundamental value, perceived by many as essential for the protection and promotion of human dignity. Hence, the access, control and dissemination of personal information are essential to ethical research.

Information that is disclosed in the context of a professional or research relationship must be held confidential. Thus, when a research subject confides personal information to a researcher, the researcher has a duty not to share the information with others without the subject's free and informed consent. Breaches of confidentiality may cause harm: to the trust relationship between the researcher and the research subject; to other individuals or groups; and/or to the reputation of the research community. Confidentiality applies to information obtained directly from subjects or from other researchers or organizations that have a legal obligation to maintain personal records confidential. In this regard, a subject-centred perspective on the nature of the research, its aims and its potential to invade sensitive interests may help researchers better to design and conduct research. A matter that is public in the researcher's culture may be private in a prospective subject's culture, for example.

There is a widespread agreement about the rights of prospective subjects to privacy and the corresponding duties of researchers to treat private information in a respectful and confidential manner. Indeed, the respect for privacy in research is an internationally recognized norm and ethical standard. It has been enshrined in Canadian law as a constitutional right and protected in both federal and provincial statutes. Model voluntary codes have also been adopted to govern access to, and the protection of, personal information.[1]

The values underlying the respect and protection of privacy and confidentiality are not absolute, however. Compelling and specifically identified public interests, for example, the protection of health, life and safety, may justify infringement of privacy and confidentiality. Laws compelling mandatory reporting of child abuse, sexually transmitted diseases or intent to murder are grounded on such reasoning; so too are laws and regulations that protect whistle-blowers. Similarly, without access to personal information, it would be difficult, if not impossible, to conduct important societal research in such fields as epidemiology, history, genetics and politics, which has led to major advances in knowledge and to an improved quality of life. The public interest thus may justify allowing researchers access to personal information, both to advance knowledge and to achieve social goals such as designing adequate public health programmes.

Historically, the benefits of the confidential research use of personal data have been substantial. Two of many such examples are: the identification of the relationship between tobacco and lung cancer; and the use of employment or educational records to identify the benefits or harms of various social factors. In the last two decades, larger data bases and newer techniques have improved the capacity of researchers to evaluate the delivery of services and the outcomes of many procedures and products. These studies have contributed to more responsive and efficient service delivery in areas such as health, education, safety and the environment.

Ethics review is thus an important process for addressing this conflict of societal values. The REB plays an important role in balancing the need for research against infringements of privacy and minimizing any necessary invasions of privacy. Individuals should be protected from harm caused by unauthorized use of personal information in which they believed they had an expectation of privacy and the benefit of confidentiality.

The situation may arise where a third party attempts to gain access to research records, and hence to breach the promise of confidentiality given by the researcher as part of a research project approved by the REB. By that time, the matter has passed from the hands of the REB. The researcher is honour-bound to protect the confidentiality that was undertaken in the free and informed consent process, to the extent possible within the law. The institution should normally support the researcher in this regard, in part because it needs to protect the integrity of its own REB. If the third party attempts to secure the research data by subpoena, it is legitimate for the researcher and the institution to argue the issue in court. The records of the REB and of the consent might be useful as part of this counter-argument, or may be requested by those seeking access. However, if the court issues a subpoena, legal appeals will probably be the only legal option open to the researcher to protect the confidentiality of the records.

In the free and informed consent process, researchers should indicate to research subjects the extent of the confidentiality that can be promised, and hence should be aware of the relevant law.

The Articles below articulate the general rule to protect privacy and confidentiality through notification and consent of the individuals whose personal information is involved. For the purposes of this Policy, identifiable personal information means information relating to a reasonably identifiable person who has a reasonable expectation of privacy. It includes information about personal characteristics such as culture, age, religion and social status, as well as their life experience and educational, medical or employment histories. However, Article 1.1(c) excludes from REB review research that is based exclusively on publicly available information. This includes documents, records, specimens or materials from public archives, published works and the like, to which the public is granted access.

As a general rule, the best protection of the confidentiality of personal information and records will be achieved through anonymity. If the data being stored are truly anonymous, the research project will need only minimal REB scrutiny.

A. Accessing Private Information: Personal Interviews

Article 3.1 **Subject to the exceptions in Article 1.1(c), researchers who intend to interview a human subject to secure identifiable personal information shall secure REB approval for the interview procedure used and shall ensure the free and informed consent of the interviewee as required in Article 2.4. As indicated in Article 1.1, REB approval is not required for access to publicly available information or materials, including archival documents and records of public interviews or performances.**

Article 3.1 requires REB approval for collection of information through personal interviews, which may be described as including such means as face-to-face, telephone or other electronic encounters, or individualized questionnaires, which the researcher uses to gather materials for such purposes as a biographical study or other research involving specific personalities. To assist the review of such activities, REBs may wish to encourage faculties and departments which use individual interviews extensively to develop standard interview procedures based on Article 2.3, this Article, and on the requirements of their professional organizations, if they so wish. Prior approval of such interview procedures may greatly simplify further review of similar protocols, though the dangers of attempting to enforce a single interview procedure on the varied circumstances within a complex institution are evident.

The task of the REB is to ensure that individuals who are approached for interviews are given the information required by this Policy in order to be able to give free and informed consent. It is clear that individuals have the right to refuse to be interviewed, if they so wish.

Nothing in this article should be interpreted to mean that REBs should engage in prior censorship of research concerning those in the public arena or in artistic and literary life (see Article 1.1(c)).

B. Accessing Private Information: Surveys, Questionnaires and the Collection of Data

Article 3.2 **Subject to Article 3.1 above, researchers shall secure REB approval for obtaining identifiable personal information about subjects. Approval for such research shall include such considerations as:**

(a) The type of data to be collected;

(b) The purpose for the which the data will be used;

(c) Limits on the use, disclosure and retention of the data;

(d) Appropriate safeguards for security and confidentiality;

(e) Any modes of observation (e.g., photographs or videos) or access to information (e.g., sound recordings) in the research that allow identification of particular subjects;

(f) Any anticipated secondary uses of identifiable data from the research;

(g) Any anticipated linkage of data gathered in the research with other data about subjects, whether those data are contained in public or personal records; and

(h) Provisions for confidentiality of data resulting from the research.

Article 3.2 requires researchers to secure REB review before commencing research involving identifiable personal information collected from subjects by such means as interviews, questionnaires, observation, access to private files or records, etc.

Researchers should ensure that the data obtained are stored with all the precautions appropriate to the sensitivity of the data. Data released should not contain names, initials or other identifying information. While it may be important to preserve certain types of identifiers (e.g., region of residence), these should be masked as much as possible using a standardized protocol before the data are released for research purposes. However, legitimate circumstances may exist where such information is critical for the research project. Accordingly, information that identifies individuals or groups should be kept in different databases with unique identifiers. Researchers should take reasonable measures to ensure against inadvertent identification of individuals or groups, and must address this issue to the satisfaction of the REB.

Article 3.2 states that subjects have a right to know who will have access to identifying information and its nature. In particular, the researcher should inform the subject if the information will be provided to the government, government agencies, personnel from an agency that monitors the research, the research sponsor (e.g., a pharmaceutical company), the REB or a regulatory agency. This would also include situations in which mandatory reporting is required, such as under laws requiring reporting of child abuse, infectious diseases or homicidal intent. The REB and the researcher should be sensitive to the interests of those who might suffer from stigmatization. For example, when records of prisoners, employees, students or others are used for research purposes, the researcher should not provide authorities with results that could identify individuals, unless the prior written consent of the subjects is obtained. Researchers may, however, provide aggregated data that cannot be linked to individuals to administrative bodies for policy decision-making purposes.

Article 3.2 refers not only to the secondary uses of information in research, but also for other purposes such as the subsequent use of research videos for educational purposes. It is essential that subsequent uses of data be specified in sufficient detail that prospective subjects may give free and informed consent; it is inappropriate to seek a blanket permission for "research in general." Article 3.2(g) is important because information that may on its own be seen as innocuous by the subject may take on a completely different meaning if linked to other data (see Article 3.6).

C. Secondary Use of Data

Secondary use of data refers to the use in research of data contained in records collected for a purpose other than the research itself. Common examples are patient or school records or biological specimens, originally produced for therapeutic or educational purposes, but now proposed for use in research. This issue becomes of concern only when data can be linked to individuals, and becomes critical when the possibility exists that individuals can be identified in the published reports.

Article 3.3 **If identifying information is involved, REB approval shall be sought for secondary uses of data. Researchers may gain access to identifying information if they have demonstrated to the satisfaction of the REB that:**

(a) Identifying information is essential to the research; and

(b) They will take appropriate measures to protect the privacy of the individuals, to ensure the confidentiality of the data, and to minimize harms to subjects;

(c) Individuals to whom the data refer have not objected to secondary use.

Data bases can vary greatly in the degree to which personal information is identifiable. A proportionate approach should be applied by the REB to evaluate the sensitivity of the information in the database and to modulate its requirements accordingly. If it is impossible to identify individuals whose records exist within a database, then researchers should be allowed access to that database. The REB must carefully appraise the possibility of identification, in particular with regard to the extent of the harm or stigma which might be attached to identification. The REB and the researcher should also be aware of legal provisions that affect the database(s) to be used in the research.

REBs and researchers should also be sensitive to the context in which the database was created, such as a confidential relationship, as well as to the expectations of the groups or individuals at the time of the collection of the data with regard to its use, retention and disclosure. When it is unclear as to whether information is to be regarded as personal, researchers should consult their REBs. Confidential information collected in this manner should normally not be transmitted to authorities, unless required by law, the courts or similar legally constituted bodies.

Article 3.4 **The REB may also require that a researcher's access to secondary use of data involving identifying information be dependent on:**

(a) The informed consent of those who contributed data or of authorized third parties; or

(b) An appropriate strategy for informing the subjects; or

(c) Consultation with representatives of those who contributed data.

Article 3.4 is based on the concept of a proportionate approach to ethical assessment of research. Under it, the REB should focus on projects above minimal risk, or modulate requirements and protection proportionate to the magnitude and probability of harms, including the likelihood that published data can be linked to individuals. In highly sensitive situations such as when identifiable data will be published or other instances when there is a significant risk of breach of confidentiality, Article 3.4(a) indicates that such deliberations and balancing may lead the REB to seek consent to use the stored data from those who made the contribution.

It may be impossible, difficult or economically unfeasible to contact all subjects in a study group to obtain informed consent. This can occur when the group is large or its members are deceased, geographically dispersed or difficult to track. In such cases, Article 3.4(b) requires that the researcher propose an appropriate strategy for informing the relevant parties or, in accord with Article 3.4(c), that there be consultation with representative members of the affected group (e.g., in an AIDS study, contacting one or a number of AIDS advocacy groups), or that there be some way to sample the opinions of a subset of individuals in the group.

Article 3.5 **Researchers who wish to contact individuals to whom data refer shall seek the authorization of the REB prior to contact.**

In certain cases, the research goal may only be achieved by follow-up contact and interviews with persons. It is evident that individuals or groups might be sensitive if they discover that research was conducted on their data without their knowledge; others many not want any further contact. This potential harm underlines the importance for researchers to make all efforts to allow subjects the right to consent that their data and private information be part of a study.

D. Data Linkage

Article 3.6 **The implications of approved data linkage in which research subjects may be identifiable shall be approved by the REB.**

Advances in our abilities to link databases create both new research opportunities and new threats to privacy. These techniques may provide avenues for addressing previously unanswerable questions and for generating better social and health-related information. The values underlying the ethical obligation to respect privacy oblige researchers and REBs to exercise caution in the creation and use of data of this kind. REBs should also be aware of relevant statutory frameworks, and the criteria required by government for authorization of use of data in governmental data banks.[2]

Endnotes

1 Canada Standards Association, *Model Code for the Protection of Personal Information* (CSA; 1996).

2 See the *Statistics Act*, R.S.C., c. S-19 1985

[Section 4]

CONFLICT OF INTEREST

Researchers hold trust relationships with research subjects, research sponsors, institutions, their professional bodies and society. These trust relationships can be put at risk by conflicts of interest that may compromise independence, objectivity or ethical duties of loyalty. Although the potential for such conflicts has always existed, pressures to commercialize research have led to increased concerns. Researchers, their institutions and REBs should identify and address conflicts of interest — real or apparent — to maintain the public confidence and trust, discharge professional obligations and ensure accountability.

Article 4.1 **Researchers and REB members shall disclose actual, perceived or potential conflicts of interest to the REB. REBs should develop mechanisms to address and resolve conflicts of interest.**

A. Conflicts of Interest Involving Researchers

The REB should assess the likelihood that the researcher's judgement may be influenced, or appear to be influenced, by private or personal interests, and assess the seriousness of any harm that is likely to result from such influence or from the mere appearance of undue influence. Competing interests may arise from family relationships, financial partnerships or other economic interests.

The appearance of a conflict may in some cases be as damaging as a real conflict. Two approaches can be suggested for assessing the potential implications of apparent or real conflicts of interest. One might ask whether an outside observer would question the ability of the individual to make a proper decision despite possible considerations of private or personal interests; alternatively, one might ask whether the public would believe that the trust relationship between the relevant parties could reasonably be maintained if they had accurate information on the potential sources of conflict of interest.

When a significant real or apparent conflict of interest is brought to its attention, the REB should require the researcher to disclose this conflict to the prospective subjects during the free and informed consent process. In accord with Article 2.3(e), research subjects should be fully informed of a researcher's potential or actual conflict of interest. To identify and address conflicts properly, REBs should be provided with details on the research project, budgets, commercial interests, consultative relationships and other relevant information (see Article 7.3).

REB management of conflicts of interest requires a proportionate approach. Sometimes, the conflict of interest is so pervasive that it is not enough merely to disclose it to the research subjects, the sponsors of research, institutions, relevant professional bodies or the public at large. In such instances, the REB may require that the researcher abandon one of the interests in conflict. A conscientious researcher will, under such circumstances, either withdraw from the research or allow others to make research-related decisions without being directed to do so. However, in some cases, the REB might conclude that the identified conflict of interest does not warrant specific

actions. When significant conflicts of interest are identified, the continuing ethics review process by the REB may also help to manage them (see Section 1). When a conflict of interest is unavoidable, the continuing ethics review process should be made more stringent, to help ensure that conflicts are managed appropriately.

B. Conflicts of Interest by REB Members

To maintain the independence and integrity of ethics review, it is of the highest importance that members of the REB avoid real or apparent conflicts of interest (see Article 1.12). For example, REB members are in a clear conflict of interest when their own research projects are under review by their REB or when they have been in direct academic conflict or collaboration with the researcher whose proposal is under review. To manage such conflicts, REB members must withdraw from the committee when such projects are under consideration. In some instances, individual members of the REB may also have a conflict of interest in accepting undue or excessive honoraria for their participation in the REB (e.g., on commercial REBs).

C. Institutional Conflicts of Interest

The REB must act independently from the parent organization. Therefore, institutions must respect the autonomy of the REB and ensure that the REB has the appropriate financial and administrative independence to fulfil its primary duties. Situations may arise where the parent organization has a strong interest in seeing a project approved before all ethical questions are resolved. As the body mandated to maintain high ethical standards, however, the public trust and integrity of the research process require that the REB maintain an arms-length relationship with the parent organization and avoid and manage real or apparent conflicts of interest.

[Section 5]

INCLUSION IN RESEARCH

A. Introduction

As indicated in the Ethics Framework in Part 1, an important aspect of the principle of justice is the fair distribution of benefits and burdens. Historically, concern for justice in research involving human subjects has focused on whether research subjects were treated fairly: were they overburdened relative to the direct benefits they received from their participation in research? Contemporary concerns with justice in research have broadened: are the overall benefits and burdens of research distributed fairly, and have disadvantaged individuals and groups received a fair share of the benefits of research?

The above two concerns form the basis of the principle of distributive justice: members of society should neither bear an unfair share of the direct burdens of participating in research, nor should they be unfairly excluded from the potential benefits of research participation. The concerns raised by the principle reflect broader obligations to respect human dignity and diversity. They should, therefore, receive the formal attention of researchers, REBs, research institutions and sponsors.

Unfortunately, the history of research involving human subjects contains chapters on the misuse or serious abuse of research subjects. Continuing concerns about such abuses have sharpened ethical focus on the relative levels of benefits and harms that research would impose on prospective subjects. The important concerns about exploiting vulnerable populations and visiting harms on research subjects are also relevant to the Sections of this Policy on free and informed consent, privacy and REBs. Accordingly, this Section focuses on the fair distribution of the direct and indirect benefits of research.

A number of sources of unfair distribution of the benefits of research can be identified. Sometimes the harms have resulted from intentional exclusion, such as that inspired by concerns about the misuse or abuse of research subjects. Thus, some have argued that the principle of free and informed consent means that only competent individuals should be permitted to participate in research that would likely be harmful or of no benefit to them. Strict application of such a principle would deny incompetent individuals many of the benefits of research participation, either directly or indirectly. In a sense, such beneficence-based reasoning and practices intentionally exclude certain groups from research. In attempting to avoid the moral problem of exploiting vulnerable research subjects, such practices may incur the moral problem that individuals in need of the benefits of research may be denied them.

Exclusion from research has also arisen indirectly. For example, concerns about legal liability associated with particular populations have prompted the exclusion of women of child-bearing age from drug trials because of possible harms to potential offspring. Further exclusions have been based (a) on concerns about factors such as the effects of the female hormone cycle on drug trials; (b) on the choice of criteria for inclusion or exclusion, such as those based on age that had the effect of including most male heart attack victims but excluding most females suffering from the same disease; and (c) on financial and other impediments to changing the direction of established research programmes.

As another example, age has been used unfairly to exclude individuals from participation in research. The result of such exclusion is that insufficient research has been done on the young and on the elderly. As the Canadian population ages, the necessity for research on the aging process and on the conditions that disproportionately affect the elderly grow concomitantly. Participation of elderly individuals poses significant questions for researchers, one of the most important being how to establish and maintain a balance between respect for the dignity and welfare of the individual and the provision of necessary protection for those who are, or who may become, incompetent (see Section 1). Article 5.1 also imposes a duty to guard against the exclusion of elderly research subjects on the basis of biases that they may be unable to comply with the researcher's directions.

Whether intentional or inadvertent, the exclusion of some from the benefits of research violates the commitment to societal justice. A commitment to distributive justice in research imposes obligations on, and concerted activities by researchers, institutions and REBs. All have important roles to play in ensuring a fairer distribution of the benefits and burdens of research. As the following articles make clear, distributive justice imposes on researchers and REBs a duty not to act in a discriminatory fashion. Sometimes it may impose positive duties to include disadvantaged groups in research involving human subjects.

Article 5.1

(a) Where research is designed to survey a number of living research subjects because of their involvement in generic activities (e.g., in many areas of health research or in some social science research such as studies of child poverty or of access to legal clinics) that are not specific to particular identifiable groups, researchers shall not exclude prospective or actual research subjects on the basis of such attributes as culture, religion, race, mental or physical disability, sexual orientation, ethnicity, sex or age, unless there is a valid reason for doing so.

(b) This article is not intended to preclude research focused on a single living individual (such as in a biography) or on a group of individuals who share a specific characteristic (as in a study of an identifiable group of painters who happen to be all of one sex, colour or religion, or of a religious order which is restricted to one sex).

The principle of distributive justice inspires Article 5.1. It imposes a duty on researchers not to discriminate against disadvantaged groups. Groups that have been disadvantaged in the context of research include women, people of colour or of different ethnicity, the elderly, children and restricted or dependent people. The intention of this section is not to discourage research which focuses on a particular group, particularly research in the social sciences and the humanities. Rather, the intention is to achieve a more just distribution of the benefits of research across all groups.

B. Research Involving Women

As indicated, women have historically been excluded from participating in some research largely because of concerns about: damaging either the foetus or the woman's reproductive capacity; harming the newborn through breast-feeding; the influence of hormonal cycles; or failing to recognize that diseases and conditions might affect men and women differently, for example at different ages; and fear of liability by research sponsors. Such exclusions retard the advance of knowledge, deny potential benefits to women and may expose women to heightened risk. For example, the exclusion of women as research subjects raises serious concerns regarding the generalizability and reliability of some research data; and research data on drug dosages, the effects of devices, treatments, cultural norms, moral development and social behaviour obtained from male-only studies likely will not be generalizable to women. As a result, data for women are lacking and often must be inferred, despite important differences which may render such inferences inaccurate and treatments or interventions based thereon more harmful. The inclusion of women in research is essential if men and women are equally to benefit from research. It advances both the commitment to justice and to rigorous scholarly or scientific analysis.

Article 5.2 **Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity.**

Like Article 5.1, Article 5.2 imposes obligations of equitable treatment of potential subjects on REBs and researchers. While some research is properly focused on particular populations that do not include women or only include very few women, in most studies women should be represented.

The Article is also clear about presumptive or automatic exclusion from research on the basis of sex or reproductive capacity. If in the past many women have been automatically excluded from research on such grounds, Article 5.2 rejects such an approach as a discriminating and unethical use of inclusion or exclusion criteria. Rather, in considering research on pregnant women, researchers and REBs must take into account potential harms and benefits for the pregnant woman and her embryo, foetus or infant. The ethical duty to assess the harms and benefits of research thus extends to the special case of research involving pregnant or breast-feeding women.

C. Research Involving Those Who Are Incompetent to Consent for Themselves

Although ethical duties to vulnerable populations preclude the exploitation of those who are incompetent to consent for themselves for research purposes, there is nonetheless an obligation to conduct research involving such people because it is unjust to exclude them from the benefits that can be expected from research (see Section 2).

Article 5.3 **Subject to the provisions in Articles 2.6 to 2.8, those who are not competent to consent for themselves shall not be automatically excluded from research which is potentially beneficial to them as individuals, or to the group that they represent.**

Article 5.3 expresses the need for research that involves those who, though not competent to consent for themselves, are unique individuals who command all the respect, justice and inclusiveness that are accorded to competent individuals. The behaviour, psychology, biology and diseases of infants and children who are incompetent because of immaturity often differ markedly from those of adults; also, incompetence is often caused by disease, which cannot be studied only in those without the disease. However, the ethical imperative for research as expressed in Article 5.3 must be interpreted in the context of the safeguards expressed in Articles 2.6 to 2.8.

[Section 6]

RESEARCH INVOLVING ABORIGINAL PEOPLES

During the drafting of this Policy Statement, suggestions were made to create a Section dealing with research involving aboriginal peoples. The Councils, however, have not held sufficient discussions with representatives of the affected peoples or groups, or with the various organizations or researchers involved. The Councils have therefore decided that it is not yet appropriate to establish policies in this area. The text of Section 6, which builds on the extensive literature on research involving aboriginal peoples, is intended to serve as a starting point for such discussions.

A. Introduction

There is growing recognition that some research involving aboriginal individuals may also involve the communities or groups to which they belong. The Councils affirm that in developing ethical standards and practices, aboriginal peoples have rights and interests which deserve recognition and respect by the research community. This Section thus has three aims: to assist researchers and REBs in determining which projects might involve research on such groups; to illustrate ethical issues and conduct for such research; and to indicate good practices that researchers should consider.

Guidance on these issues comes from at least two sources. The first is the ethical principles, standards and procedures articulated throughout this Policy. Thus, for example, ethics review should be proportionate to the risks of potential harm. As well, informed consent and the concepts of harm, benefits and confidentiality should be informed by the perspective of the participant group.[1] For the expertise essential to effective ethics review, REBs may need to involve academic or community members from representative groups, or advisory committees drawn from relevant communities (see Article 3.4(c)). Such approaches and the principles are consistent with the work of the SSHRC some two decades ago.[2]

The second source of ethical guidance comes from the specific additional provisions developed in Canada and in other countries for research involving aboriginal peoples. Beginning in Australia in 1986, research agencies and aboriginal peoples have set out guidelines for the conduct of research in aboriginal communities. These guidelines do not replace ethical standards for the conduct of research on individuals; they seek to suggest additional requirements to ensure that the rights and interests of the community as a whole are respected. International,[3] Australian,[4] Canadian (see below) and American[5] guidelines are currently available. The high degree of agreement and consensus among these guidelines is remarkable, perhaps reflecting commonalities in the experience of these communities and the sharing of existing guidelines among communities.

Three documents are especially relevant to research on aboriginal peoples in Canada. They were prepared by the Association of Canadian Universities for Northern Studies,[6] the Royal Commission on Aboriginal Peoples[7] and the Inuit Circumpolar Conference. Researchers and REBs considering research involving aboriginal communities should be familiar with the relevant documents. All three documents agree on the following requirements for research involving aboriginal communities.

Research may involve aboriginal communities when it focuses on the community, its subgroups or individuals as members. The research may seek information on the characteristic beliefs, values, social structures or other features by which members identify themselves as group members. Alternatively, the group may be involved in the conduct, direction, sponsorship or implementation of the research. A general principle is that the obligation to respect human dignity in research involving aboriginal groups gives rise to both special considerations and to basic ethical duties regarding ethics review, informed consent, confidentiality, conflict of interest and inclusion (see Sections 1-5). This principle is not intended to preclude critical inquiry and research, or research that may come to negative conclusions; rather it seeks to advance accurate, informed and ethical research.

In Canada and elsewhere, aboriginal peoples have distinctive perspectives and understandings embodied in their cultures and histories. This Policy Statement recognizes the international consensus that has developed over recent decades that aboriginal peoples have a unique interest in ensuring accurate and informed research concerning their heritage, customs and community.

Research involving aboriginal communities may raise difficult ethical issues, sometimes novel and sometimes old. As indicated in the Ethics Framework described in this document, for example, research that is premised on respect for human dignity entails high obligations to individuals and groups. Indeed, there are historical reasons why indigenous or aboriginal peoples may legitimately feel apprehensive about the activities of researchers. In many cases, research has been conducted in respectful ways and has contributed to the well-being of aboriginal communities. In others, aboriginal peoples have not been treated with a high degree of respect by researchers. Inaccurate or insensitive research has caused stigmatization. On occasion, the cultural property and human remains of indigenous peoples have been expropriated by researchers for permanent exhibition or storage in institutes, or offered for sale. Researchers have sometimes treated groups merely as sources of data, and have occasionally endangered dissident indigenous peoples by unwittingly acting as information-gatherers for repressive regimes. Such conduct has harmed the participant communities and spoiled future research opportunities.

Other aspects of research involving aboriginal peoples present ethical challenges. Since researchers may belong to a different culture, for example, debates may arise because of different definitions of public and private life. Notions of property will sometimes differ between the researcher, sponsors and the community. Language differences may impede clear communication and understanding that is instrumental to the informed consent process. A researcher may also be confronted by ethical dilemmas because of competing interests among different sections of the community.

For reasons such as these, when research involves aboriginal individuals, researchers and REBs should consider the interests of the aboriginal group, when any of the following considerations applies:

(a) Property or private information belonging to the group as a whole is studied or used.

(b) Leaders of the group are involved in the identification of potential participants.

(c) The research is designed to analyze or describe characteristics of the group.

(d) Individuals are selected to speak on behalf of, or otherwise represent, the group.

The considerations above outline the proposed situations in which REBs should review the need for involving the community in research involving aboriginal peoples. Item (a) includes cultural properties[8] as understood by the aboriginal community in question and may include human tissue (Section 10). Item (b) covers research where the group is asked to assist in recruiting its members, or to give official approval and permit access to their property. Together, items (c) and (d) would include research in which members are interviewed as spokespersons for the group as a whole. The central issue for discussion is when it is legitimate for researchers to interview individuals in their own right as individuals, without regard to the interests of the group as a whole and without seeking permission from any group authority or spokesperson or, conversely, when the approval of the community as a whole should be required.

B. Good Practices

Researchers and REBs involved with aboriginal communities should consider the following "good practices" which have been drawn from the documents referred to above:[9]

- To respect the culture, traditions and knowledge of the aboriginal group;
- To conceptualize and conduct research with aboriginal group as a partnership;
- To consult members of the group who have relevant expertise;
- To involve the group in the design of the project;
- To examine how the research may be shaped to addresses the needs and concerns of the group;
- To make best efforts to ensure that the emphasis of the research, and the ways chosen to conduct it, respect the many viewpoints of different segments of the group in question;
- To provide the group with information respecting the following:
  - Protection of the aboriginal group's cultural estate and other property;
  - The availability of a preliminary report for comment;
  - The potential employment by researchers of members of the community appropriate and without prejudice;
  - Researchers' willingness to cooperate with community institutions;
  - Researchers' willingness to deposit data, working papers and related materials in an agreed-upon repository.
- To acknowledge in the publication of the research results the various viewpoints of the community on the topics researched; and

- To afford the community an opportunity to react and respond to the research findings before the completion of the final report, in the final report or even in all relevant publications (see Section 2 on information disclosure).

  Aboriginal peoples may wish to react to research findings. It is inappropriate for researchers to dismiss matters of disagreement with the group without giving such matters due consideration. If disagreement persists, researchers should afford the group an opportunity to make its views known, or they should accurately report any disagreement about the interpretation of the data in their reports or publications.

Endnotes

1 Medical Research Council of Canada, *Guidelines on Research Involving Human Subjects*, Ottawa, 1987, pp 27-28.

2 Social Sciences and Humanities Research Council of Canada, *Ethics Guidelines for Research with Human Subjects*, Ottawa, 1977, p.1-2. (Affirming, as regards collective rights, the right to be fully informed about the nature and purpose of the research to enable the informed choice of the group; the right to assurance that privacy will not be invaded and that any information disclosed will remain confidential; the right of living members of a society regarding the entry of 'outsiders' to examine their burial grounds, cultural property or to exhibit and dispose of these objects.)

3 Inuit Circumpolar conference. *Principles and Elements for a Comprehensive Arctic Policy*, Alaska, Greenland, Canada; Council for International Organizations of Medical Sciences. *International Guidelines for Ethical Review of Epidemiological Studies.* Geneva: WHO, 1991.

4 National Health and Medical Research Council of Australia, *Guidelines of Ethical Matters in Aboriginal and Torres Strait Islander Health Research*. Canberra: NHMRC, 1991.

5 American Anthropological Association, *Statement on Ethics: Principles of Professional Responsibility*, Adopted by the Council of the American Anthropological Association, May 1971; American Public Health Association Task Force. National Arctic Health Science Policy. Washington, D.C.: APHA, 1984; American Indian Law Center. Model Tribal Research Code. Albuquerque, 1994; and U.S. Interagency Arctic Research Policy Committee, *Principles for the Conduct of Research in the Arctic.* Arctic Research of the United States 1995; 9(Spring): 56-57.

6 Association of Canadian Universities for Northern Studies, *Ethical Principles for the Conduct of Research in the North*, Ottawa: ACUNS, 1982, reprinted, 1988.

7 Royal Commission on Aboriginal Peoples. Appendix B: *Ethical Guidelines for Research.* Ottawa: RCAP, 1993.

8 See, e.g., UNESCO, *Convention on Cultural Properties*...of 14 Nov. 1970.

9 See, e.g., American Anthropological Association, Statement on Ethics (1991); American Indian Law Center, Inc., *Model Tribal Research Code* (2d ed., 1994); Board of the Swiss Academy of Humanities and Social Sciences and of the Swiss-Liechtenstein Foundation for Archaeological Research Abroad, *Principles for Partnership in Cross-Cultural Human Sciences Research with a Particular View to Archaeology* (1994). Canadian Archaeological Association, *Statement of Principles for Ethical Conduct Pertaining to Aboriginal Peoples* (1996); Canadian Association of Universities of Northern Studies, *Ethical Principles for the Conduct of Research in the North* (1997).

[Section 7]

CLINICAL TRIALS

Clinical trials are most frequently undertaken in biomedical or health research, although other clinically related disciplines, such as psychology, also conduct research that evaluates interventions, usually by comparing two or more approaches. In this Section, clinical trials will be discussed in the context of biomedical research with emphasis on pharmaceutical trials.

Researchers conducting clinical trials seek different research objectives under various research formats. Clinical trials may include questions that are not directly related to therapy (for example, cost effectiveness, drug metabolism), in addition to those that directly affect the treatment of the subjects. They may also take the form of case studies, cohort studies, case control studies, "n of 1" studies, or multicentre clinical trials. Although the types and forms of clinical trials naturally create methodological differences, they all can accommodate the ethical principles and procedures articulated in this Policy. Four topics of clinical trials that give rise to ethical issues are reviewed: the phases of pharmaceutical research, multicentre trials, placebo-controlled studies, and the analysis and dissemination of the results of clinical and multicentre trials.

A. Clinical Equipoise

"….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."[1]

Clinical equipoise means a genuine uncertainty on the part of the expert medical community about the comparative therapeutic merits of each arm of a clinical trial. The tenet of clinical equipoise provides a clear moral foundation to the requirement that the health care of subjects not be disadvantaged by research participation.[2]

B. Phases of Pharmaceutical Research

Four conventional phases of pharmaceutical research in clinical trials are emphasized because they create different ethical issues:

- Phase I clinical trials conventionally examine the acute, dose-related pharmacological toxicities of new pharmaceutical drugs; they are often conducted in healthy subjects, but may involve patients in studies with interventions that are known to be toxic.

- Phase II clinical trials primarily examine the short-term pharmacological toxicities of and, to a lesser extent, the efficacy of new drugs; they are conducted in populations with specific diseases.

- Phase III clinical trials primarily examine the pharmacological efficacy and, to a lesser extent, the short-term toxicities of new drugs. Phase III and IV clinical trials are designed to increase the survival or the quality of life of subjects suffering from a specific disease or condition.

- Phase IV clinical trials, also known as post-marketing surveillance studies, primarily examine the long-term efficacy and toxicity of already marketed drugs.

It should be noted that Phase I clinical trials now increasingly include persons with specific diseases — persons for whom all conventional therapies have failed (e.g., terminal cancer or AIDS). Such studies may be designated as Phase I clinical trials where, in fact, they properly should be designated as mixed Phase I/II or pure Phase II clinical trials.

Article 7.1 **Phase I non-therapeutic clinical trials shall undergo both stringent review and continuous monitoring by an REB independent of the clinical trials sponsor.**

Conventional Phase I clinical trials depend on generally healthy subjects who are paid by the sponsors of newly developed drugs. These considerations raise ethical concerns about the selection and recruitment of subjects, the free and informed consent process, the meaning of free and informed consent under these circumstances, the membership and procedural adequacies of the REB (if any) and the duties of the federal regulator.

The development of a plethora of new pharmaceutical drugs and the private setting of Phase I clinical trials invites vigilance from an ethical perspective. As more of these trials are conducted in the academic sector, academic REBs must carefully monitor all aspects of such trials including unexpected adverse events, for example, unforeseen drug toxicity. These are matters of continuing ethical concern.

Article 7.2 **In combined Phase I/II clinical trials, researchers and REBs shall carefully examine the integrity of the free and informed consent process. Where appropriate, the REB may require an independent monitoring process.**

Combined Phase I/II clinical trials raise particular ethical concerns because they are often conducted with desperate populations whose therapeutic options have been exhausted. Patients afflicted with terminal cancer and HIV AIDS are examples. Such situations may distort the perceptions by patients and their families, as well as by researchers, of the balances between the harms and benefits of the research. Such factors not only relate to the free and informed consent process, they also influence the clarity and strength of stopping and withdrawal procedures. Because of these considerations, it is essential that researchers and REBs collaborate and consult with each other throughout the course of Phase I/II clinical trials.

Phase II and III clinical trials, unlike combined Phase I/II clinical trials, often include placebo controls to detect and quantitate the acute toxicity and efficacy of an experimental drug. In such studies, and in addition to the other ethical concerns raised for combined Phase I/II clinical trials, the use of placebos (discussed below) can further stress the duty of researchers to maximize the benefit and minimize harm to subjects.

Phase IV clinical trials are usually designated as post-marketing surveillance studies. Often, however, they serve the purpose of post-marketing advertising conducted in the private practices of physicians. For example, a physician may be paid a per capita fee by the sponsor to assess the side effects and the acceptance by patients of an already-marketed drug. Such Phase IV clinical trials may compromise physicians' professional integrity with respect to finders' fees, billing practices and utilization of public resources, as well as with respect to conflicts of interest. Researchers and REBs must examine the scientific and ethical implications of Phase IV clinical trials with the same diligence accorded to other phases of clinical trials.

Clinical trials of medical devices, whether implanted in human subjects or not, raise ethical concerns similar to those encountered in the four phases of pharmaceutical research. In addition, clinical trials with some implants can create unique ethical dilemmas concerning the free and informed consent processes, as well as raise potential conflicts of interest. For example, newly developed heart rhythm pacemakers, which may cost thousands of dollars, must be implanted surgically to assess their efficacy and possible harmful side effects. In some jurisdictions, health plans pay the surgical fees, while intellectual property rights related to the experimental devices usually remain with the sponsor of the trial. In such clinical trials, and to whatever extent is practical, researchers and REBs must ensure that subjects are accorded all opportunities to exercise their rights to the initial and continuing free and informed consent processes.

The REB must carefully examine such clinical trials to assist researchers in avoiding potential conflicts of interest concerning the selection and recruitment of subjects, and payments by sponsors to the researchers. The REB should also examine (1) the issue of continuing access after the trial, (2) the treatments, especially medical devices to which the subjects may have become accustomed or, (3) if impossible, the provisions taken to ensure adequate replacement. To discharge its duties to protect the welfare of subjects, the REB should also be aware that numerous safety standards (e.g., mechanical and electrical) apply to medical devices and receive assurances that these standards will be respected.

Clinical investigators undertaking research intended for use in seeking regulatory approval for pharmaceuticals should also generally respect the ICH Guidelines which were developed by the United States, Europe and Japan and have been adopted by Canada.[3]

Article 7.3 **REBs shall examine the budgets of clinical trials to assure that ethical duties concerning conflict of interest are respected.**

Budgets for clinical trials usually are calculated by per capita costs, that is, the sponsor pays the researcher a fixed sum for each research subject recruited. Per capita payments raise ethical concerns because of the potential to place the researcher in a conflict between maximizing economic remuneration and serving the best health interests of subject-patients, especially if the researcher also holds a therapeutic or clinical or other fiduciary relationship with the subjects. Disclosure of the amount of the per capita payment, and other budgetary details, will assist the REB in assessing potential conflicts of interest, and may also assist the researcher in resolving them. As a general guide, per capita payments should be comparable to the physician's or researcher's usual professional fee. When trials take place within a public institution, such as a hospital or a long-term care facility, recovery of utilization costs for institutional and other resources (such as radiological and diagnostic services) should be considered essential, and should be in addition to any overhead charge stipulated by the institution.

Examination of the clinical trials within the ethical perspectives of the phases outlined above for clinical trials will assist REBs and researchers in identifying those ethical issues that are both generic for all clinical trials and specific for a given trial.

C. Multicentre Clinical Trials

Multicentre clinical trials are now commonplace, and reflect not only the need for increased numbers of research subjects but also the multidisciplinary nature of contemporary human research. For REBs, multicentre trials raise particular difficulties for REBs, some of which are discussed in Section 1.

D. Placebo-Controlled Studies

Article 7.4 **The use of placebo controls in clinical trials is generally unacceptable when standard therapies or interventions are available for a particular patient population.**

Clinical equipoise is widely regarded as the moral foundation of the randomized-controlled trial. In order for a clinical trial to proceed ethically, a state of clinical equipoise must exist at the trial's inception (see A above). Consistent with clinical equipoise, a placebo may be used as the control treatment in a clinical trial in the following circumstances:

(a) There is no standard treatment;

(b) Standard therapy has been shown to be no better than placebo;

(c) Evidence has arisen creating substantial doubt regarding the net therapeutic advantage of standard therapy;

(d) Effective treatment is not available to patients due to cost constraints or short supply. (This may only be applied when background conditions of justice prevail within the health care system in question; for example, a placebo-controlled trial is not permissible when effective but costly treatment is made available to the rich but remains unavailable to the poor or uninsured.)

(e) In a population of patients who are refractory to standard treatment and for whom no standard second-line treatment exists;

(f) Testing add-on treatment to standard therapy when all subjects in the trial receive all treatments that would normally be prescribed; or

(g) Patients have provided an informed refusal of standard therapy for a minor condition for which patients commonly refuse treatment and when withholding such therapy will not lead to undue suffering or the possibility of irreversible harm of any magnitude.

When a clinical trial involving a placebo control is undertaken, the researcher and the REB must ensure that patients or authorized third parties are fully informed about any therapy that will be withdrawn or withheld for purposes of (1) the research, (2) the anticipated consequences of the withdrawing or withholding of the therapy, and (3) the reasons why investigators deem a placebo-controlled trial to be necessary (see also Article 2.4).

E. Analysis and Dissemination of the Results of Clinical Trials

In many clinical trials, the sponsors obtain contractual rights to the initial analysis and interpretation of the resultant data. Researchers and REBs must ensure, however, that final analysis and interpretation of such data remain with the researchers, whose duty it is to ensure the integrity of their research. When stopping rules are required in Phase I, II and III clinical trials, monitoring of the interim results must be done independently. It should also be remembered that, with a stopping rule in place, long-term positive or negative effects might be masked by short-term harms or benefits.

Equally important, though sometimes difficult to achieve, is the researchers' duty to disseminate the analysis and interpretation of their results to the research community. Unfortunately, negative results and outcomes of research frequently are not published or disseminated. Silence on such results may foster inappropriate and potentially harmful clinical practices or needless and wasteful duplication. Researchers and REBs may exert pressure to alleviate this deficiency in the dissemination of research results by resisting publication bans proposed in research protocols, on the basis of ethical obligations of truthfulness and the integrity of research. Research journalists, journal editors, members of editorial peer review boards, sponsors and regulators should address this as an issue of scientific and ethical urgency.

Endnotes

[1] Freedman, B., *Equipoise and the Ethics of Clinical Research*, New England Journal of Medicine, 317.3 (1987): 141-145.

[2] World Medical Association, *Declaration of Helsinki* (1964, as revised 1996), para. II.3.

[3] *"Good Clinical Practice: Consolidated Guidelines of the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use"*, published by the Therapeutic Products Directorate, Health Canada, Ottawa, K1A 0L2, and obtainable from http://www.hc-sc.gc.ca/hpb/dgps/therapeut.

[Section 8]

HUMAN GENETIC RESEARCH

Human genetic research involves the study of genetic factors responsible for human traits and the interaction of those factors with each other and, in some instances, with the environment. Research in this area includes identification of the genes that make up the human genome, the functions of the genes, and the characterization of normal and disease conditions in individuals, biological relatives, families and groups. Observation of different forms of the gene may be important among biological relatives and within and among different groups.

Accordingly, human genetic research is concerned with the use of genetic material. Genes and their alleles are being identified as part of the Human Genome Project, but the function of each gene and its relationship to human health may not be clear. Although the research is both exciting and rapidly changing, the recently acquired knowledge regarding genes and their mutations is not yet matched with a full understanding of the implications for human subjects.

In single gene disorders, for example, a mutation altering a biochemical pathway is directly related to disease. However, the presence of other genes or environmental factors will modulate expression. In disorders that are influenced by multiple genes and environmental factors (i.e. multifactorial inheritance), there may not be a clear differentiation between the normal and the abnormal. In addition, identification of genetic factors may only indicate predisposition because other genetic and non-genetic factors may also influence the development of disease (e.g., an inherited predisposition to breast cancer). Such factors indicate that identifying a particular genetic predisposition (e.g., by predictive testing) in individuals, biological relatives or a population may not mean that the person will definitely suffer from the disease, but may be perceived as such; the benefits of predictive testing, however, can include intervention strategies (e.g., such as dietary management with an inherited hypercholesterolemia).

Because genetic material is by its very nature shared by biological relatives, identifying a genetic causative agent has implications beyond the individual. Thus, issues of privacy and confidentiality may affect the individual, the family and the group to which the individual belongs. For example, in population studies, a particular group can be identified by common descent, geographic location, ethnic origin, etc. The results, if revealed and publicized, may stigmatize the other individuals in that group.

New technologies to analyze genetic material are being developed at an unprecedented rate. Indeed, new discoveries may be quickly incorporated into health care practices without sufficient research into their effectiveness or means of delivery. Given the present inability to know the limits or effects of such research, or the context in which genetic information is interpreted and used, caution should be exercised. These rapid changes and the potential financial gain from marketing the technologies drive the need to be sensitive to ethical issues in genetic research.

The potential ability to identify all human genes and their mutations has profound social implications. Misunderstanding or misuse of the results of genetic testing has the potential to interfere with an individual's self identity and sense of self-worth, and to stigmatize the entire group to which that individual belongs. A number of issues remain unresolved and require continuing deliberation by the research community and the public.

Accordingly, this Section reviews some of the major unique ethical issues presented by genetic research involving human subjects. The Section should be read particularly in the context of other Sections of this Policy.

A. The Individual, Families and Biological Relatives

Article 8.1 **The genetics researcher shall seek free and informed consent from the individual and report results to that individual if the individual so desires.**

Article 8.1 extends the general requirement for free and informed consent of Section 2, to their particular application in genetic research. Because genetic research involves the family and/or the community — in terms of family history, linkage and other studies — a potential tension exists between the individuals in the study and the families who are thereby implicated. Therefore, free and informed consent shall also involve those social structures, as far as is practical and possible. Because genetic counselling and research studies begin with a family history provided by a family member, medical genetic charts will reflect the health and social history of the entire family, not just the individual. Because linkage and mutation analyses involve biological relatives, interpreting the results may not be possible without the co-operation of the family or the cultural group (see Section 6). The researcher should be aware that, in certain situations, members within a family may be coerced by other members to join the study. Further conflict within a family may exist if some members hold that the rights of the family to genetic information override the rights of the individual.

When the wishes of the family or a group are in conflict, enhancing communication is preferable to compelling either the group or the individual to overcome their reluctance. The researcher should recognize the potential for conflict within a family regarding participation in research endeavours but, above all, should honestly present to family members the goals, advantages and disadvantages of the research.

B. Privacy, Confidentiality, Loss of Benefits and Other Harms

Article 8.2 **The researcher and the REB shall ensure that the results of genetic testing and genetic counselling records are protected from access by third parties, unless free and informed consent is given by the subject. Family information in databanks shall be coded so as to remove the possibility of identification of subjects within the bank itself.**

Because the potential for gathering genetic knowledge about biological relatives or groups by studying only a few individuals is unique to genetic studies, an individual may not be assured of privacy within the group, unless extra precautions are taken. The status of an individual may be known simply from data obtained on a parent or a child. Consequently, the knowledge by a third party (e.g., an employer or insurer) of a specific risk or diagnosis may lead to discrimination in employment, insurance, etc.

Article 8.2 should be read in conjunction with the general provisions on privacy and confidentiality of Section 3. The Article recognizes the special privacy and confidentiality issues that may arise due to the unique nature of genetic information. Unless special precautions are taken, for example, databases containing genetic information may identify multiple biological relatives. Similarly, publication of pedigrees from families having rare conditions may identify not only the particular family, but also specific individuals within that family, because such families tend to be known within the genetics research community. The researcher is then faced with a dilemma: maintaining accuracy of the data, or publishing an altered pedigree that potentially contains either sensitive social information (e.g., non-paternity) or sensitive diagnostic information (e.g., where individuals have inherited a particular disease allele); however, an altered pedigree can wrongly target others, and alteration may impair replication in future research or lead to flawed conclusions by other researchers.

DNA banking allows family histories, clinical details and genetic material to be available for other researchers to make specific diagnoses of genetic alterations, to allow studies of genotype/phenotype correlations, or to answer basic questions regarding human development. If appropriate guidelines are not respected, confidentiality may be compromised by DNA banking (see Article 8.6).

Accordingly, the researcher should be aware of these potential risks to confidentiality, and be able to inform the REB as to how the publication of data or other handling of such information will be accomplished. In particular, the researcher should clarify how subjects will be made aware of limits to the protection of confidentiality.

Article 8.3 **Researchers and genetic counsellors involving families and groups in genetic research studies shall reveal potential harms to the REB and outline how such harms will be dealt with as part of the research project.**

Article 8.3 obliges researchers to address the potential harms of genetic research. With the exception of gene therapy, physical risks in genetic research are generally similar to those seen in other forms of research. However, the potential for social and psychological harm as a consequence of genetic research is a reality. Harm in genetic research includes moral, physical, psychological and social harms. Merely being involved in a study may lead to harm for a subject. For example, receiving information regarding susceptibility to genetic disease or even carrier status may provoke anxiety, disrupt relationships or undermine an individual's sense of life opportunities. The individual's position within the family may be challenged by the decision of whether to participate. Such issues may be exacerbated in cases involving single gene disorders where confirmation of high risk or carrier status cannot be followed by effective therapy or prevention. As well, even receiving information of low-risk status may be psychologically harmful if the individual is perceived as no longer sharing the family burden.

As in other areas of research ethics, genetic research involving children involves special ethical obligations and protection. Children may be at particular risk for stigmatization both within and beyond the family because of knowledge gained through genetic studies. Therefore, genetic research involving children should not be done unless an effective intervention is available and the information to be gained outweighs the risk of harm. It may be appropriate, for example, to offer testing to children in a family for an early onset condition such as polyposis coli, for which the knowledge affects treatment options, but inappropriate to test children for an adult onset condition such as Huntington Disease for which no effective prevention yet exists.

C. Genetic Counselling

Article 8.4

Genetics researchers and the REB shall ensure that the research protocol makes provision for access to genetic counselling for the subjects, where appropriate.

Genetic counsellors who are formally trained to impart genetic information have two main roles in dealing with a family: The first is to educate regarding the condition in question, and the second is to counsel by presenting options or possible action scenarios in a non-directive manner. The complexity of genetic information and its social implications usually requires that free and informed consent be supplemented with genetic counselling.

Genetic research involves families and groups in different ways. Individuals questioned about intimate family details and groups approached for a study may be unaware of harms beyond those of a physical nature. Accordingly, counselling regarding the potential benefits, harms and limitations of each study is crucial both before the individual gives free and informed consent and after results are available. For example, in predictive testing for Huntington Disease, pre- and post-test counselling have been essential.

In studies examining allelic differences or predisposing alleles in a particular condition, the clinical implications may as yet be unknown. Accordingly, the researcher will need to advise research subjects and the REB about the potential meaning of the anticipated results to the subjects, and how counselling will be handled. Subjects may also need follow-up, and the question will remain as to when follow-up should occur and where the researcher's obligation ends. One option is for the researcher to identify a contact person within the family to be given information to be shared. Even though the onus should be on the researcher to outline suggestions for such ongoing education and counselling, new genetic knowledge and therapeutic interventions are being developed unpredictably. It is, therefore, sometimes only practical to explain to research subjects that they will need to contact their physician to keep informed, because researchers may not be able to maintain contact after the research is completed. The extent of continuing duties should be discussed with the REB.

In newer applications of predictive testing, such as inherited breast cancer, pre- and post-test counselling are integral to the research project. Therefore, the researcher must recognize that educating the subjects regarding the factors involved in predictive testing (e.g., interpreting the results and providing further counselling when results are available) is essential in this complex area. Consideration should also be given to combining clinical expertise with that of the research geneticist.

At present, the geneticist or genetic counselor may have the most expertise regarding the counselling issues involved in research projects. However, as technology continues to outpace our understanding of the impact and consequences of genetic knowledge, even the most experienced genetic counsellors may be unable to predict future consequences. The prudent researcher cannot assume that he or she can anticipate all harms inherent in a particular project.

Families may define themselves in different ways in terms of biological, social and cultural relationships. There may be important cultural differences regarding notions of genetic inheritance. There is also a problem that the higher frequency of disease and/or genetic changes in a group or region that has historically confined reproduction to within its own members could reinforce discriminatory use of ethnicity, culture or racial labels. Researchers who propose to study ethnically related genetic changes should understand this issue and be able to provide the necessary counselling.

D. Gene Alteration

Article 8.5

Gene alteration (including "gene therapy") that involves human germline cells or human embryos is not ethically acceptable. Gene alteration for therapeutic purposes and involving human somatic cells may be considered for approval.

Gene alteration involves the transfer in various vectors (or carriers) of genes into cells to induce an altered capacity of the cell. Commonly used vectors are viruses that introduce the gene into the host genome or plasmids (where integration does not occur, e.g., a method used with DNA vaccines). Alteration of human genes may be used to treat disease in an individual, alter germ cells to prevent the disease or alter for cosmetic "improvement." Since gene alteration remains experimental and is not "therapy" in the accepted sense of the word, the use of animal models continues to be crucial in this area of incomplete knowledge. At present, the most common research in gene alteration concerns serious single gene disorders, such as adenosine-deaminase deficiency, a subtype of an immune disorder, or life-threatening malignancies.

The possible use of germline alteration in the embryo implies alteration of cells not yet committed to specific organs, and therefore would alter future reproductive cells. Accordingly, resulting changes could be transmitted to future generations. Two Canadian documents, the Medical Research Council's *Guidelines on Somatic Cell Gene Therapy in Humans* (1990) and the *Report of the Royal Commission on New Reproductive Technologies* (1993), report that germline therapy has serious ethical concerns and should not be undertaken.

Gene alteration outside the context of well-defined serious single gene conditions or malignancies poses the following concerns: long-term follow-up of already treated individuals is not available; the numbers of such individuals is small; and the lack of information regarding long-term harms makes it inappropriate for such technology to be used for enhancement purposes or for non-life-threatening disorders.

Gene alteration is irreversible; the cell and its descendants are forever altered and cannot be removed from the patient. In addition, the need for lifetime follow-up is crucial to establish harms, benefits and unrecognized concerns. The special circumstances of gene alteration must be clarified to potential subjects, and sometimes their families, in advance of participation.

The following issues, which are articulated in the Medical Research Council's *Guidelines on Somatic Cell Gene Therapy in Humans* (1990), should be considered when evaluating the harm/benefit ratio in gene alteration projects:

- A dilemma exists in that the most likely diseases to be considered for gene alteration are severe, progressive and fatal in childhood (e.g., immune deficiencies). Early treatment for maximal effect means the subject is less able to give free and informed consent because of immaturity. Furthermore, long-term effects are unknown in this age group. However, if research is restricted to those who are able to give consent, many severely affected children would be excluded.

- The withdrawal of the subject from the research project makes early recognition of harms less likely and denies knowledge of such harms to future subjects and researchers involved in gene alteration.

- *In utero* uses of somatic cell gene alteration may not involve the embryo because the germ cells may be affected.

- The potential risks of gene alteration include reinfectivity and oncogenicity of the viral vector, interruption of a normal host gene with negative consequences, bacterial contamination, establishment of the inserted gene in germ cells with unanticipated consequences, and only partial correction of the genetic disease, thus converting a fatal condition to a chronic progressive one.

- In the case of rare genetic diseases, the survival and subsequent reproduction of treated subjects is unlikely to have a significant impact on the gene pool.

E. Eugenic Concerns

The aim of genetic research should be to advance knowledge or to alleviate disease, not to "improve" or "enhance" a population by cosmetic manipulation. Further, the aim should be to better understand genetic disease, the genetic contribution to health and disease, the human genome, and to help individuals and families with genetic conditions. Accordingly, care should be taken to avoid isolating specific populations so that the group either feels stigmatized by the genetic disorder or targeted for "improvement."

The rights and freedoms attached to personal relationships, reproduction, and the support of those with handicapping conditions should also be maintained. The freedom of couples who are at risk to plan and carry potentially affected pregnancies, and the support of children and adults with handicapping conditions, should not be compromised.

F. Banking of Genetic Material

Article 8.6

Though the banking of genetic material is expected to yield benefits, it may also pose potential harms to individuals, their families and the groups to which they may belong. Accordingly, researchers who propose research involving the banking of genetic material have a duty to satisfy the REB and prospective research subjects that they have addressed the associated ethical issues, including confidentiality, privacy, storage, use of the data and results, withdrawal by the subject, and future contact of subjects, families and groups.

Consistent with the data confidentiality provisions of Section 3, above, Article 8.6 outlines the duty of researchers to address ethical issues raised by the banking of genetic material. In this context, although consensus has not been reached, a number of issues need to be considered by the researcher and clarified for the REB, particularly concerning privacy, confidentiality of records, and information derived from stored genetic material. A special concern arises when it is difficult to separate genetic information on an individual from information on his or her biological relatives or community. Access to genetic material and to the results of the research should be limited to the researcher, and if such limitation will not be the case, then the issue should be discussed with the research subject. Similarly, unauthorized access to stored genetic material or results by third parties should be prevented. Specifying whether banked genetic material will be anonymized, i.e., without identifiers, may help alleviate the concerns that other biological relatives may inadvertently be identified by linked data.

Though no international consensus currently exists regarding long-term banking of genetic material for the purposes of genetic research, the storage of samples should be for a defined term; some researchers state five years, while others prefer 25 years to allow another generation to potentially benefit from the information. In the case of immortalized cell lines, researchers have a duty to explain that the sample may be stored indefinitely. The researcher should outline, in the protocol, future uses of genetic material or research data. In some cases, the genetic material will be used to investigate only the specific genetic condition affecting the biological relatives. In other cases, a variety of genetic mutations may be evaluated using this material, and, in yet other cases, future uses may simply be unknown.

Suggested methods to handle secondary use of genetic material or research data include a comprehensive consent form, which allows the research subject to choose from a number of options (e.g., use of the material only in the present study, use restricted to the condition, or other clearly specified use) or a more limited consent form, which specifies arrangements to maintain contact with the subject regarding future uses. Either method must be clearly explained during the free and informed consent process.

As stated previously, the biological aspects of genetic variability or disease-causing mutations implies that information gained from banked genetic material pertains not only to the individual, but also to biological relatives. If possible, researchers should clarify with the subject whether results are to be used for the individual and/or for biological relatives. In addition, clarifying whether results will be available from any analysis, and whether the subject wishes to receive results, assists the subject in the free and informed consent process.

The right to withdraw from a research study is a necessary component of the free and informed consent process. Where banking is concerned, withdrawal affects not only the individual but also the biological relatives. Therefore, withdrawal could involve actual destruction of genetic material or research data, or the removal of all identifiers. These options need to be discussed with the subject.

Differentiating between already-stored genetic material (e.g., materials previously obtained perhaps without consideration of the factors referred to throughout this Section) and a proposed banking project is important. In the latter situation, the REB should expect that the researcher has considered all of the factors referred to herein in the description of the study and in the free and informed consent process. In projects involving already-stored genetic material, an REB should consider the importance of the factors on a project by project basis since the research subjects may no longer be living, or the material to be used was obtained from samples previously collected or left over after routine care. Until consensus has been reached in the area of genetic banking, full disclosure to the research subject of the factors referred to herein would seem to be the prudent course.

G. Commercial Use of Genetic Data

Article 8.7

At the outset of a research project, the researcher shall discuss with the REB and the research subject the possibility and/or probability that the genetic material and the information derived from its use may have potential commercial uses.

Article 8.7 adds a specific obligation to the disclosure requirements for obtaining free and informed consent from those being subjected to genetic research: the potential for commercial use of genetic data. There is significant legal and moral controversy regarding ownership of genetic material or research data, and concepts of ownership may vary from one cultural group to another and between legal systems. It is unethical for a researcher to claim ownership of genetic material by claiming that the concept of private ownership did not exist in the community involved. Consistent with the free and informed consent provisions of Section 2, the researcher may have to seek further permission from the group. The fact of commercial sponsorship of genetic research should be revealed to the subject at the beginning of the project. Similarly, possible commercialization occurring after involvement in research should also be revealed at the outset if possible.

[Section 9]

RESEARCH INVOLVING HUMAN GAMETES, EMBRYOS OR FOETUSES

Because the topic of human reproduction invokes a discussion of fundamental values, research involving new reproductive technologies engenders acute ethical concerns for both the research community and the public at large. Respect for human dignity remains a paramount consideration in evolving ethical, policy and societal deliberations. Within this scenario, researchers and REBs have a continuing duty to remain abreast of the public interest in these issues, and to respect the developing policy, legal and regulatory frameworks.

The Report of the Royal Commission on New Reproductive Technologies[1] is an authoritative and thorough analysis of current Canadian viewpoints, reflecting both the divisions and areas of consensus, within society, on these important matters. Statements of Government policy in effect at the time of drafting this Policy Statement have arisen from the Royal Commission Report. A moratorium on certain practices was announced by the Minister of Health in July 1995, and draft legislation (Bill C-47) was under consideration in the House of Commons at the time of the 1997 election.

Informed by such public and scholarly discussions, this Policy suggests to REBs a pragmatic position on research involving human reproduction. The position recognizes the following:

- That the present status of the law, ethics and health care in Canada regarding research in human reproduction is broadly consistent with a graduated approach that correlates permitted interventions with the developmental stages of the human embryo or foetus;

- That a careful, moderate and controlled approach to human reproductive research is preferred to the relatively uncontrolled introduction of new practices as therapy.

In addition to the considerations expressed elsewhere in this Policy, the following bear specifically on research involving the conception and development of human embryos and foetuses. REBs and researchers should be mindful of these guidelines in reviewing and conducting research:

- Research on human reproductive tissues or cells that are intended to result in an ongoing pregnancy is unacceptable — if the knowledge sought may be obtained by the use of other systems or models.

- Research involving the conception and development of human embryos and foetuses may prove beneficial due to the present lack of knowledge and its impact on the adequacy of care.

Such research raises many complex concerns, including possible physical harms to the embryo or foetus, the question of who may consent for the foetus, and an overall concern of respect for the embryo or foetus.

A. Research Involving Human Gametes

Article 9.1 **Researchers shall obtain free and informed consent from the individual whose gametes are to be used in research.**

Human reproductive cells (ova or sperm) may be obtained from a research subject as part of standard care, or may be requested solely for research. Sperm is relatively easy to obtain, while ova can only be obtained by a surgical procedure. As elaborated more generally in Section 2, researchers have a duty to seek the free and informed consent of prospective subjects for research involving their reproductive cells. Consistent with general requirements of full disclosure, subjects should be informed of the purpose of the proposed research, such as research involving infertility or birth control. The requirement for free and informed consent applies, of course, if the gametes were originally provided for a purpose other than research. Researchers and REBs should also pay close attention to the social sensitivity of such research.

The moratorium announced by the Minister of Health in July 1995 prohibits research involving gametes derived from cadavers. Respect for human dignity also means that it is unacceptable to obtain gametes from foetuses or individuals unable to consent for themselves.

Article 9.2 **In research, it is not ethical to use ova or sperm that have been obtained through commercial transactions, including exchange for service.**

Inspired by the fundamental ethical principle of respect for human dignity, Article 9.2 expresses the moral prohibition against the commercialization of human reproduction.

Article 9.3 **It is not ethically acceptable to create, or intend to create, hybrid individuals by such means as mixing human and animal gametes, or transferring somatic or germ cell nuclei between cells of humans and other species.**

Combining human genetic material with that of other species has the potential to create new life. The creation of hybrid individuals or species which may survive, which are intended to survive, violates our basic norm of respect for human life and dignity. Article 9.3 expresses this concern, while acknowledging that other related research may raise fewer ethical objections.

B. Research Involving Human Embryos

Research where fertilization occurs should be regarded as research on embryos.

Article 9.4 **It is not ethically acceptable to create human embryos specifically for research purposes. However, in those cases where human embryos are created for reproductive purposes, and subsequently are no longer required for such purposes, research involving human embryos may be considered to be ethically acceptable, but only if all of the following apply:**

(a) **The ova and sperm from which they were formed are obtained in accordance with Articles 9.1 and 9.2;**

(b) The research does not involve the genetic alteration of human gametes or embryos;

(c) Embryos exposed to manipulations not directed specifically to their ongoing normal development will not be transferred for continuing pregnancy; and

(d) Research involving human embryos takes place only during the first 14 days after their formation by combination of the gametes.

Research potentially altering the embryo by chemical or physical manipulation should be distinguished from research directed at ensuring normal development. For example, evaluation of potential teratogens and their effects on certain cell lineages may use early embryos, but those embryos must not be implanted for an ongoing pregnancy. On the other hand, pre-implantation diagnosis of a serious genetic disorder may involve testing of one cell of the early embryo, but not manipulation of the embryo itself ultimately destined for implantation (see Section 8).

The broad consensus restricting research on embryos to the first 14 days of development is based on the stages of biological development. Implantation usually begins at approximately the sixth or seventh day of development, and is usually completed around 14 days, beyond which time the embryo proper starts to develop the primitive streak, or the first indication of neural development.

Article 9.5 **It is not ethically acceptable to undertake research that involves ectogenesis, cloning human beings by any means including somatic cell nuclear transfer, formation of animal/human hybrids, or the transfer of embryos between humans and other species.**

Article 9.5 recognizes that while some research involving human reproduction is inherently objectionable to some schools of ethical and religious thought, it may not be so for others. Such techniques have provoked vigorous debates arising from conflicts in values, and such discussion and reflection need to continue. In the meantime, the intrinsic ills, potential harms, and the scientific and ethical uncertainty weigh in favour of not approving such research.

C. Research Involving Foetuses

Research may be undertaken on methods to treat, in utero, a foetus that is suffering from genetic or congenital disorders. Because the foetus and the woman cannot be treated separately, any intervention on one involves an intervention on the other. Accordingly, and consistent with the requirements of Section 2, research involving a human foetus requires the free and informed consent of the woman. Research methods on the treatment of foetuses in utero thus pose no issues that are not addressed elsewhere in this Policy.

D. Research Involving Foetal Tissue

Research involving the use of foetal tissue should be guided by respect for the woman's dignity and integrity. Researchers should thus obtain the free and informed consent of the woman whose foetal tissue is to be used for research. As a corollary of such respect, it is unacceptable to undertake research interventions that compromise the woman's decision on whether or not to continue her pregnancy. A former Minister of Health, responding to a question concerning the transplantation into patients of tissues obtained from elective abortions, stated that he would not approve federal funding for such a procedure.[2] The Royal Commission on New Reproductive Technologies has recommended that "Research projects using foetal tissue (including those related to transplantation in human beings) be eligible for funding by the Medical Research Council of Canada and other public agencies, provided they meet applicable ethical and scientific research standards and tissue is obtained in accordance with the recommendations of the Royal Commission on New Reproductive Technologies." These recommendations include the establishment of a well defined regulatory and licensing structure.[3]

There are few absolutes in areas such as these, where ethical deliberation and societal values continue to evolve rapidly. Hence, while a women's autonomy to consent to the use of her foetal tissue shall be respected, countervailing ethical considerations hold that a woman should not direct the use of such tissue to particular individuals, such as choosing to have foetal tissue used for Parkinson Disease research in a relative. The objection is based on concerns that the foetus not be used simply as a source of tissue, but should be recognized as a potential person deserving of respect.

Endnotes

1 Report of the Royal Commission on New Reproductive Technologies, *Proceed with Care*, Ottawa, 1993.

2 Hansard, Question Period, July 15, 1988.

3 Report of the Royal Commission on New Reproductive Technologies, *Proceed with Care*, Ottawa, 1993.

[Section 10]

HUMAN TISSUE

The use of human tissue for the purpose of research has proven to be of immense importance to the advancement of knowledge. The ethical considerations raised by research involving human tissue centre on the moral status of human tissue, on access to and the use of data from the tissue, and, consequently, on the standards that define precisely how those involved in research relate to one another. In this regard, it is a fundamental ethical principle that researchers, in the collection and use of human tissue, respect individual and community notions of human dignity and physical, spiritual and cultural integrity.

The status accorded the human body and its parts varies among individuals and cultures. It varies in part due to how people perceive, identify with or relate to their bodies. Some people or cultures take little interest in tissue removed from their bodies. Other cultures regard certain parts of the body (e.g., the placenta) as sacred. Other parts of the body may be regarded as appropriate for gift-giving, provided that the use for research does not compromise medical diagnosis or care. What some regard as an invasive method to acquire tissue samples, other individuals or cultures will not. These examples illustrate the continuing importance of assessing the ethics of research involving human subjects through a subject-centred perspective.

In Canadian society, it is generally held that human tissue itself deserves some degree of respect, for reasons of the dignity of the person from whom tissue is obtained. These principles are reflected in Canadian law and public policy, which generally allow competent individuals to donate, but not sell, human tissues for research. In this context, it is reasonable to draw the ethical conclusion that the use of tissue for research depends on an individual's altruism in donating the tissue with the expectation that social good will be advanced and human knowledge increased. In the case of genetic research, this altruistic gift has an added dimension: tissue obtained from the individual may reveal information about one's current or future health as well as that of biological relatives (see Section 8).

A. Privacy and Confidentiality

It is essential to protect the privacy of the individual and ensure confidentiality. Four categories of tissue can be distinguished:

- Identifiable tissue can be immediately linked to a specific individual (e.g., by way of an identifying tag or patient number).
- Traceable tissue is potentially traceable to a specific donor provided there is access to further information such as a patient record or a database.
- Anonymous tissue is anonymous due either to the absence of tags and records or the passage of time (e.g., tissue recovered from archaeological sites).
- Anonymized tissue was originally identified but has been permanently stripped of identifiers.

Genetic testing has greatly narrowed the concept of anonymous tissue (see Section 8), but the concept of traceable tissue is now wider, since it is now possible to identify biological relatives by using genetic markers.

A researcher may request REB approval for use of non-traceable tissue in research when such tissue was left over from different research or, for instance, from a pathological examination. In giving approval, the REB should address such issues as privacy, confidentiality, and, where appropriate, continuing consent or free and informed consent concerning the new research project.

The researcher and the REB should also address how likely it is that traceable tissue will be traced back to an individual. Although rendering tissue anonymous has the advantage of increasing confidentiality, it has the disadvantage of making it impossible to offer the benefits of research to donors and their families. This is particularly significant when research may disclose previously undiagnosed conditions, such as HIV infection or an inherited predisposition to breast cancer.

In the case of incompetent individuals, the principles developed in Section 2 regarding harm and third-party authorization should be observed. For example, the post-mortem acquisition of brain tissue from a person suffering from dementia would require the free and informed consent of an authorized third party if there were no prior directive of the deceased. Special care should also be taken to avoid apparent or real coercion when the subjects are drawn from groups in the care, or under the authority, power or control of others.

B. Free and Informed Consent

It is essential to pay attention to the issues related to free and informed consent developed in Section 2; all relevant information should be provided to enable the potential subject to decide whether to give free and informed consent. Thus, reasonably anticipated harms, such as the possibility of future identification, must be disclosed. Advance directives, for example, may include donations of tissue. Since the law in some provinces requires that the free and informed consent be based on an understanding of the specific uses of tissue for research, researchers and REBs must be aware of, and conform to, the specific requirements of applicable law.

Article 10.1 **Research proposing the collection and use of human tissues requires ethics review by an REB. Amongst other things, the researcher shall demonstrate the following to the REB:**

(a) That the collection and use of human tissues for research purposes shall be undertaken with the free and informed consent of competent donors;

(b) In the case of incompetent donors, free and informed consent shall be by an authorized third party;

(c) In the case of deceased donors, free and informed consent shall be expressed in a prior directive or through the exercise of free and informed consent by an authorized third party.

Article 10.1 generally applies prospectively, that is prior to the recovery of tissue intended for research purposes. It applies the general elements of free and informed consent in Section 2 to the specific case of tissue for particular types of potential donors. It should be read in conjunction with the requirements outlined below in Article 10.3 for the use of previously collected tissue. Article 10.1 also applies when the tissue to be used in research is acquired incidentally to therapeutic interventions. Individuals who do not wish to contribute tissue to particular research projects should be free to withhold consent without fear of penalty.

Article 10.2 **For the purpose of obtaining free and informed consent, researchers who seek to collect human tissue for research shall, as a minimum, provide potential donors or authorized third parties information about:**

(a) The purpose of the research;

(b) The type and amount of tissue to be taken, as well as the location where the tissue is to be taken;

(c) The manner in which tissue will be taken, the safety and invasiveness of acquisition, and the duration and conditions of preservation;

(d) The potential uses for the tissue including any commercial uses;

(e) The safeguards to protect the individual's privacy and confidentiality;

(f) Identifying information attached to specific tissue, and its potential traceability; and

(g) How the use of the tissue could affect privacy.

By providing individuals with information set out in Article 10.2 about the uses of their tissue, potential subjects will be empowered to decide if their concerns about privacy and confidentiality are met. Measures to protect privacy, confidentiality and anonymity should be proposed by the researcher and be considered adequate by the REB.

Disclosing such information also ensures that researchers and subjects understand that tissue gathered for one purpose (e.g., medical) may have serious implications from other perspectives (e.g., legal). Data linkage issues should also be addressed (See Section 3). It is also important to pay special attention to cultural or religious concerns regarding certain tissue or human products, such as zygotes, embryos and foetuses (see Section 9), and concerns that some individuals may have about certain types or applications of research.

C. Previously Collected Tissue

Article 10.3

(a) When identification is possible, researchers shall seek to obtain free and informed consent from individuals, or from their authorized third parties, for the use of their previously collected tissue. The provisions of article 10.2 also apply here.

(b) When collected tissue has been provided by persons who are not individually identifiable (anonymous and anonymized tissue), and when there are no potential harms to them, there is no need to seek donors' permission to use their tissue for research purposes, unless applicable law so requires.

Article 10.3 applies the general principles of research involving identifying data of Section 2 to the specific case of tissue. The article, which should be read in conjunction with Articles 10.1 and 10.2, applies broadly to research in areas such as health sciences, anthropology and genetics. Identification is a matter of sensitivity for individuals, families and members of groups. As such, Article 10.3(a) requires consent for the use of previously collected tissue from which persons may be identified; Article 10.3(b) provides an exception to the consent requirement when the tissue does not permit identification and poses no potential harms.

Though it may not be possible to identify the individuals who provided the tissue, other ethical issues may warrant scrutiny. Some individuals may not want their tissue used for any research purposes regardless of anonymity. The interests of biological relatives or members of distinct cultural groups or other communities may be adversely affected through research uses of their anonymous tissue. Issues may also arise concerning any duties, in extraordinary circumstances, to make traceable tissue identifiable for purposes of providing significant or beneficial information to those who have provided the tissue (see Section 2). Researchers should address such issues to the satisfaction of the REB.

[Appendix 1]

SCOPE OF RESEARCH REQUIRING ETHICS REVIEW

The following which is adapted from the University of Alberta, *General Faculty Council Policy Manual* indicates the range of research projects or instances that should be reviewed by the REB.

- Whether the research is funded or not;
- Whether the funding is internal or external;
- Whether the subjects are from inside or outside the institution;
- Whether the subjects are paid or unpaid;
- Whether the research is conducted inside or outside Canada;
- Whether the research is conducted inside or outside the institution;
- Whether the research is conducted by staff or by students;
- Whether the research is conducted in person or remotely (e.g., by mail, electronic mail, fax or telephone);
- Whether the information is collected directly from subjects or from existing records not in the public domain;
- Whether the research is to be published or not;
- Whether the focus of the research is the subject;
- Whether the research is observational, experimental, correlational or descriptive;
- Whether a similar project has been approved elsewhere or not;
- Whether the research is a pilot study or a fully developed project;
- Whether the research is to acquire basic or applied knowledge; and
- Whether the research is primarily for teaching or training purposes or whether the primary purpose is the acquisition of knowledge.

[Appendix 2]

ARTICLES INCLUDED IN *TRI-COUNCIL POLICY STATEMENT: ETHICAL CONDUCT FOR RESEARCH INVOLVING HUMANS*

For easy reference, the following is a comprehensive listing of all articles included in this document

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 should 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.

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 which is conducted within, or by members of, the institution, using the considerations set forth in this Policy as the minimum standard.

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.

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.

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 which 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 organisations. 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.

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.

Article 1.7 REBs shall meet regularly to discharge their responsibilities.

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 1.9 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 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.

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

Article 1.11 (a) In cases when researchers and REBs can not reach agreement through discussion and reconsideration, an institution should permit review of an REB decision by an appeal board, provided that the board is within the same institution and its membership and procedures meet the requirements of this Policy. No *ad hoc* appeal boards are permitted.

(b) The Councils will not entertain any appeals of REB decisions.

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.

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 shall 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.

Article 1.14 Research to be performed outside the jurisdiction or country of the institution which employs the researcher shall undergo prospective ethics review both (a) by the REB within the researcher's institution; and (b) by the appropriate REB, where such exists, which has authority in the country or jurisdiction where the research is to be done.

Article 2.1 (a) Research governed by this Policy (see Article 1.1) may begin only if (1) prospective subjects, or authorized third parties, have been given the opportunity to give free and informed consent about participation, and (2) their free and informed consent has been given and is maintained throughout their participation in the research. Articles 2.1(c), 2.3 and 2.8 provide exceptions to Article 2.1(a).

(b) Evidence of free and informed consent by the subject or authorized third party should ordinarily be obtained in writing. Where written consent is culturally unacceptable, or where there are good reasons for not recording consent in writing, the procedures used to seek free and informed consent shall be documented.

(c) The REB may approve a consent procedure[1] which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent, provided that the REB finds and documents that:

i. The research involves no more than minimal risk to the subjects;
ii. The waiver or alteration is unlikely to adversely affect the rights and welfare of the subjects;
iii. The research could not practicably be carried out without the waiver or alteration;
iv. Whenever possible and appropriate, the subjects will be provided with additional pertinent information after participation; and
v. The waivered or altered consent does not involve a therapeutic intervention.

(d) In studies including randomization and blinding in clinical trials, neither the research subjects nor those responsible for their care know which treatment the subjects are receiving before the project commences. Such research is not regarded as a waiver or alteration of the requirements for consent if subjects are informed of the probability of being randomly assigned to one arm of the study or another.

Article 2.2 Free and informed consent must be voluntarily given, without manipulation, undue influence or coercion.

Article 2.3 REB review is normally required for research involving naturalistic observation. However, research involving observation of participants in, for example, political rallies, demonstrations or public meetings, should not require REB review since it can be expected that the participants are seeking public visibility.

Article 2.4 Researchers shall provide, to prospective subjects or authorized third parties, full and frank disclosure of all information relevant to free and informed consent. Throughout the free and informed consent process, the researcher must ensure that prospective subjects are given adequate opportunities to discuss and contemplate their participation. Subject to the exception in Article 2.1(c), at the commencement of the free and informed consent process, researchers or their qualified designated representatives shall provide prospective subjects with the following:

(a) Information that the individual is being invited to participate in a research project;

(b) A comprehensible statement of the research purpose, the identity of the researcher, the expected duration and nature of participation, and a description of research procedures;

(c) A comprehensible description of reasonably foreseeable harms and benefits that may arise from research participation, as well as the likely consequences of non-action, particularly in research related to treatment, or where invasive methodologies are involved, or where there is a potential for physical or psychological harm;

(d) An assurance that prospective subjects are free not to participate, have the right to withdraw at any time without prejudice to pre-existing entitlements, and will be given continuing and meaningful opportunities for deciding whether or not to continue to participate; and

(e) The possibility of commercialization of research findings, and the presence of any apparent or actual or potential conflict of interest on the part of researchers, their institutions or sponsors.

In light of (b) and (c), REBs may require researchers to provide below:

TABLE 1

Additional information that may be required for some projects

1. An assurance that new information will be provided to the subjects in a timely manner whenever such information is relevant to a subject's decision to continue or withdraw from participation;

2. The identity of the qualified designated representative who can explain scientific or scholarly aspects of the research;

3. Information on the appropriate resources outside the research team to contact regarding possible ethical issues in the research;

4. An indication as to who will have access to information collected on the identity of subjects, and descriptions of how confidentiality will be protected, and anticipated uses of data;

5. An explanation of the responsibilities of the subject;

6. Information on the circumstances under which the researcher may terminate the subject's participation in the research;

7. Information on any costs, payments, reimbursement for expenses or compensation for injury;

8. In the case of randomised trials, the probability of assignment to each option;

9. For research on biomedical procedures, including health care interventions; information about (a) foregoing alternative procedures that might be advantageous to the subject, (b) which aspects of the research involve the use of procedures that are not generally recognized or accepted; and, (c) particularly in trials of therapeutic interventions, the care provided if the potential subject decides not to consent to participation in the study;

10. The ways in which the research results will be published, and how the subjects will be informed of the results of the research.

Article 2.5 Subject to applicable legal requirements, individuals who are not legally competent shall only be asked to become research subjects when:

(a) the research question can only be addressed using the identified group(s); and

(b) free and informed consent will be sought from their authorized representative(s); and

(c) the research does not expose them to more than minimal risks without the potential for direct benefits for them.

Article 2.6 For research involving incompetent individuals, the REB shall ensure that, as a minimum, the following conditions are met:

(a) The researcher shall show how the free and informed consent will be sought from the authorized third party, and how the subjects' best interests will be protected.

(b) The authorized third party may not be the researcher or any other member of the research team.

(c) The continued free and informed consent of an appropriately authorized third party will be required to continue the participation of a legally incompetent subject in research, so long as the subject remains incompetent.

(d) When a subject who was entered into a research project through third-party authorization becomes competent during the project, his or her informed consent shall be sought as a condition of continuing participation.

Article 2.7 Where free and informed consent has been obtained from an authorized third party, and in those circumstances where the legally incompetent individual understands the nature and consequences of the research, the researcher shall seek to ascertain the wishes of the individual concerning participation. The potential subject's dissent will preclude his or her participation.

Article 2.8 Subject to all applicable legislative and regulatory requirements, research involving emergency health situations shall be conducted only if it addresses the emergency needs of individuals involved, and then only in accordance with criteria established in advance of such research by the REB. The REB may allow research that involves health emergencies to be carried out without the free and informed consent of the subject or of his or her authorized third party if ALL of the following apply:

(a) A serious threat to the prospective subject requires immediate intervention; and

(b) Either no standard efficacious care exists or the research offers a real possibility of direct benefit to the subject in comparison with standard care; and

(c) Either the risk of harm is not greater than that involved in standard efficacious care, or it is clearly justified by the direct benefits to the subject; and

(d) The prospective subject is unconscious or lacks capacity to understand risks, methods and purposes of the research; and

(e) Third-party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so; and

(f) No relevant prior directive by the subject is known to exist. s dissent will preclude his or her participation.

Article 3.1 Subject to the exceptions in Article 1.1(c), researchers who intend to interview a human subject to secure identifiable personal information shall secure REB approval for the interview procedure used and shall ensure the free and informed consent of the interviewee as required in Article 2.4. As indicated in Article 1.1c, REB approval is not required for access to publicly available information or materials, including archival documents and records of public interviews or performances.

Article 3.2 Subject to Article 3.1 above, researchers shall secure REB approval for obtaining identifiable personal information about subjects. Approval for such research shall include such considerations as:

(a) The type of data to be collected;

(b) The purpose for the which the data will be used;

(c) Limits on the use, disclosure, and retention of the data;

(d) Appropriate safeguards for security and confidentiality;

(e) Any modes of observation (e.g., photographs or videos) or access to information (e.g., sound recordings) in the research that allow identification of particular subjects;

(f) Any anticipated secondary uses of identifiable data from the research;

(g) Any anticipated linkage of data gathered in the research with other data about subjects, whether those data are contained in public or personal records; and

(h) Provisions for confidentiality of data resulting from the research.

Article 3.3 If identifying information is involved, REB approval shall be sought for secondary uses of data. Researchers may gain access to identifying information if they have demonstrated to the satisfaction of the REB that:

(a) Identifying information is essential to the research; and

(b) They will take appropriate measures to protect the privacy of the individuals, to ensure the confidentiality of the data, and to minimize harms to subjects;

(c) Individuals to whom the data refer have not objected to secondary use.

Article 3.4 The REB may also require that a researcher's access to secondary use of data involving identifying information be dependent on:

(a) The informed consent of those who contributed data or of authorized third parties; or

(b) An appropriate strategy for informing the subjects; or

(c) Consultation with representatives of those who contributed data.

Article 3.5 Researchers who wish to contact individuals to whom data refer shall seek the authorization of the REB prior to contact.

Article 3.6 The implications of approved data linkage in which research subjects may be identifiable shall be approved by the REB.

Article 4.1 Researchers and REB members shall disclose actual, perceived or potential conflicts of interest to the REB. REBs should develop mechanisms to address and resolve conflicts of interest.

Article 5.1 (a) Where research is designed to survey a number of living research subjects because of their involvement in generic activities (e.g., in many areas of health research or in some social science research such as studies of child poverty or of access to legal clinics) that are not specific to particular identifiable groups, researchers shall not exclude prospective or actual research subjects on the basis of such attributes as culture, religion, race, mental or physical disability, sexual orientation, ethnicity, sex or age, unless there is a valid reason for doing so.

(b) This article is not intended to preclude research focused on a single living individual (such as in a biography) or on a group of individuals who share a specific characteristic (as in a study of an identifiable group of painters who happen to be all of one sex, colour or religion, or of a religious order which is restricted to one sex).

Article 5.2 Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity.

Article 5.3 Subject to the provisions in Articles 2.6 to 2.8, those who are not competent to consent for themselves shall not be automatically excluded from research which is potentially beneficial to them as individuals, or to the group that they represent.

Article 6 (None)

Article 7.1 Phase I non-therapeutic clinical trials shall undergo both stringent review and continuous monitoring by an REB independent of the clinical trials sponsor.

Article 7.2 In combined Phase I/II clinical trials, researchers and REBs shall carefully examine the integrity of the free and informed consent process. Where appropriate, the REB may require an independent monitoring process.

Article 7.3 REBs shall examine the budgets of clinical trials to assure that ethical duties concerning conflict of interest are respected.

Article 7.4 The use of placebo controls in clinical trials is generally unacceptable when standard therapies or interventions are available for a particular patient population.

Article 8.1 The genetics researcher shall seek free and informed consent from the individual and report results to that individual if the individual so desires.

Article 8.2 The researcher and the REB shall ensure that the results of genetic testing and genetic counselling records are protected from access by third parties, unless free and informed consent is given by the subject. Family information in databanks shall be coded so as to remove the possibility of identification of subjects within the bank itself.

Article 8.3 Researchers and genetic counsellors involving families and groups in genetic research studies shall reveal potential harms to the REB and outline how such harms will be dealt with as part of the research project.

Article 8.4 Genetics researchers and the REB shall ensure that the research protocol makes provision for access to genetic counselling for the subjects, where appropriate.

Article 8.5 Gene alteration (including Agene therapy") that involves human germ-line cells or human embryos is not ethically acceptable. Gene alteration for therapeutic purposes and involving human somatic cells may be considered for approval.

Article 8.6 Though the banking of genetic material is expected to yield benefits, it may also pose potential harms to individuals, their families and the groups to which they may belong. Accordingly, researchers who propose research involving the banking of genetic material have a duty to satisfy the REB and prospective research subjects that they have addressed the associated ethical issues, including confidentiality, privacy, storage, use of the data and results, withdrawal by the subject, and future contact of subjects, families and groups.

Article 8.7 At the outset of a research project, the researcher shall discuss with the REB and the research subject the possibility and/or probability that the genetic material and the information derived from its use may have potential commercial uses.

Article 9.1 Researchers shall obtain free and informed consent from the individual whose gametes are to be used in research.

Article 9.2 In research, it is not ethical to use in research ova or sperm that have been obtained through commercial transactions, including exchange for service.

Article 9.3 It is not ethically acceptable to create, or intend to create, hybrid individuals by such means as mixing human and animal gametes, or transferring somatic or germ cell nuclei between cells of humans and other species.

Article 9.4 It is not ethically acceptable to create human embryos specifically for research purposes. However, in those cases where human embryos are created for reproductive purposes, and subsequently are no longer required for such purposes, research involving human embryos may be considered to be ethically acceptable, but only if all of the following apply:

(a) The ova and sperm from which they were formed are obtained in accordance with Articles 9.1 and 9.2;

(b) The research does not involve the genetic alteration of human gametes or embryos;

(c) Embryos exposed to manipulations not directed specifically to their ongoing normal development will not be transferred for continuing pregnancy; and

(d) Research involving human embryos takes place only during the first 14 days after their formation by combination of the gametes.

Article 9.5 It is not ethically acceptable to undertake research that involves ectogenesis, cloning human beings by any means including somatic cell nuclear transfer, formation of animal/human hybrids, or the transfer of embryos between humans and other species.

Article 10.1 Research proposing the collection and use of human tissues requires ethics review by an REB. Amongst other things, the researcher shall demonstrate the following to the REB:

(a) That the collection and use of human tissues for research purposes shall be undertaken with the free and informed consent of competent donors;

(b) In the case of incompetent donors, free and informed consent shall be by an authorized third party;

(c) In the case of deceased donors, free and informed consent shall be expressed in a prior directive or through the exercise of free and informed consent by an authorized third party.

Article 10.2 For the purpose of obtaining free and informed consent, researchers who seek to collect human tissue for research shall, as a minimum, provide potential donors or authorized third parties information about:

(a) The purpose of the research;

(b) The type and amount of tissue to be taken, as well as the location where the tissue is to be taken;

(c) The manner in which tissue will be taken, the safety and invasiveness of acquisition, and the duration and conditions of preservation;

(d) The potential uses for the tissue including any commercial uses;

(e) The safeguards to protect the individual's privacy and confidentiality;

(f) Identifying information attached to specific tissue, and its potential traceability; and

(g) How the use of the tissue could affect privacy.

Article 10.3

(a) When identification is possible, researchers shall seek to obtain free and informed consent from individuals, or from their authorized third parties, for the use of their previously collected tissue. The provisions of Article 10.2 also apply here.

(b) When collected tissue has been provided by persons who are not individually identifiable (anonymous and anonymized tissue), and when there are no potential harms to them, there is no need to seek donors' permission to use their tissue for research purposes, unless applicable law so requires.

Endnotes

[1] Article 2.1(c) was adapted from *Protection of Human Subjects*, U.S. Dept. Of Health & Human Services, Title 45; *Code of Federal Regulations, Part 46.116(d).*

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