[Appendix 2]

ARTICLES INCLUDED IN THE *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 that 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 that poses, at most, minimal risk shall not normally be required by the REB to be peer reviewed.

(d) Certain types of research, particularly in the social sciences and the humanities, may legitimately have a negative effect on public figures in politics, business, labour, the arts or other walks of life, or on 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 those researchers may not be present when the REB is making its decision. When an REB is considering a negative decision, it shall provide the researcher with all the reasons for doing so and give the researcher an opportunity to reply before making a final decision.

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

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

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

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 that 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] that does not include, or that 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 waived 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 process of free and informed consent, 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 process of free and informed consent, 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 of 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 randomized 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 risk 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.

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.

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 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;

(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; and

(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 that 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 that 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 process of free and informed consent. 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 “gene 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. Among 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).