SECTION I

INFORMED CHOICE

Informed choice is at the heart of ethical research involving humans and should be seen as a process that begins with the initial contact and carries through to the end of the research project. Detailed guidance is provided within this Section, however, it is essential to follow the spirit, as well as the letter, of the Articles that follow.

In this Code, the definition of **informed choice** includes three key elements: 1) competence; 2) disclosure/understanding; and 3) voluntariness. The National Council on Bioethics in Human Research expands on this definition of informed choice and states:

> A morally valid choice [i.e. an informed choice] concerning research participation is made: (1) by a competent person; (2) on the basis of adequate information concerning the nature and foreseeable consequences of the research (as these are known at the time the request is made) and all available alternatives; and (3) without controlling influences such as 'force, fraud, deceit, duress, over-reaching, or other ulterior forms of constraint or coercion' (Nuremberg Code).[1]

The principle of autonomy grounds the requirement for informed choice. As indicated in Part 1, researchers do not have the right to require individuals to participate in research. Rather, research participation involves a partnership between the researcher and research participants; the ethical principle of informed choice is basic to this partnership.

Article 1.1

Research with prospective participants may only begin if they or any authorized third parties are given the opportunity to make an informed choice about participation and only when their consent is thereby secured and thereafter maintained throughout their participation in the research.

Care must be taken to avoid selecting prospective participants merely because of the convenience of their recruitment or other characteristics that might impede the informed choice process (see below on incompetence and involuntariness). If the research hypothesis concerns such groups, then additional measures must be taken to ensure that the choice by prospective participants is an adequately informed one. (This may include a prior directive for competent persons who anticipate future incompetence - see Article 1.6).

Article 1.2

Incompetent individuals, or those who are not free to make voluntary choices, may only be recruited when the knowledge sought cannot be obtained from competent individuals or from those who are able to make voluntary choices.

---

[1] National Council on Bioethics in Human Research (NCBHR), Facilitating Ethical Research: Promoting Informed Choice. Discussion Document, Vol. 7, No. 2, December 1996

The principle of respect for persons brings a strong moral preference for recruiting competent over incompetent research participants, and for those who meet conditions of voluntariness. Of course, in many types of research (e.g., with infants), such participants may neither be suitable nor available. Indeed, if research participation were limited only to those who could make informed choices, then some of the most **vulnerable** members of society (e.g., immature children or persons in a coma) would be denied the **benefits** of research (see Section VI). As a result, strict adherence to the ethical principle of informed choice by the research participant could act against the ethical principle of justice in the distribution of benefits of research.

The REB plays an essential educative and consultative role in the process of informed choice. When in doubt about an issue involving informed choice, researchers should consult their REB.

In this examination of informed choice, researchers and REBs must address three components: competence, information disclosure, and voluntariness.

A. COMPETENCE

1. General Conditions

Competence refers to the ability of prospective participants to make informed choices in accord with their own fundamental values; it involves the ability to understand the information presented, appreciate the potential consequences of a choice and, do make an informed choice. This ability may vary according to the choice being made (e.g., a medical versus a financial decision), the circumstances (e.g., a decision made in the home or in a prison), or the time in question (e.g., intermittent competence in earlier stages of Alzheimer's disease). It is important, then, not to treat competence as an "all or nothing" condition. Competence in choosing to participate does not require that prospective participants be competent for making every kind of choice but, rather, that they be competent for making an informed choice regarding participation in a research project.

As indicated in Article 1.2, there are strong ethical principles which fortify the role of competence in the informed choice process. It should be remembered that in law, adults and, in some provinces, older children are presumed competent unless there is evidence to the contrary. Although Common Law and the Civil Code differ in interpretation, from an ethics perspective, the competence of adults and older children should be presumed unless there is reasonable evidence to the contrary.

Certain safeguards must be in place in order to protect the interests and dignity of **incompetent individuals**. One safeguard is the requirement for **third party authorization**. For example, when involving infants and immature children, researchers must secure the **informed consent** of parents or guardians. For other incompetent participants, those individuals legally qualified to provide third party authorization usually include next of kin, a court appointed guardian, or a person authorized to act under the appropriate legislation. Beyond the legal requirements for third party authorization, it is worth noting that family members and friends can provide information about the interests and previous wishes of prospective participants who are no longer competent.

A second safeguard is to respect perceived meaningful expressions of preferences, that is, **assent** or **dissent**. Many individuals who are not fully competent are still able to express their wishes in a meaningful way, even though such expression may fall short of meeting the requirements for informed choice; that is, prospective participants may be capable of verbally or

physically assenting to or dissenting from participation in research. The interpretation of such verbal or physical assent and dissent is often difficult and may require independent adjudication. Included in this category are prospective participants whose competence is in the process of development (e.g., **children** as their capacity for judgement and self-direction is maturing), those who once were capable of making informed choices but whose competence is now considerably, but not completely, diminished (e.g., an individual with early Alzheimer's disease), and those whose competence remains only partially developed (e.g., those suffering from permanent cognitive impairment).

Article 1.3

Research involving incompetent individuals is acceptable under special circumstances. In such cases, enrolment in research or continued participation requires that the researcher explain to the REB how third party authorization and the participants' assent will be obtained, and how the participants' best interests will be protected. In addition:

(a) when individuals are incompetent, third party authorization must be obtained. Such authorization must not be given by the researcher or any other member of the research team;

(b) the authorization of a relevant third party to permit recruitment of an incompetent participant for research is valid only while the participant remains incompetent; and

(c) should participants become competent during the research project, their informed choice must be sought.

Article 1.3 details various considerations relevant to the use of third party authorization. In some cases, the REB will have to determine from whom authorization should be sought (e.g., in some cases authorization would come from a school principal, in other cases it would come from a parent).

Third party authorization is only a partial means of protecting the research participant. Many legal and ethics experts regard such consent as inadequate when the prospective participant is not expected to derive direct benefit, especially if that individual will be exposed to **risk of harm**; experts also argue that the powers given by the law to the authorized third party only equip them to protect the welfare of those dependent on them, and to advance those dependants' interests. These experts believe that the courts might take a restrictive view of the extent to which these powers can be exercised, particularly respecting the approval of invasive procedures for research purposes. Such restrictive views could, for example, extend to the prevention of taking blood samples required to study a method of treatment or to the investigation of the normal development of a disease process. REBs must be aware of this potential conflict between research permitted under this Code and research permitted under the law.

Other legal and ethics experts dispute this view, arguing that third party authorization is sufficient to proceed when there is little or no risk to participants;[1] that is, they argue that research may proceed provided that the risk of harm is within the threshold for **normally acceptable risk**

[1] National Council on Bioethics in Human Research (NCBHR), Reflection on Research Involving Children, Ottawa, December 1993.

and that it is likely to be of sufficient social benefit. In all cases, researchers and REBs should be aware of the applicable laws in their own jurisdiction and in the jurisdiction where the research is to take place.

Article 1.4

The assent or dissent of incompetent individuals must be respected by researchers. Normally, assent is a necessary condition for research to proceed and dissent is a sufficient condition for the research to stop, unless there are sufficient compensating benefits for the participant that can only be provided through research participation.

Article 1.4 states that researchers must respect the assent or dissent of those who are incapable of making an informed choice, that is, those who are **incompetent** or those whose **voluntariness** is seriously compromised. Article 1.4 is designed mainly for research that produces no direct benefits for the participant. However, there may be cases (e.g., research on therapies) where research participation offers a direct benefit to the participant that could not otherwise be secured. In this situation, a judgement has to be made, first by the researcher and then by an authorized third party, as to whether the benefits are sufficient to override the prospective participant's lack of assent or expression of dissentand take into account their significance.

The interpretation of assent or dissent may be problematic for researchers for it may be difficult to determine what, precisely, the participant is assenting to or dissenting from. These difficulties may be greater in cross-cultural situations, for example, when the prospective participants, their families, and any authorized third parties are from a culture that has a different attitude toward certain types of research or is more risk-averse than members of the researcher's own culture. It is important in such cases to work with families, authorized third parties, and knowledgeable professionals or caregivers to develop an accurate interpretation of assent and dissent. If assent or dissent is still unclear, the researcher should use the standard for risk prescribed in Article 1.5.

To respect the interests and dignity of incompetent research participants, a conservative approach must be taken by the REB in determining an acceptable balance between the benefits of a research project and its potential harms.

Article 1.5

In the absence of a prior directive, incompetent individuals, or individuals who are of doubtful competence or those who are unable to make voluntary choices, should not be included in research that exposes them to risks beyond the threshold for normally acceptable risk without the potential for greater benefits for them. (For exceptions to this Article, see Articles 1.7 and 1.8.)

2. Previously Competent Individuals

In anticipation of future incompetence or **involuntariness**, prospective participants may have given **prior directives** of their desire to participate in research.

Article 1.6

For participants who made an informed choice when competent, but who later become incompetent, participation in research is permissible provided a prior directive and/or specific authorization is in place.

Competent individuals who anticipate future incompetence may prepare prior directives and/or a **specific authorization** which can be extended to future research participation, provided the consent is specific to the type and manner of participation (e.g., research specific to the person's illness). Nonetheless, as indicated in Article 1.4, assent or dissent remain important inclusion or withdrawal criteria. Researchers and REBs should be aware of local regulations which may be more restrictive than this Code.

Important research also takes place in emergency, acute or critical care settings. Given time constraints and the often unforeseeable occurrence of life-threatening situations, it may be impossible to secure the informed choice of prospective participants or authorized third parties. Not allowing such research would deny potentially beneficial therapies to those individuals and to those in future situations. Nonetheless, it is important that researchers understand that the moral criterion for assessing the potential harms and benefits of proposed research remains **standard efficacious care**.

Article 1.7

Consent to research in emergency or life-threatening situations may be forgone when the patient is unable to give consent and third party authorization cannot be secured in sufficient time. The researchers must only address questions concerning the condition that caused the emergency or life-threatening situation and must not expose the participant to more than reasonable additional anticipated harms over standard efficacious care.

The interests, rights, and welfare of prospective participants in emergency research situations must be protected by special safeguards requested by REBs which may include the following:

- additional scientific, medical or REB consultation;
- consultation with former and potential participants or community groups;
- 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.

Underlying Article 1.7 is the assumption that potential research benefits could not be secured without forgoing informed choice or third party authorization. The research hypothesis must support a realistic possibility of significantly improving the participant's condition compared to the relevant standard efficacious care. There is no simple formula, however, for determining what is "a **reasonable additional anticipated harm**" and professional judgement must be used in making such an assessment. Concern for the patient's well-being must be paramount.

Article 1.8

When research has commenced without the informed choice of the participant or the third party authorization, in accordance with Article 1.7, a now competent participant or the authorized third party must be informed of the research participant status as soon as possible. Informed consent or authorization must be obtained for continuation in the project and for subsequent examinations or tests related to the study.

Research under the conditions established in Articles 1.7 and 1.8 raise important ethical concerns. For example, since informed choice and consent cannot be obtained, respect for the autonomy of the research participant is jeopardized. For this reason, Article 1.8 requires that research participants who become competent again have the opportunity to make an informed choice concerning continued participation or to have their data withdrawn, as the case may be.

3. Incompetent Individuals

This category includes infants, immature children, and individuals who have never been competent (such as those with permanent cognitive impairment). Although principles of assent and dissent in Article 1.4 are generally relevant to this subsection, the main ethical test used here is that of the best interests of research participants. As is the case with assent, dissent, and unclear prior directives, disagreements may arise about whether or not it is in the best interests of the individual to participate in a research project. Researchers must propose to REBs satisfactory ways of resolving these disagreements.

B. INFORMATION DISCLOSURE

Article 1.9

Researchers must provide sufficient information to prospective participants or authorized third parties so that they can make an informed choice. Throughout the informed choice process, the researcher must ensure that prospective participants are given adequate opportunities to discuss and contemplate their participation. At the commencement of the informed choice process, researchers or their qualified designated representatives must provide prospective participants, either verbally or in writing, with the following:

(a) information that the individual or collectivity 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;

(d) an assurance that prospective participants 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 conflict of interest on the part of researchers, their institutions or sponsors.

If signed consent is required, the participant must be given a copy of such consent form and any relevant written information.

There must be no statement that by consenting, participants waive any legal rights or waive rights other than those specified in the consent form.

In light of (b) and (c), REBs may require researchers to provide prospective participants with additional information (See Table 1).

TABLE 1 - ADDITIONAL INFORMATION THAT MIGHT BE REQUIRED BY THE REB

1.1	an assurance that new information will be provided in a timely manner whenever such information is relevant to the participant's decision to continue or withdraw from participation;
1.2	the identity of the **qualified designated representative** who can explain scientific or scholarly aspects of the research;
1.3	information on the appropriate resources outside the research team to contact regarding possible ethical issues in the research;
1.4	an indication as to who, including personnel from institutional monitoring agencies, will have access to information collected on the identity of participants and a description of how **confidentiality** will be protected and anticipated uses of data;
1.5	an explanation as to the responsibilities of the participant;
1.6	information on the circumstances under which the researcher may terminate the individual's or group's participation in the research;
1.7	information on any costs, reimbursement, and compensation for research participants;
1.8	in the case of randomised trials, the probability of assignment to each option;
1.9	for research on biomedical procedures (including health care interventions), information about forgoing alternative procedures that might be advantageous to the participant and a clear indication of which aspects of the research involve the use of procedures that are not generally recognized or accepted; or
1.10	the ways in which the research results may be disseminated.

Article 1.9 indicates that it is crucial that prospective participants be given the information they need to make an informed choice of whether or not to be involved in the research project. In deciding what is relevant information, a participant-centred perspective must be taken (see Part 1). It also requires that the qualified designated representative of the research team be knowledgeable about the research project (Table 1.2), be able to explain the items in Article 1.9 to prospective participants, and be able to answer any questions. The principal researcher is ultimately responsible for the actions of all those acting with delegated authority.

Researchers need to be aware that research participants, whether inside or outside Canada, may have cultural values different from those of the researcher. In such situations, the researcher has special responsibilities to ensure that prospective participants are provided with adequate opportunities for making informed choices. Thus, researchers must explain the nature and goals of the research listed in Article 1.9, and other additional information, in clear terms and in a manner that is appropriate for each prospective participant.

In some cultures, written consent is the norm whereas in others, verbal consent may not only be the norm, but it also may be regarded as the only acceptable mode of formal consent. Similarly, in some types of research, verbal consent may also be preferable, whereas in others, written consent is mandatory. Where verbal consent is appropriate, the researcher may wish to make a contemporaneous journal entry of the event and circumstances.

It is important for the researcher to communicate in ways that are appropriate to the prospective participants' cultural setting. With some cross-cultural research projects, it may not be possible to offer an adequate "translation" of the researcher's understanding to prospective participants. REBs should proceed cautiously in such cases and require very stringent protection for the interests of participants (e.g., appointing an individual to act in an independent advocacy role).

Under the appropriate circumstances, the distinction between research and care must be clearly explained to prospective participants. It is essential to provide information about which parts of the procedures in question are professionally accepted and recognized therapies, and which parts involve research.

The issue of participants' pre-existing entitlements to care, education, and other services to which the participant is entitled is set out in Article 1.9(d). Accordingly, a physician must ensure that continued clinical care is not linked to research participation. Similarly, teachers must not provide prospective participants drawn from their classes, or under their supervision, with undue inducements for research participation. Also under Article 1.9(d) is the provision that researchers must specifically ascertain that there is continuing consent from participants.

In doing this, researchers provide suitable opportunities for reviewing any new information that had arisen in the course of the research.

Researchers must also 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 participant. Furthermore, the researchers must articulate, during the recruitment process and throughout the project (to the satisfaction of the participant and the REB), how they have dissociated their role as researcher from that of caregiver.

With respect to Table 1.2 the qualified designated representative is usually someone on the research team. When the research poses risks to participants beyond the threshold for normally

acceptable risk, however, it may be advisable to have a person who is independent of the research team in this role. Regarding Table 1.3 some institutions may decide to name an ombudsman for research participants, or designate an individual in the institution's research office as the resource person to handle queries, receive complaints, and transmit them to the REB.

The issue in Table 1.7 is intended to prevent the development of a payment structure for research participation that might place undue pressure on research participants either to join or withdraw from a research project; it does not imply that participants should be paid for their participation in research. In research projects where participants will be compensated, REBs should be sensitive to the possibility of undue inducement for participation, (e.g., payments that would lead participants to run risks they would not ordinarily run). REBs must pay attention to both the situation of those in the pool of prospective participants (e.g., their economic circumstances) and to the amount and kind of risk (in particular, whether the risk exceeds the threshold for normally acceptable risk described in Part 1).

In accord with Table 1.10 participants have the right to know whether they will be identified directly or indirectly in publications resulting from the research. It is important that prospective participants know whether or not they will be given an opportunity to comment on research findings prior to publication. (Affording participants an opportunity to review and comment on research results is one way of building a stronger trust relationship between researchers and participants.) In some cases (e.g., when there has been a history of alleged misrepresentation), individuals or groups may be unwilling to participate unless they are guaranteed the right to review research results and even have their comments incorporated in resulting publications. Reviewing research results with participants may also improve the quality of research (e.g., in terms of correcting mistaken impressions on the part of researchers or by including a more comprehensive perspective) and also help protect the researcher (e.g., against claims of libel).

Rushing the informed choice process or treating it as a perfunctory routine may cause conflict for prospective participants. The time required for the informed choice process is relative to the degree of risk, the setting where the information is given (e.g., hospital or home) and the participant's situation (e.g., level of anxiety, maturity or seriousness of disease). (For exceptions to Article 1.9 regarding emergency situations, see Articles 1.7 and 1.8).

In some circumstances, it is appropriate to have the consent form witnessed. The importance of having someone witness that the choice to participate is voluntary increases as the level of risk increases and as the likelihood of incompetence increases. Using the notion of a proportionate approach to ethics assessment, the REB should decide whether a witness is required. In law, the role of the witness is to provide evidence that participants provided oral or written consent. Hence, for credibility, it is essential that witnesses be independent of the research team.

1. Research Which May Affect the Reproductive Capacity of Participants or their Future Children

The general provisions presented in Article 1.1 also apply to research that may affect a participant's ability to reproduce, or may affect women who are pregnant or breast-feeding. Hence, those who are able to reproduce should be informed before the project begins of potential risks to themselves (including potential **teratogenicity**) resulting from the research, including adverse effects on their reproductive capacities and on future children.

In presenting for REB review a project that recruits pregnant or potentially pregnant women, researchers must demonstrate that they will provide the opportunity for prospective

participants to discuss what potential harms the research could cause to the gestation of the embryo or foetus, the availability of standard efficacious therapy, and the availability of the option of terminating the pregnancy. Should unforeseen findings relevant to these issues be made during the research project, the participant must be informed.

Similarly, in accord with Article 1.9, women who are breast-feeding should be informed of potential risks to themselves and to their infants. Researchers should remember that involving breast-feeding women as research participants may affect both the women and their infants. In such cases, the REB must make an evaluation of the risk both to the women and to their infants.

C. VOLUNTARINESS

As stated in Article 1.2, there is a strong preference for research with those whose voluntariness is not diminished. Voluntariness is especially relevant in research involving **restricted or dependent participants**. Prisoners, members of highly-disciplined organizations (such as the military, some religious groups, and street gangs), residents in long-term care facilities or psychiatric institutions, and employees and students can all fall under this category because they share the characteristic of being within an institutional context where the potential exists for an undue pressure on their free choice.

The pervasiveness of authority relationships on voluntary choice must be judged according to the particular context of prospective participants (e.g., the difference between a maximum and minimum security institution). Similarly, authority figures in some short-term care facilities will have much less effect on their residents' abilities to make voluntary choices than in long-term care facilities. Even within institutions, some participants will be susceptible to greater pressure from authorities and fellow inmates or residents than will others.

Voluntariness will be seriously compromised if research is secured by the order of authorities or as a result of coercion or manipulation on the part of others. Hence, the manipulation of the participant's perception of likely harms or benefits must be avoided. The consent of authorities is not generally permissible as a substitute for the consent of individual research participants. The offer of some benefits in such contexts, for example, a sentence remission for prisoners, will amount to undue inducement. Such inducements limit the freedom of such populations who may perceive such offers as a way to gain favour or improve their situation within their institutional setting.

For the researcher and the REB, issues of privacy and confidentiality are important considerations affecting voluntariness. The research community must appreciate that the danger of disproportionate burdens being imposed on these populations by research participation is very real (see Section VI). Researchers and REBs have an obligation to tailor the choice process to mitigate these risks.

Restricted or dependent participants must be granted their right to make informed choices. Researchers working with such populations must pay attention to conditions which might adversely affect the voluntariness of their choices. In the past, there has been abuse of participants under the authority of or in the care of others because they were convenient populations or because they could be ordered to participate (e.g., human radiation experiments). There is an overwhelming consensus in the research community that such abuses must never again occur.

The permission of authorities or caregivers should not be used to induce or compel participation in research. The researcher should propose to the REB whether prospective

participants should be made aware that such permission has been secured from authorities. Considerable care must be exercised in constructing relationships between researchers and authorities so as not to compromise either the informed choice process or the privacy and confidentiality of participants. Although permission from authorities and caregivers is normally necessary for research to proceed, researchers should avoid being put in a position of becoming informants, unless required to do so by law (e.g., child abuse), or for the protection of health and safety of others.

1. Naturalistic Observation

Naturalistic observation refers to the systematic recording of naturally occurring behaviour outside a controlled setting (e.g., a laboratory). A naturalistic setting is one generally not perceived as established for the sole or primary purpose of conducting research. Behaviour may be recorded in several ways, including continuous or time-sampled verbal or written note-taking, audio recording, video recording or checking off observed behaviours on a previously designed score sheet; naturalistic observation may also involve the researcher as a participant-observer.

The primary ethical issues raised here concern respect for the autonomy of those being observed. In some cases, those being observed know they are being observed for research purposes; in other cases, they do not. Obviously, individuals cannot choose to participate if unaware that they are being watched. However, there seems to be a general consensus that naturalistic observation is within ethical guidelines as long as it is limited to essentially public behaviour, that is, settings that are generally regarded as open to public observation (e.g., a cafeteria), and if the data are collected without reference to specific individuals.

Researchers and REBs should appreciate, however, that there are debates over what constitutes public behaviour, a public place or an acceptable mode of public observation. This may be especially important when researchers make observations outside their own cultural context or in multi-cultural settings in which there are significantly different understandings as to what is or is not public observation. If the research involves any changes in, or the manipulation of, the public environment, REBs should carefully scrutinize the research for its effect on the dignity or interests of prospective participants.

Article 1.10

REB review is required for research involving naturalistic observation. However, if the naturalistic observation takes place in a public setting or in a setting that is normally open to public observation, then the REB would not normally require the informed choice of those observed.

If there is any uncertainty as to whether the behaviour is public, the mode of observation acceptable, or if there is any chance that observation will harm either participants or members of the research team, then the REB may require that prospective participants be notified or even that they ask for their informed choice.

2. Partial Disclosure and Deception

In the ordinary course, informed choice is established through candid disclosure. However, there are exceptions to this standard (e.g., instances where candid disclosure could seriously compromise the research and thus render the research unable to produce benefits which would

make it ethically acceptable). This subsection deals only with the special ethical problems presented by research in which partial disclosure and/or deception is essential for obtaining research objectives.

Partial disclosure refers to cases in which participants are given only partial information as to the true purpose of the research. **Deception** refers to cases in which participants are deliberately given misleading information about the purpose of the research. What is ethically crucial in these situations is that prospective participants not be deceived about the risk of harm of participation (that is, the magnitude of potential harm, its probability or general characteristics).

Questionnaires are one example of a research tool in which partial disclosure or deception may be justified. In this method (as is sometimes also the case in interviews or structured diaries), the information that is central to the researcher's hypothesis may be embedded in **distractor questions**. Distractor questions are used to decrease the likelihood that participants will adapt their responses to their perceptions of the true nature of the research question.

The primary ethical consideration raised by partial disclosure and deception is that the principle of autonomy be maintained and, further, that the trust relationship between researchers, their participants, and the community not be eroded. REBs should use a participant-centred perspective in deciding if a particular project involves either partial disclosure or deception. The use of partial disclosure and deception should be scrutinized with increasing levels of concerns for detail as the level of risk increases. Normally, deception is acceptable only when the harms are below the threshold for normally acceptable risk.

REBs should recognize that in some areas of research, the use of either partial disclosure or deception is generally regarded as methodologically and ethically acceptable.[1] In other areas of research, especially in research on health care that requires forgoing generally accepted and recognized interventions, the use of these techniques requires significant justification and should occur rarely.[2] (This is an area where the community representatives on the REB can play an important role). The use of randomization in clinical trials does not involve either partial disclosure or deception since participants are informed of the probability of being randomly assigned to one arm of the study or another before the project commences (see Table 1.8).

Article 1.11

Researchers must justify to the REB the use of either partial disclosure or deception and must show that:

(a) partial disclosure or deception is the only feasible method for realizing research objectives;

(b) nothing will be withheld from the participants that might, if divulged, cause them to refuse to participate; and

(c) prospective participants will be informed about the magnitude, probability, and general characteristics of any risks they may be exposed to by the research.

[1] Social Sciences and Humanities Research Council of Canada (SSHRC), Ethics. Guidelines for research with human subjects, Ottawa, 1976.
[2] Medical Research Council of Canada (MRC), Guidelines on Research Involving Human Subjects, Ottawa,1987.

Article 1.11(c) should be understood in light of Article 1.9(c) and (d) as requiring researchers to provide accurate information on the magnitude, probability, and general characteristics of potential harms from research participation.

When partial disclosure or deception is used, reasonable efforts must be taken to avoid, or at least to minimize, risk of harm, including embarrassment or humiliation. Researchers should attempt to enroll participants who, if given full disclosure, would likely consent.

Article 1.12

For research involving the use of partial disclosure or deception, the REB, in accord with a proportionate approach to ethics assessment:

(a) may require debriefing following participation when the risk of harm to participants is within the threshold for normally acceptable risk;

(b) must require debriefing following participation when the risk of harm to participants is above the threshold for normally acceptable risk;

(c) may require that the researcher provide the participants a second opportunity for consent when the risk of harm to those participants is above the threshold for normally acceptable risk; and

(d) may require that participants be given the opportunity to withdraw their data from the study when the risk of harm to participants is above the threshold for normally acceptable risk.

As indicated in Article 1.12(a) and (b), **debriefing** should be proportionate to the sensitivity of the issue. Often debriefing can be quite simple and straightforward; however, it also can also involve much more than providing candid disclosure as to the purpose of the research. In such cases, researchers must provide a full explanation as to why deception was necessary, being candid and sincere about their belief in the importance of the research, their regret at having to resort to deception, and their concern about the welfare of the participant. In areas where sensitivities are high, debriefing conducted in an indifferent fashion may compound a feeling of insult with embarrassment or diminishment. Considerable care must be taken to eliminate or reduce the possibility of the participant suffering loss as a result of participating in a research project. Debriefing is an important mechanism in maintaining the participant's trust in the research community.

Debriefing may not be feasible in all cases, (e.g., large scale questionnaires). However, it may be possible to accomplish the same objectives by providing participants with the opportunity to obtain information about the research results, including a discussion of the need for partial disclosure and deception. In cases of greater potential harm, debriefing may be ethically insufficient and may require supplementation by the measures set out in Article 1.12(c) and (d). In some cases, for example research involving immature children, it may be more appropriate to provide debriefing to parents, guardians or authorized third parties rather than to the participants themselves. In other cases, it may be more appropriate to provide debriefing to the entire family or community. When participants express significant concern about the use of partial deception or disclosure in the research project during the debriefing process, the researcher is to report those concerns to the REB.

SECTION II

ETHICS REVIEW

A. SCOPE OF RESEARCH REQUIRING ETHICS REVIEW

All research involving humans requires **ethics review**. In a research institution, ethics review by an REB is required:

- whether the research is funded or not;
- whether the funding is internal or external;
- whether the participants are from inside or outside the institution;
- whether the participants are paid or unpaid, (including the researcher as participant);
- 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 participants or from existing records not in the public domain (see Article 3.1);
- whether the research is to be published or not;
- whether the focus of the research is the participant or something with which the participant interacts;
- 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.[1]

In any situation where there is uncertainty as to whether ethics review is required, the REB must be consulted.

[1] Adapted from University of Alberta, General Faculty Council Policy Manual.

B. RESEARCH ETHICS BOARDS

1. Role of the REB

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

The REB must function impartially and provide reasoned and well-documented decisions. In other words, not only must an REB make decisions about ethics, but it must also make those decisions in an ethical way.

2. Authority of the REB

Article 2.1

The REB must be vested by its institution with the authority to approve, reject, propose modifications to or terminate all proposed or ongoing research involving humans within the institution's jurisdiction on grounds of the ethical considerations set forth in this Code.

Institutions must respect the authority of the REB and ensure they have the appropriate financial and administrative independence to fulfil their primary duties. Both the authority and the mandate of the REB should be established by the highest officer in the institution. In this sense, an REB's authority is delegated authority and, consequently, the legal responsibility for all decisions made rests with the officer who delegated the authority. It must be emphasized, however, that this relationship does not give that officer the authority to override negative REB decisions reached on ground of ethics.

Nothing in this Code is intended to limit the right of the institution to refuse certain research within its jurisdiction, even though the REB may find such research acceptable with respect to the ethical standards and the principles set forth in this Code.

In defining the REB's mandate and authority, the institution should make clear the jurisdiction of the REB and its relationship to others concerned with research and ethical matters within the institution. It is important that the REB have the authority to review research conducted by persons employed by the institution or under the supervision of such persons inside or outside the institution.

3. Terms of Reference of the REB

Article 2.2

Terms of reference shall be adopted for each REB which must include:

(a) protecting participants from research harms;

(b) respecting the duties and rights of researchers; and

(c) reviewing proposed and ongoing research to ensure that it complies with this Code.

Article 2.2(a) should be understood in light of the discussion in Part 1 of a participant-centred perspective. Article 2.2(b) is based on the discussion of the researcher's duty to advance knowledge, and of other rights and responsibilities that flow from that duty.

4. Membership of the REB

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 humans. REB members should also have the ability to educate new members in the technique of ethics review.

The REB has the obligation to reflect the ethical values of this Code in the context of the society within which it operates. The REB's membership must be broad enough to reflect that society.

Article 2.3

The minimum acceptable membership of an REB is 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 who is knowledgeable in the discipline of ethics;

(c) at least one member is a lawyer; and

(d) at least one member has no affiliation with the institution, but is recruited from the community served by the institution and, if possible, from potential participants.

The institution's legal counsel must not be a member of the REB.

To ensure the adequate and thorough review of research, the institution may need to exceed these minimum requirements. The Councils consider it essential that effective community representation be maintained; accordingly, as the size of an REB increases beyond the minimum of five members, the number of community representatives should also increase.

The roles of the lawyer and the member knowledgeable in the discipline of ethics include alerting the REB to potential issues relating to those disciplines. Since there is an ethical obligation to follow the law, the presence of a lawyer on the REB is essential. The institution's legal counsel is not an appropriate member of the REB because the professional obligation to protect the institution may be in conflict with the REB's obligation to protect research participants.

In the event the REB is reviewing a project that requires particular community or research participant representation, or a project that requires specific research methodological expertise not available from its regular members, the REB Chair should nominate appropriate *ad hoc* members for the duration of the review. Should this become a frequent or recurrent event generally or with regard to one specific area of research, then the composition of the REB should be modified to include these *ad hoc* members.

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.

5. Number of REBs within an Institution

The size and complexity of the institution will determine, in large part, how many REBs need to be established and what their focus of research should be (e.g., biomedical, behavioural, humanities, social or natural sciences). In smaller institutions, a single REB may be sufficient; in larger institutions, the authority to review projects may be delegated to more than one REB. In such cases, it is important that the jurisdiction of each REB be defined clearly.

It is essential that review be at arm's length from the researcher. For this reason, departmental REBs normally are not acceptable. Similarly, a multiplicity of REBs with small workloads within the same institution should be avoided.

6. Relationships among REBs

When more than one REB has been established within the same institution, it is desirable that all REBs strive to apply the same ethical standards. Accordingly, a mechanism should be established to co-ordinate the practices of all REBs within the institution.

When an institution, such as a large university, has within it an entity such as a college with additional ethical requirements, the REB responsible for research in that entity must comply with the same minimal standards as the REB responsible for other parts of the institution, namely the standards set forth in this Code. Institutions are free, however, to add requirements to meet special needs (e.g., regulations from a professional college applying to those in a professional faculty).

When an institution has more than one REB and the jurisdiction of each REB has been stipulated by the institution, it is incumbent upon the researcher to apply to the REB which has the jurisdiction over the proposed research. 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 to keep each aware of the research under review and of the decisions made.

C. REVIEW PROCEDURES

1. Scholarly Review Requirements

As noted in Part 1, there is broad consensus among researchers that research that poses risk of harm above the threshold for normally acceptable risk should be reviewed with respect to **scholarly standards**. There is disagreement, however, among various research communities as to whether research at or below this threshold should be assessed with respect to scholarly standards. REB's should use the approach that is appropriate to the research discipline in question and clearly indicate to the researchers submitting proposals for review their approach to this issue.

In evaluating a research proposal with respect to scholarly standards, the REB's assessment "should be based on a global assessment of the degree to which the research might further the understanding of a phenomenon; it should not be based on methodological biases or a preference for particular procedures or on the judgement that another approach is possible."[1] REBs should

[1] Adapted from University of Alberta, General Faculty Council Policy Manual.

not reject research proposals because they are controversial, challenge mainstream thought or offend powerful interest groups, whether within the institution or within the community. The primary tests to be used by REBs should be **ethical probity** and scholarship.

To ensure that the research meets the appropriate scholarly standards, the following mechanisms are among those that should be considered by the REB:

- an **independent external peer review**;
- a **permanent internal peer review committee** reporting directly to the REB;
- where a permanent internal peer review committee is not available or feasible, the REB may arrange for independent review on an *ad hoc* basis; and
- the REB may assume complete responsibility for the scholarly and/or scientific merit, which would require that it have the necessary expertise to carry out peer review of the research in question.

To ensure that the research has sufficient overall value to counter-balance risk of harm to participants, the researchers must clearly explain the evidence that they have of the general benefits of the research including advancement of knowledge. Researchers must also clearly explain the harms that may be incurred by the participants, and explain how the benefits outweigh the harms.

2. A Proportionate Approach to Ethics Assessment

Some research involving humans poses difficult ethical questions both for the researcher and for the REB and may require lengthy deliberation and consultation; most research does not. To ensure that limited resources are used most appropriately, REBs are encouraged to adjust their level of scrutiny to the potential harms perceived in the research — a strategy referred to in this Code as a proportionate approach to ethics assessment (see Part 1). This concept is applied both to the review of proposed research and to the review of ongoing research.

While ensuring that all research is reviewed adequately, in this strategy REBs are encouraged to reserve their most intensive scrutiny for the most ethically challenging research. (The REB may find it useful to develop alternative review mechanisms to concentrate its resources where they are most needed.) Ordinarily, the REB would adopt a procedure in which proposals judged to be below the threshold for normally acceptable risk are reviewed initially by a subcommittee, which makes its recommendations to the REB. The REB would ordinarily accept the subcommittee's positive recommendations. The REB as a whole must review proposals not recommended by the subcommittee. The subcommittee must not have sole authority to reject a proposal.

The REB's authority and responsibility must not be assigned to any other body. The REB may, however, authorize the Chair, another member or a subcommittee to act on its behalf in approving minor changes made by the researcher to comply with conditions of approval stipulated by the REB. Such approvals are reported to the REB for information purposes only. Further, the REB may ask a department to undertake review of its own undergraduate research proposals. In this case, the department would provide the REB with a summary of recommended approvals for ratification by the REB. The REB has the responsibility for auditing the departmental review process at its discretion. Regardless of the review strategy, the REB continues to be responsible for the ethics of all research within its jurisdiction.

3. Meetings

Article 2.4

REB decisions concerning research ethics must be reached in face-to-face meetings, and must be based upon review of fully detailed research proposals or, where applicable, progress reports.

Face to face meetings are essential for the 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 within a reasonable time so that the research can be planned in an orderly way. REBs should also have general meetings, retreats, and educational workshops where members can take advantage of educational opportunities that may benefit the overall operation of the REB, discuss any general issues arising out of the REB's activities or create new local policies for the REB. The funds and other resources required to support activities to enhance the overall expertise and efficiency of the REB are the responsibility of the REB's parent institution.

4. Attendance

Regular attendance by REB members at scheduled meetings is important, and frequent unexplained absences should be construed as a notice of resignation; institutions should also establish quorum rules for REBs. In cases where there is less than full attendance, it is essential that ethics review decisions be adopted only if the members attending the meeting possess the range of background and expertise stipulated in Article 2.3.

5. Decision Making

Article 2.5

The REB must function impartially and provide reasoned and appropriately documented written decisions. When an REB is considering a negative decision, it must provide the researcher with all the reasons for doing so and give the researcher an opportunity to reply.

As indicated in Part 1, it is essential in ethics review that there be congruence between principles and procedures. Article 2.5 indicates the need for REBs to act, and be seen to be acting, fairly and reasonably.

In the event that an REB member 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.

The Chair must monitor consistency in the REB's decisions, 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. When research has been approved subject to conditions, the REB should not, under ordinary circumstances, impose additional conditions subsequent to the original approval.

6. Records of Meetings

Article 2.6

Minutes of all REB meetings must be prepared and maintained by the REB. These minutes shall clearly document the REB's decisions and the reasons for them, and will be accessible to authorized representatives of the institution, researchers, and funding agencies to assist those conducting internal and external audits or research monitoring and to facilitate appeals.

Maintaining satisfactory records is essential to maintaining the reputation of the institution, the researcher, and the REB. Failure to do so may result in loss of research funding and may create situations exposing researchers and institutions to legal liability.

7. Participation by Researchers

To expedite and facilitate the development of ethical research projects, REBs may request that researchers meet with them to discuss the research in question. Where it is feasible, REBs should accommodate requests from researchers to be present for any discussion of their research. In no case should the researcher be present when the REB is making its decision.

If an REB is reviewing research in which a member of that REB has a personal interest (e.g., as researcher), that member must not be present when the REB is making its decision (see Section IV). This does not, however preclude the researcher from participating in any discussion of the research.

8. Review Procedures for Ongoing Research

Article 2.7

All ongoing research must be subject to continuing ethics review. The rigor of this review must follow the principle of a proportionate approach to ethics assessment. The minimal requirement for continuing review is submission to the REB of a brief final report at the conclusion of the project.

In keeping with the principle of proportionate review, a **continuing ethics review** for research exceeding the threshold for normally acceptable risk can include:

- review of annual reports;
- formal review of the informed choice process;
- establishment of a **safety monitoring committee**;
- periodic review by a third party of the documents generated by the study;
- review of the impact of the research on a collectivity;
- review of reports of adverse events;
- review of patients' charts; or
- a random audit of the choice process.

Other models of a continuing ethics review may be designed by researchers and REBs to fit particular circumstances; for example, research that exposes participants to the risk below the threshold for normally acceptable risk requires only a minimal review process.

Article 2.8

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

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. The REB should receive reports at intervals to be determined by it on a case-by-case basis on the progress of the research project from those reviewers identified by the researcher and/or the REB. These reports should include an assessment of how closely the researcher and the research team have complied with the ethical safeguards initially proposed.

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 of scholarly standards. Research institutions must strive to educate researchers on the process of a continuing ethics review through workshops, seminars, and other educational opportunities.

9. Review of Multi-centre Research

Multi-centre research poses particular difficulties as several REBs consider the same proposal from the perspectives of their respective institutions. Inevitably there will be differences of opinion among REBs concerning some aspect of the research. At the same time, there are core elements of any research project which cannot be altered without invalidating the pooling of data from the participating institutions.

Article 2.9

When submitting a proposal for multi-centre research, the researcher must distinguish between core elements of the research and those elements that can be altered to comply with local requirements without invalidating the pooling of data.

While knowledge of approval by the REB of the originating institution will be helpful, the other REBs must avoid being pressured into making a *pro forma* review; it must conduct a complete review and, when feasible, should communicate any concerns with other REBs dealing with the same project. To facilitate this communication, the researcher should provide the names and addresses of the other REB Chairs (if known) dealing with this project. The local REB must maintain full responsibility for the ethical acceptability of research undertaken by the researcher in its institution.

10. Review of Research in Other Jurisdictions

Article 2.10

When research is to be performed outside the jurisdiction of the institution which employs the researcher, the researcher must obtain approval of the institution's REB as well as the approval of the REB (if any) having responsibility 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 or jurisdiction where the research is carried out. 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.

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

Researchers should normally send a copy of every research report/and or publication arising from research to the host university and/or a university, which is best suited to act as a repository and disseminator of the results. This may not be necessary in richer countries when the results are readily available in print or electronically. However, such reporting is particularly important in Third World countries where western publications frequently are prohibitively expensive. If possible, a copy of the field material ought to be provided as well, with due regard to commitments concerning anonymity and confidentiality of research participants. 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. This may take the form of information-sharing, training for local personnel both in the host country and in Canada, or health care or similar services. Scholars, however, are not aid agencies and REBs should not try to force them to undertake expensive aid work which Canadian aid agencies will not fund.

Any rules pertaining to research abroad should be created and interpreted in the spirit of the Helsinki Accords and subsequent documents which encouraged the free movement of scholars across national boundaries for the purposes of research.

11. Reconsideration

Article 2.11

Researchers have the right to request reconsideration by the REB of decisions affecting their research.

When a request is made for reconsideration, the REB should respond quickly, respect the right of the researcher to appear in person for discussion of the research, conduct the reconsideration proceedings without antagonism, and communicate its written decision as soon as possible.

12. Appeals

Article 2.12

Should an institution permit review of an REB decision by an appeal board, that board must be within the same institution and its membership must meet the requirements of Article 2.3 of this Code. No *ad hoc* appeal boards are permitted.

The intent of this Article is to ensure that **appeal boards** have at least the same level of expertise as the REB that made the initial decision. Beyond the foregoing, nothing in this Code is intended to specify substantive or procedural limits to an institution's appeal process. Institutional reversals of REB decisions that have disallowed a research project on ethical grounds are not permitted. The Councils will not conduct an appeal of an REB decision.

13. Other Ethics Review Bodies

In this Code, an REB determines the ethical acceptability of research involving humans which is conducted within the jurisdiction of one or more of those institutions usually qualifying for Council research funding. Insurance and legal liability considerations frequently deny other groups and agencies access to these REBs. Other organizations (e.g., pharmaceutical companies, non-profit agencies, community groups or government research agencies) may establish their own REBs or for-profit review bodies (e.g., private companies in the business of reviewing research projects involving humans).

It is recognized that, in the absence of relevant legislation in Canada, other ethics review bodies are not required to adopt this Code. Because there are clear advantages in harmonizing the ethical standards for REBs evaluating research involving humans, it is hoped that other ethics review bodies will regard this Code as an appropriate model to follow. Adopting this Code will ensure that the minimal standards for research involving humans have been met. This, ultimately, will preserve and enhance the public trust and confidence in Canadian researchers.

SECTION III

PRIVACY, CONFIDENTIALITY, ACCESS TO PERSONAL RECORDS, SECONDARY USE OF DATA, AND DATA LINKAGE

Respect for the autonomy of research participants is the ethical basis for respect for participants' **privacy**: a zone of exclusivity that makes it possible to decide which private attitudes, behaviours, and beliefs will be made available to others in public forums and which will be kept private or will be shared with a few select intimates, that is, family, friends, legal or health care advisors. Privacy is valued not only because certain information is felt to be embarrassing, shameful, or in other ways hurtful to the participant, but also because privacy is essential for intimate, personal, and even spiritual relationships, that is, with what is thought to be "sacred" in a variety of ways.

When a research participant confides in a researcher, unless laws are in place to protect the public interest (e.g., mandatory reporting of child abuse), the researcher is obliged not to share this information with others without the participant's agreement. Breaches of confidentiality may result in irreparable harm to the trust relationship between the researcher and the research participant as well as to other individuals and collectivities.

In order to understand what information is regarded as private and confidential by prospective participants, it is necessary to adopt a participant-centred perspective. For example, a matter that is public in the researcher's culture may be private in a prospective participant's culture. In some cases, it is the type of research that is sensitive (e.g., into someone's sexual or psychiatric history). In other cases, even aspects of the researcher's identity may be seen as invading privacy (e.g., some research participants may be more comfortable with a researcher of their own sex or status). In other cases, it can be the context of the research (e.g., an authoritarian or oppressive institutional context where, in some countries, police have used research data to assist in tracking dissidents). The place of research (e.g., a clinic for sexually transmitted diseases) and the researcher's manner can be seen as potential violators of a research participant's privacy.

There is widespread social consensus about the rights of prospective participants to privacy and the corresponding duties of researchers to treat certain information in a respectful and confidential manner; this is reflected in social practice and in legislation on freedom of information and protection of privacy. Researchers and REBs should be aware of relevant legislation in their jurisdiction and familiarize themselves with the expectations participants may have about privacy and confidentiality. In light of rapid developments in information technology, researchers and REBs must also take appropriate steps to safeguard confidential information.

Notwithstanding the caution expressed above, without access to private information in **personal records**, **secondary use of data**, and **data linkage**, it would be extremely difficult to conduct important research. Research in such fields as epidemiology, history, genetics, and politics, for example, has led to major advances in knowledge and to a greatly improved quality of life. Clearly, there is significant public interest in allowing researchers access to private information not only in order to advance knowledge, but also to achieve a number of social goals, such as designing adequate public health programmes and maintaining democratic processes. The researcher must

ensure that a favourable balance exists between the research participants' interests to privacy and confidentiality and the researcher's quest for knowledge and beneficial research.

A substantial amount of health, social, economic, and psychological research relies on secondary uses of data. Examples include the use of comprehensive registries to identify harmful exposures such as the relationship between tobacco and lung cancer, or employment or educational records to identify the benefits or harms of various social factors.

In the last two decades, the development of larger databases, and the techniques to update and analyze them, has resulted in a significant improvement in the capacity of researchers to design and conduct studies that monitor and evaluate the delivery of services and the outcomes of many procedures and products. These studies have contributed to a more responsive and efficient service delivery system in many areas such as health, education, safety, and the environment.

Furthermore, it is important to note that information gathered in a research project may be shared with the participant (e.g., in the case of the discovery of important genetic information about participants and their biological relatives - see Section VIII) or, under the appropriate circumstances, with those who have a professional care relationship with the participant (e.g., the interaction of a drug under investigation with other drugs used by the participant). With sufficient thought and care, researchers and REBs can develop appropriate methods and practices for the collection, preservation, and use of private data.

A. ACCESS TO PERSONAL RECORDS

There are important precedents in Canada pertaining to the protection of confidential information in research which are found in the law and relevant institutional, professional, disciplinary, and other guidelines. The following Articles build on the good practices that have been successfully implemented by Canadian researchers.

Article 3.1

The researcher must secure REB approval for access to private information obtained directly from participants or from the secondary use of data that identifies them. The researcher must demonstrate to the REB that adequate provision has been made for keeping private information confidential. REB approval is not required for access to information in the public domain, including archival documents.

Prospective participants have the right to know how their privacy will be protected and Articles 1.9 and 3.1 recognize the role of the REB in this regard.

Article 3.2

The researcher must provide adequate information to prospective participants to enable them to make an informed choice regarding participation in the research. Specifically, researchers must inform participants about:

(a) conditions under which identifying information will be released to third parties and the identification of those third parties;

(b) any modes of observation (e.g., photographs or videos) or access to information (e.g., sound recordings) in the research that allows identification of particular participants;

(c) any anticipated secondary uses of data from the research;

(d) any anticipated linkage of data gathered in the research with other data about participants, whether that data are contained in public or private records; and

(e) provisions for confidentiality in publications resulting from the research.

Article 3.2 is based on the assumption that the participants' privacy is usually protected through anonymity, that is, through the removal of information that could be used to identify them. Researchers should not publish any part of their research that could lead to inadvertent identification of individuals; this may prove, however, to be difficult in some types of research, for example, in genetic research when pedigrees are published (see Section VIII and, in particular, Articles 8.1 and 8.2) or in sociological studies of individuals in small communities. In such cases, the researcher must address this issue to the satisfaction of the REB. Similar steps should be taken for a collectivity, if appropriate.

In order to prevent administrative actions from adversely affecting particular individuals or groups, information identifying individuals should not be released to administrative or governmental bodies; 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 participants is obtained. Researchers may, however, provide aggregated anonymous data to administrative bodies for policy decision-making purposes.

Article 3.2(a) states that participants have a right to know who will have access to identifying information and its nature. This would include the 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, for example, child abuse or infectious diseases. In some cases, communicating confidential information (that is, data sharing) is designed to directly benefit the participant (e.g., information shared with a health care provider, lawyer, teacher or counsellor, as the case may be). In other cases, it would be to the detriment of the participant, for example, if information was reported to an employer or other authority figure.

Article 3.2(c) refers not only to the secondary uses of information in research, but also for other purposes, for example, the subsequent use of research videos for educational purposes. Careful observance of Article 3.2(c) will facilitate future research because, if done properly and ethically, the researcher will not have to return to participants for subsequent permission to use their data for another research project. However, it is essential that subsequent uses of data be specified in sufficient detail in order for prospective participants to make an informed choice; it is inappropriate to seek a blanket permission for "research in general." Article 3.2(d) is important because information that may on its own be seen as innocuous by the participant may take on a completely different meaning if linked to other data (see Article 3.6).

Research organizations storing data used for research should implement storage measures that follow standard procedures appropriate to the sensitivity of the data. In general, data released should not contain names, initials or other identifying information. While it may be important to

preserve certain types of identifiers (e.g., age or sex), 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 collectivities should be kept in different databases with unique identifiers.

When working with collectivities, researchers should discuss with relevant members whether or not information allowing its identification should be made public. In this case, it may be necessary to secure both individual and collective informed consent.

Article 3.3

Researchers may gain access to identifying information from databases if they have demonstrated to the satisfaction of the REB that:

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

(b) they have taken appropriate measures to protect the privacy of the individuals, to ensure the confidentiality of the data, and to minimize harms to participants.

Databases can vary greatly in the degree to which personal information is identifiable. There are databases where it is impossible to identify individuals, and there are databases that not only identify individuals but also identify sensitive information about them. Hence, a graduated approach should be used by the REB to evaluate the sensitivity of the information in the database and 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.

Some data are collected as a result of a trust relationship between, for example, patient and physician, employee and employer or client and psychologist. In using such data, researchers must take care not to interfere with or endanger that trust relationship. Similar considerations should also extend to private information collected from families and collectivities. Here, the standard is to use information that individuals could reasonably expect to be used, given the trust relationship, and to justify any exceptions to the REB and/or seek the prospective participants' informed choice for the use of such data.

Public health officers may be mandated by law to undertake research and in such cases REB approval is not required; this does not, however, exempt public health officers from seeking REB approval when the research is outside their mandate. In such case, REB approval is mandatory and, in all cases, respect for persons must be observed.

B. SECONDARY USE OF DATA

Secondary use of data does not include the resolution of other research questions when present in the initial project. Furthermore, rules on the secondary use of data only apply when identifying information is available.

Article 3.4

If identifying information is involved, REB approval must be sought for secondary uses of data. REB approval is not required for access to non-identifying data.

As indicated in Article 3.4, permission must be obtained from the REB before identifying information can be used for another research purpose. Confidential information collected in this manner should normally not be transmitted to authorities unless required by law. When it is unclear as to whether or not information about individuals or collectivities is to be regarded as private, researchers should consult their REBs. This might be the case with sensitive information contained in privately held records on recently deceased individuals.

Article 3.5

Depending on the sensitivity of the information and on feasibility, the REB may also require that a researcher's access to secondary use of data be dependent on:

(a) the informed consent of those who contributed data; or

(b) an appropriate strategy for informing the participants; or

(c) consultation with a representative group of those who contributed data.

Article 3.5 is based on the concept of **proportionate review** of research proposals which means that an REB should focus on projects above the threshold of normally acceptable risk. According to Article 3.5(a), this may lead the REB, in highly sensitive situations, to ask permission from those who made the contribution to use the stored data.

It may be impossible, difficult or economically unfeasible to contact all participants 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 3.5(b) requires that the researcher propose an appropriate strategy for informing the relevant parties or, alternatively, in accord with Article 3.5(c), that there be consultation with representative members of the affected group (e.g., in an AIDS study, contacting an AIDS advocacy group), or there be some way to sample the opinions of a subset of individuals in the group.

Article 3.6

When researchers wish to contact individuals from whom data were obtained, permission must be secured from the REB prior to contact.

An REB must require that initial contact with individuals be made by the **record holder**, or its representative, to briefly explain the research and gain permission for the researcher to make subsequent contact.

In some cases, it is essential for the researcher to contact individuals directly. Because this may be seen by prospective participants as a breach of confidentiality, it is important that record holders or their representatives make the initial contact before permission is sought. In some cases, the researcher should seek the advice of the prospective participant's relevant professional (e.g., physician or lawyer) as to the appropriateness of contacting the patient or client. The relevant

professional may have knowledge of the health status or other possible factors that will determine whether the researcher should approach the potential participant.

The record holder's representative can be an employee of the institution, a member of the research team or an individual paid by the researcher. The representative should avoid conflicts of interest and should not receive payment of finders' fees or similar inducements to recruit participants.

C. DATA LINKAGE

Article 3.7

Data linkage that may identify research participants must be approved by the REB.

Advances in database linkage and the tools to analyze them may be seen as a threat to privacy. Notwithstanding this potential threat, these advances provide significant opportunities for addressing previously unanswerable questions and for generating better social and health-related outcomes.

Because of its analytical power, data linkage is used more and more frequently. To exercise caution, only a restricted number of individuals should perform the function of merging databases; researchers should either destroy the merged file immediately after use, or use enhanced security measures to store it. Whether the data are to be used statistically or otherwise, confidentiality of the information must be maintained by all members of the research team. (Data essentially become statistical data once databases are linked and the identifiers removed; hence, consent by the participant is not necessary under such circumstances.) When a merged database identifies a person or a group that might be at significant risk of harm, it may be appropriate to contact those at risk or the appropriate authorities. The REB and the record holder should also be notified.

SECTION IV

CONFLICT OF INTEREST

Researchers hold trust relationships with research participants, research sponsors, institutions and their relevant professional bodies, and society. These trust relationships can be put at risk by a **conflict of interest.** While the potential for conflict of interest in research has always existed, pressures to commercialize research have led to increased concerns. Therefore, researchers, their institutions, and REBs must assess conflicts of interest, real or apparent, in order to maintain the trust relationship and to ensure accountability.

Article 4.1

Researchers and REB members must disclose conflicts of interest, real or apparent, to the REB.

The REB must assess the likelihood that the researcher's or the REB members' 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 its appearance. The appearance of a conflict may in some cases be as damaging as a real conflict; hence, real and apparent conflicts must be addressed. Apparent conflicts of interest can be assessed by asking if an outside observer might reasonably question whether a decision taken by a researcher could be influenced by private or personal interests.

A useful test to identify real or apparent conflicts of interest is the "publicity test:" If information on the motives and incentives of the researcher were to be accurately presented to the general public, would the trust relationship between that researcher and all relevant parties be maintained?

When a real or apparent conflict of interest is brought to its attention, the REB may require that the researcher disclose this conflict to the prospective participants at the informed choice stage. In accord with Article 1.9(e), research participants should be fully informed of a researcher's potential on actual conflict of interest.

Sometimes the conflict of interest is so pervasive that it is not enough for the research participants, the sponsors of research, institutions, relevant professional bodies or the public at large to simply be informed that there is one; in this case, the REB may require that the researcher abandon one side of the interest in conflict. In such situations, a conscientious researcher will either withdraw from the research or allow others to make research-related decisions without being directed to do so.

When there is an apparent or real conflict of interest, the REB should be aware of the importance of the continuing ethics review process (see Section II). When a conflict of interest is

unavoidable, the continuing ethics review process should be made more stringent. This should help ensure that conflicts are managed appropriately.

In order to judge conflicts properly, REBs must be provided with details on the research project, budgets, commercial interests, consultative relationships, and other relevant information.

A. CONFLICTS OF INTEREST BY REB MEMBERS

It is of the highest importance that members of the REB avoid real or apparent conflicts of interest. For example, REB members are in a clear conflict of interest when their own research projects are under review by their REB. In order to avoid such a conflict, REB members must withdraw from the committee when decisions on their own projects are taken and refrain from using their membership on the REB to gain a favourable decision. Individual members of the REB may also have a conflict of interest in accepting undue or excessive honoraria for their participation in the REB (for example, on commercial REBs).

B. 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 fulfill 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, it is essential that the REB maintain an arms-length relationship with the parent organization to avoid a conflict of interest, real or apparent.

SECTION V

CLINICAL TRIALS

Clinical trials are most frequently conducted in biomedical or health research, although other clinically-related disciplines such as psychology, for example, also conduct clinical trials. 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. Thus, clinical trials may express therapeutic or non-therapeutic objectives and may take the form of case studies, cohort studies, case control studies, "n of 1" studies, and multi-centre 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 Code.

Accordingly, it is unnecessary to examine specific methodological differences; instead, four topics that derive from clinical trials and create ethical issues will be examined: the phases of pharmaceutical research, multi-centre trials, placebo-controlled studies, and the analysis and dissemination of the results of clinical trials and multi-centre trials.

A. 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; as such, they are non-therapeutic clinical trials and are conducted in populations of apparently healthy participants.
- Phase II clinical trials primarily examine the short-term pharmacological toxicities of and, to a lesser extent, the efficacy of new drugs; as such, they are therapeutic clinical trials because they are conducted in populations with specific diseases. These trials, as well as Phase III and IV clinical trials, are designed to increase the survival or the quality of life of participants suffering from a specific disease or condition.
- Phase III clinical trials primarily examine the pharmacological efficacy of and, to a lesser extent, the short-term toxicities of new drugs; as such, they are usually disease-specific therapeutic clinical trials.
- Phase IV clinical trials, also known as post-marketing surveillance studies, primarily examine the long-term efficacy and toxicity of already marketed drugs; as such, they are usually disease-specific, therapeutic clinical trials.

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

Article 5.1

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

Conventional Phase I non-therapeutic clinical trials depend on apparently healthy participants who are paid by the sponsors of newly developed drugs to undergo sometimes life-threatening toxicities. Such studies usually are conducted in private settings without independent public scrutiny to ensure that appropriate scientific principles are upheld and ethical safeguards are in place. These considerations raise ethical concerns about the selection and recruitment of participants, the informed consent process, the meaning of informed choice under these circumstances, the membership and procedural adequacies of the REB (if any), and the duties of the federal regulator.

Because healthy participants are invited to voluntarily take risks that might be significant, without any benefit other than financial, the ethical principles that apply to an employment relationship are relevant in this circumstance; these involve due consideration to autonomy, beneficence, and justice.[1]

The development of a plethora of new pharmaceutical drugs and the private setting of Phase I non-therapeutic 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.

Article 5.2

In combined Phase I/II therapeutic clinical trials, researchers and REBs must carefully examine the integrity of the selection, recruitment, and informed choice and consent processes. Where appropriate, the REB may require an independent monitoring process.

Combined Phase I/II therapeutic clinical trials raise particular ethical concerns because they are often conducted with desperate populations (e.g., terminal cancer and AIDS populations) whose therapeutic options have been exhausted. In such situations, autonomous choice by both participants and researchers may be distorted, as may the ratio between reasonable harms and benefits caused by the research. Such factors not only relate to the selection, recruitment, and informed choice processes, 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 therapeutic clinical trials.

Phase II and III therapeutic clinical trials, unlike combined Phase I/II clinical trials, often include placebo controls to detect and quantitate 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 can further stress the duty of researchers to maximize the benefit to participants and minimize harm in human research.

Phase IV clinical trials are usually designated as post-marketing surveillance studies; often, however, they are post-marketing advertising conducted in the private practices of physicians. For

[1] Freedman, B. Canadian Bioethics Society Annual Meeting, Montreal, Canada, October 1996: Plenary Session.

example, a physician may be paid a per capita retribution by the sponsor to assess the side effects and the acceptance by patients of an already-marketed drug. Clearly, such Phase IV clinical trials can stress 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 humans 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 informed choice and consent processes, as well as raise potential conflicts of interest. For example, newly developed heart rhythm pacemakers, which can cost thousands of dollars, must be implanted surgically to assess their efficacy and possible harmful side effects. Typically, in some Canadian jurisdictions, health plans pay the surgical fees, while "ownership" of the experimental devices usually remains with the sponsor of the trial. In such clinical trials, and to whatever extent is practical, researchers and REBs must ensure that participants are accorded all opportunities to exercise their rights to the initial and continuing informed choice process.

The REB must carefully examine such clinical trials to assist researchers in avoiding potential conflicts of interest concerning the selection and recruitment of participants, and payments by sponsors to the researchers. The REB should also examine the issue of continuous access to relevant medical devices or, if impossible, the provisions taken to ensure an adequate replacement. Finally, the REB must be aware that numerous safety standards (for example, mechanical and electrical) apply to medical devices and that these standards should be respected.

Article 5.3

REBs must examine the budgets of all clinical trials.

Budgets for clinical trials usually are calculated by per capita costs, that is, the sponsor pays the researcher a fixed sum for each research participant recruited. This form of payment raises ethical concerns because it has the potential to place the researcher in a conflict of interest if she or he also holds a therapeutic or other clinical relationship with participants. Disclosure of the amount of the per capita payment, and other budgetary details will assist the REB in assessing potential conflicts of interest and, if applicable, also assist the researcher in resolving them. As a general guide, per capita payments should be comparable to the researcher's usual professional fee. When trials take place within a public institution (e.g., 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.

B. MULTI-CENTRE CLINICAL TRIALS

Multi-centre clinical trials are now common-place and reflect not only the need for increased numbers of research participants but also the multi-disciplinary nature of contemporary

human research. As multi-centre trials raise particular difficulties for REBs, a complete discussion of this issue is held in Section II (see, in particular, Article 2.9).

C. PLACEBO-CONTROLLED STUDIES

Article 5.4

The use of placebos in clinical trials is ethically unacceptable where clearly effective therapies or interventions are available.

Researchers and REBs must be very cautious concerning the use of **placebos**.[1] In some cases, when the purpose of a clinical trial is to determine whether an established intervention does more or less good than no intervention, the use of placebos may be appropriate. When an established intervention is effective, **clinical equipoise** holds that it is unethical to withhold it from participants for research purposes: "In any medical study, every patient — including those of a control group, if any — should be assured of the best proven diagnostic and therapeutic method."[2] There is a range of therapeutic possibilities which requires careful consideration on a project-by-project basis.

Placebo drugs are commonly used in Phase II and Phase III clinical trials and multi-centre trials as a means of identifying the actual and pseudo-toxicities and efficacy of a test drug. Placebos are not necessary drugs but may include, for example, "sham" physical therapies or manipulations in physiotherapeutic, surgical or chiropractic research. Whenever a placebo intervention is proposed, the researcher must satisfy the REB that:

- the validity of the research requires the use of a placebo;
- the placebo is being compared to the best efficacious and accessible intervention;
- all other therapeutic components of the usual regimen employed for the condition being tested are included in the experimental project;
- the participant has been made aware of the likelihood of receiving a placebo; and
- in the unusual circumstance where the experimental use of a placebo cannot be revealed during the informed consent process, post-trial debriefing (see Article 1.12) and disclosure (see Article 1.9) must occur.

In the event that the use of a placebo is necessary but cannot be revealed (such as during wash-out phases), the requirement for post-trial debriefing and disclosure can strain the voluntary and informed choice and consent process; in particular, researchers must provide accurate information on the magnitude, probability, and general characteristics of potential harms from research participation - see Articles 1.9(c) and (d) and 1.11(c).

---

[1] Declaration of Helsinki-Tokyo (Helsinki II). A code of ethics for clinical research approved by the World Medical Association in 1964 and renewed in 1975, 1983, 1989, and 1996. This declaration was widely adopted by medical associations in various countries.

[2] World Medical Association

D. ANALYSIS AND DISSEMINATION OF CLINICAL TRIALS AND MULTI-CENTRE TRIALS RESULTS

In most clinical trials and multi-centre trials, the sponsors typically 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 always 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 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 denied publication and dissemination thereby fostering, for example, inappropriate clinical practices or needless and wasteful duplication. Researchers and REBs can do little to influence this deficiency in the dissemination of research results: research journalists, journal editors, members of editorial peer review boards, sponsors, and regulators should address this as an issue of scientific and ethical urgency.

SECTION VI

INCLUSIVENESS IN RESEARCH

A. INTRODUCTION

One important aspect of justice is the fair distribution of benefits and burdens, that is, distributive justice. Historically, concern for justice in research involving humans has focussed on whether or not research participants were treated fairly: were they over-burdened relative to the direct benefits they received from their participation in research? Contemporary concerns with justice in research have widened: are the overall or global benefits and burdens of research distributed fairly and, in particular, have disadvantaged individuals and groups, whether participating in research or not, received a fair share of the benefits of research?

The above two concerns form the basis for the following ethical principle: members of society, especially those in disadvantaged or vulnerable groups, should neither bear an unfair share of the direct burdens of participating in research, nor should they be unfairly excluded from the potential direct or indirect benefits of research participation. These concerns with justice are important and must receive formal attention from researchers, REBs, research institutions, and sponsors.

There are well-known cases in which researchers intentionally or negligently misused research participants, and even seriously abused them. Worries about such abuses have led to an ethical focus on the relative level of benefits and harms that research would impose on prospective participants. These issues are reflected in this Code in a variety of ways: a heightened concern with risks above the threshold for normally acceptable risk (Part 1); special attention to groups that are vulnerable because of incompetence or involuntariness (Section I); research areas of special sensitivity (e.g., Human Genetic Research in Section VIII and Reproduction, Infertility, Embryos, and Foetuses in Section IX); and research that raises specific methodological concerns (e.g., secondary use of data (Section III) and partial disclosure and deception in Section I, and the inappropriate use of placebos in Section V). Since these particular issues are covered in other Sections of this Code, the main thrust of this Section is the fair distribution of the direct and indirect benefits of research.

Experience has identified a number of sources of unfair or unjust distributions of the benefits of research. One source is specifically tied to concerns about the misuse or abuse of research participants. Thus, some scholars and ethicists have argued that, in principle, only competent individuals should be permitted to participate in research that would likely be harmful or non-beneficial to them and, hence, that it would be wrong and perhaps illegal, for example, to subject an infant to venipuncture to withdraw blood for research purposes unless there was some direct compensating benefit for that infant. The rigid application of such a principle could potentially deny specific infants the direct benefits of research participation as well as deny indirect benefits to infants as a group. In a sense, then, avoiding one moral problem, the unfair exploitation of vulnerable research participants, leads to another moral problem, that individuals most in need of the benefits of research can be denied those benefits.

Another source of unfair or unjust distributions has been the fear of legal liability and litigation which, for example, led to the exclusion of women of child-bearing age from drug trials presumably because of possible harms to potential offspring. There was not, however, a similar

exclusion of men of reproductive age. Further exclusions were based on concerns about confounding effects (e.g., the effects of the female hormone cycle on drug trials); choice in the **inclusion** or **exclusion** criteria (e.g., setting a low age as the upper limit of inclusion includes most male heart attack victims but excludes many female heart attack victims); and financial and other costs of changing the direction of established research programmes.

With this second concern about distributive justice in research, it is not nearly as easy to focus on researchers and REBs as it is for the first type of concern (appropriately benefiting and not overburdening research participants). There are multiple agents involved in setting "the research agenda," that is, the general direction of current and future research: attitudes and beliefs of colleagues, availability of funding, technology and infra-structure, and multiple diverse and sometimes conflicting demands by research institutions and society. This is not to deny that individual researchers and REBs have a role to play in the fair distribution of the benefits and burdens of research; rather, it is easier to avoid specific harms in areas under one's own control than to bring about a larger social good (in this case, a fairer distribution of the general benefits of research).

To be effective in setting and maintaining a just research agenda, there must be responsible interaction by all those directing the research project. The Councils have for their part engaged in a variety of endeavours in this area, including this Code, the Report of MRC's Advisory Committee on Women in Clinical Trials, the Programme of Co-Operation on Women's Health, and research projects sponsored by the Councils with populations that are the subject of this Section (e.g., the elderly, children, and women), to name a few.

Article 6.1

Researchers must not discriminate against prospective or actual research participants on the basis of culture, religion, race, mental or physical disability, ethnicity, sex or age.

The aim of this Article is, therefore, to discourage discrimination against disadvantaged groups and, more positively, to encourage research which benefits members of such groups, either directly through participation in research or indirectly through research which ultimately produces such benefits.

While there may be disagreement at the margins about who has or has not been disadvantaged in terms of receiving the direct and indirect benefits of research, there is general agreement that certain groups have been disadvantaged: women, people of colour, Aboriginal peoples, the elderly, children, and restricted or dependent participants. The intention of this Section, then, is not to discourage research involving more advantaged groups but, rather, to achieve a more just distribution of the overall benefits of research. The due representation in studies of those to whom the studies are intended to apply is a matter of both ethical and methodological concern.

B. CULTURE, RELIGION, RACE, ETHNICITY, AND MENTAL OR PHYSICAL DISABILITIES

Article 6.2

Researchers and REBs must endeavor to distribute equitably the potential benefits of research. Accordingly, depending on the themes and objectives of the research, researchers and REBs must:

(a) select and recruit research participants from disadvantaged social, ethnic, racial, and mentally or physically disabled groups; and

(b) ensure that the design of the research reflects appropriately the participation of these groups.

In general terms, Article 6.2 requires researchers to explain to REBs how they have taken into account the provisions of the Article or why its provisions should not be applied to their research. The words, "depending on the theme and objectives of the research project" indicate that Article 6.2 is relevant to some but not all research. REBs should take into account difficulties posed by the size of samples, limitations in participant availability, funding requirements, cultural and linguistic differences, and the like.

Article 6.2(a) is important for the validity of the research and for justice in the distribution of the benefits of research. Article 6.2(b) places an onus on researchers to explain how the project's design affects the recruitment of members of relevant groups. (Inclusion and exclusion criteria, particularly those that exclude members of relevant groups, would be especially relevant to Article 6.2(b).

C. RESEARCH INVOLVING WOMEN

Historically, women have been excluded as research participants. The justifications for this exclusion have included fear of damage to the foetus including teratogenicity, the confounding influence of hormonal cycles, and fear of liabilities of research sponsors. Women have also been excluded because of a failure to recognize that certain diseases and conditions might affect men and women differently.

The exclusion of women as research participants also raises serious concerns regarding the generalizability and reliability of the data collected. Research data on, for example, drug dosages, device effects, treatments, cultural norms, moral development, and social behaviour obtained from male-only studies likely will not be generalizable to women. As a result, data necessary for the treatment or understanding of women often must be inferred despite important differences which may render such inferences inaccurate. When women, or any group, are excluded from research studies, they may be deprived of the possible benefits that come from participating as research subjects, and may suffer as a result. The inclusion of women in research is essential if men and women are to equally benefit from research. Careful attention to these issues is essential to both justice and the quality of research.

Article 6.3

Researchers and REBs must endeavor to distribute equitably the potential benefits of research. Accordingly, depending on the themes and objectives of the research, researchers and REBs must:

(a) select and recruit women from disadvantaged social, ethnic, racial and mentally or physically disabled groups; and

(b) ensure that the design of the research reflects appropriately the participation of this group.

While some research is properly focussed on particular populations that do not include women or only include very few women, in most studies women should be represented in proportion to their presence in the population affected by the research. In designing and implementing research projects, particular attention also should be paid to the need to include women of colour, women who are members of cultural or religious minorities, and women who are socially or otherwise disadvantaged.

Article 6.4

No woman should be automatically excluded from research relevant.

Many women have been automatically excluded from research (e.g., the possibility of pregnancy was used as justification for excluding presumably fertile women, especially those not using contraceptives). Concerns for the embryo, foetus or a new-born infant were used as justifications for excluding pregnant or breast-feeding women. Excluding women, or requiring contraception in women but not men, created an ethically unjustifiable imbalance (see Section I).

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. This extends the standard practice for the assessment of harms and benefits of research to the special case of research involving pregnant or breast-feeding women. Research with substantial potential benefit, beyond the benefits of generally accepted efficacious care (see Section I), for pregnant or breast-feeding women, and minimal potential harm (that is, below the threshold for normally acceptable risk) for their embryos, foetuses or infants can be justified on simple utilitarian grounds. Research with substantial potential benefit to pregnant women and potential substantial harm (above the threshold for normally acceptable risk) for their embryos and foetuses can sometimes be justified on various grounds, including respect for the autonomy of women. An example of such a project might be a clinical trial of chemotherapy for highly malignant cancer undertaken when all alternative standard therapies have failed that is potentially life-saving for the woman but life-threatening to her embryo.

D. AGE AS AN INCLUSION OR EXCLUSION CRITERION

Article 6.5

Depending on the theme and objectives of the research project, the researcher must justify to the REB the use of age as a criterion for the inclusion or exclusion of research participants.

Age has been used to unfairly exclude individuals from participation in research with the result that insufficient research has been done on the young and on the elderly. There are concerns with members of both groups regarding competence, but these concerns should be addressed in their own right and not masked with arbitrary age dependent criteria.

Moreover, 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 autonomy of the individual and the provision of necessary protection for those who are, or who may become, incompetent (see Section I). Researchers and their sponsors should guard against the bias that elderly persons, in general, are unable to comply with the researcher's directions and hence must be excluded as research participants.

Age is not valid as an independent criterion for the capacity to consent. The elderly are a heterogeneous group, and, as with other heterogeneous groups, their competence should be assessed directly rather than on the basis of age. This has been a particular concern with drug studies but also has implications for a broad range of research, such as studies on loss of cognitive skills.

E. RESEARCH INVOLVING INFANTS, CHILDREN, AND ADOLESCENTS

While the exploitation of children for research purposes must not be allowed, there is an obligation to encourage and pursue research involving children. This obligation is rooted in three principles:

- harm could come to infants, children, and adolescents if research about them is not pursued (see Section I);
- it is unjust to exclude these populations from research that may be to their benefit; and
- respect must be given to the rights and obligations of parents or guardians to ensure the well-being of their children.

The notion of harm as it applies to these three groups should be understood differently from harm as it applies to adults. Any harm induced in children may have longer term consequences in their growth and development. Furthermore, harms and benefits for children with chronic disabilities and terminal illnesses should be understood differently from harms and benefits for other children. Every researcher working with child participants 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 6.6

Infants, children and adolescents should not be excluded from participating in research which is potentially directly beneficial to them as individual participants and, with appropriate safeguards, indirectly beneficial to them as a group.

In some cases, children benefit directly from participation in research. For example, some research produces improved health, social or educational outcomes for child participants. Where the benefits are significant, researchers must make serious efforts to recruit children from groups which are disadvantaged. In general, children ultimately benefit from research done on other children; this is a good reason for including children as research participants. However, it is essential that there be adequate safeguards to protect child participants from undue risks of harm (see Section I).

As already noted, there is a general social obligation to extend to children the benefits of research which makes it permissible, and even mandatory, to conduct research involving children. However, care must be taken not to exploit these young research participants for the benefit of others. This is especially important when children are unable to consent or assent to being involved in the research project.

F. RESEARCH INVOLVING RESTRICTED OR DEPENDENT PARTICIPANTS

Restricted or dependent participants, that is, those in the care, or under the authority, power, or control, of others (e.g., students, employees, incarcerated populations, persons in care), should neither bear an unfair share of the burden of participating in research nor should they be excluded from its benefits. Researchers working with such participants must take into account the particular vulnerabilities of these populations. Issues pertaining to the voluntary and informed choice for these participants are discussed in Section I.

G. PATIENTS IN EMERGENCY OR LIFE THREATENING SITUATIONS

The provisions in Section I (and, in particular, Articles 1.7 and 1.8) regarding patients in emergency or life-threatening situations constitute other populations previously excluded from the benefits of research that are now included.

SECTION VII

RESEARCH INVOLVING COLLECTIVITIES AND THEIR MEMBERS

A. INTRODUCTION

Some research involving humans is with individuals as members of groups or with the groups themselves as reflected in the following examples: an anthropologist investigates community self-governance in a small Aboriginal community for a protracted period of time as a participant-observer; a researcher intends to involve an ethnic community in a predictive genetic study specific to members of that biologically related group; or a team of researchers seeks the help of an advocacy organization dealing with issues of spousal abuse in the recruitment of members for a crime-prevention study.

Sometimes in research involving **collectivities**, the researcher is attempting to achieve an understanding of the group in terms of the characteristic beliefs, values, social structures, and other features by which members identify themselves as group members. In some instances, research on or about collectivities is not relevant to this Code (e.g., the information is in the public domain - see Article 3.1). However, in other instances, the collectivity itself should be seen as a research participant. For example, the group might regard the information sought in the research as belonging to the group and as private, e.g., sacred songs, community records, or life histories.

Collectivities may also be considered research participants because the group is formally or informally involved in the conduct, direction, sponsorship or implementation of the research. For instance, the researcher may be soliciting a group's assistance in conducting research on its institutions or members; or a group may be asked to perform a collective task (e.g., have a discussion of a hypothetical question and then vote on its resolution); a group may be asked to approve and commit resources to the research project (e.g., co-sponsorship of a clinic in which research will take place, or provide the researcher with an audience to explain a community-oriented research project); or the researcher may wish to speak with various spokespersons of the group for an oral history project.

There are sound historical reasons for many groups, and not only oppressed minority groups, being apprehensive about the activities of researchers. While in many cases, research with groups has been conducted in respectful and responsive ways, there have been other cases where group members have felt that researchers have abused their trust. For example, in some instances researchers have expropriated the cultural properties and human remains of minority groups, particularly indigenous peoples and those who have been colonized. Properties and remains of certain groups have been taken to research institutes for examination, exhibition, and permanent storage, and some have even been placed on the market for sale. Concerns have been expressed about "parachute scientists" who treat groups merely as a source of data and, in return, give nothing of value back to the community. In some instances, researchers have endangered dissident minorities by wittingly or unwittingly acting as information-gatherers for repressive regimes. Besides the inherent wrongness of such actions, these researchers have through these behaviours also impaired research opportunities for others.

Research involving collectivities can raise difficult and novel ethical issues. A central issue that can arise is setting mutually agreeable terms of engagement when the researcher is from a different culture than the one being studied. As noted in Section I, there are debates over what constitutes public behaviour, public space or what is an acceptable mode of public observation. Similarly, private information or artifacts that are private possessions subject only to individual control in one culture, may be collective and inalienable property in another. Confusion and misunderstanding may also arise over whose expectations are to prevail. Another area of ethical difficulty can arise for the researcher when there is a conflict between a group and one or more of its members. The researcher and REB must ascertain whether the informed choice of the group or the dissidents will ultimately have priority.

B. AIMS OF THIS SECTION

This Section is designed to assist researchers and REBs in deciding which projects involve (are "on" or "with") collectivities, and then what types of research conduct are ethically appropriate. The first objective of this Section is to ensure that collectivities will be treated ethically in research. The second objective is to encourage good practice in research involving collectivities.

The positions taken in this Section represent a natural continuation of the 1977 SSHRC *Guidelines for Research With Human Subjects*[1] on the treatment of collectivities. In the 1977 SSHRC *Report of the Consultative Group on Ethics*[2], which formed the basis for the *Guidelines*, the fundamental ethical principles of research are described as follows:

> While recognizing the vital importance of research to human progress, we affirm that consideration for the welfare and integrity of the particular collectivity must prevail over the advancement of knowledge and the researcher's use of human subjects for that purpose. Given this premise, it follows that certain individual/collective rights must be maintained, such as the right to be fully informed about the precise nature and purpose of the research in which participation is sought so that consent may be given and withheld advisedly; the right to know of the risks and benefits involved in participation in the proposed research; 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, to remove and store sacred and cultural objects or to exhibit and dispose of these objects; the right of cultural groups to accurate and respectful description of their heritage and customs and to the discreet use of information on their daily lives and aspirations.
>
> Such a listing is neither original nor exhaustive. Many of Canada's institutional and professional codes of ethics for research on human subjects make reference to these or similar individual/collective 'rights. In so doing they are unanimously sympathetic to our primary concern'[3].

This Code also draws upon the participant-centred perspective contained in MRC's 1987 *Guidelines on Research Involving Human Subjects* regarding cross-cultural studies, where it is stated that

[1] Ethics. Guideline for research with human subjects. Social Sciences and Humanities Research Council of Canada, Ottawa, 1977é
[2] Ethics. Report of the Consultative Group on Ethics. Canada Council (Social Sciences and Humanities Research Council of Canada), Ottawa, 1977.
[3] *Ibid*, pp. 1-2.

crucial concepts such as informed consent, privacy and confidentiality "must always be viewed from the perspective of the culture studied as well as from that of the investigator."[1]

C. SCOPE OF THIS SECTION

As indicated in the 1977 SSHRC *Report* and in the resultant *Ethics Guidelines*, the general principle is that all moral and legal rights, be they individual or collective rights, must be respected. While collective rights are a recognized part of Canadian law and jurisprudence and have received attention over the last several years in philosophy and in political science, they are less familiar than individual rights to a substantial part of the Canadian academic and lay communities. Yet, even from a purely individual rights perspective, it is possible to argue that individuals can pool their rights by vesting them in groups and organizations (e.g., governments, trade unions, and corporations). Moreover, it is plausible to claim that individual autonomy finds its expression and support in collective autonomy. (As will be noted below, this has particular importance in the case of vulnerable groups.) In any case, for many people, collective rights are more fundamental than individual rights and, therefore, it would be inappropriate to simply disregard or override such deeply held convictions.

D. COLLECTIVITIES AS RESEARCH PARTICIPANTS

Article 7.1

Researchers must seek REB approval for research on or with a collectivity when one or more of the following applies:

(a) property or private information belonging to the group as a whole is studied or used;

(b) the research requires the delegated participation or permission of those occupying positions of authority, whether formal or informal, in the group; or

(c) the research involves the participation of members acknowledged as representatives of the group as a whole.

As stated in Article 3.1, this Article does not apply to research involving collectivities which only uses information, including archival documents, in the public domain.

Article 7.1 provides guidance to researchers and REBs about when collectivities are to be counted as research participants and, as a result, come under the provisions of this Code with respect to such important matters as informed choice (Section I), privacy (Section III), and inclusion (Section VI). Article 7.1(a) includes cultural properties as understood by the group in question;[2] human tissue also may fall under this category (Section X). In accord with Article 7.1(b), research involves a collectivity if the researcher, for example, asks the group to assist in recruiting its members (e.g., asking a gay advocacy group to recruit members to a study of discrimination), or if the group is asked to give official approval (e.g., asking Band elders for approval for the use of Band records in a study of the effects of residential schools on Native children). While Article 7.1(b) takes into account the actions or involvement of groups with recognized authority structures (i.e., groups in which some person or group of persons acts officially on behalf of the collectivity), Article 7.1(c) applies more broadly and includes groups that do not have such structures but are

[1] Medical ResearchCouncil of Canada, Guidelines on Research Involving Human Subjects, Ottawa, 1987, pp 27-28.
[2] See Appendix 5. Report of the Consultative Group on Ethics. *Op. Cit.*

nonetheless collectivities, (i.e., groups in which there is mutual recognition of membership). Together, Article 7.1(b) and (c) would include the research in which members of a collectivity are interviewed as spokespersons for the group as a whole.

E. PROTECTION FOR VULNERABLE COLLECTIVITIES

Article 7.1 applies broadly to many types of groups. It applies to large and well-defined groups, including those generally recognized in law and in social opinion, for example, governments and corporations, as well as unrecognized and relatively powerless groups. Insofar as any of these groups have collective rights to property, information, and action, those rights should be respected by everyone including researchers. The rights of powerful groups are usually widely respected and, in any case, are easily enforced by the groups themselves. The primary aim of Articles 7.2 and 7.3, however, is to underscore the need for researchers to protect the collective rights of groups that are vulnerable because their rights might not be recognized and because they lack the resources to enforce their rights.

As noted in reference to populations who have been unfairly excluded from the potential direct or indirect benefits of research participation (see Section VI), there may be disagreement at the margin about which groups are vulnerable. There is, however, a general consensus about the main groups in this category: Indigenous peoples, in Canada and elsewhere, and minority groups who are or have been oppressed or discriminated against. Such minorities often have been defined in terms of race, gender, ethnicity, religious belief, physical or mental disability, disease status, occupation or class.

The relative vulnerability of a group does not always depend on the explicit intentions or actions of particular researchers. How vulnerable a group is vis à vis a researcher may be as much a product of the appearance of the researcher's power in relation to the group as it is of more tangible power differentials (e.g., expertise, control of information and, in some cases, control of or authority over the research population). Hence, vulnerability due to an actual or perceived power imbalance may be historical (e.g., a history of abuse by researchers in the past), symbolic (e.g., religious or cultural sensitivities in a particular group may dictate that research interviews or physical examinations may only be conducted by members of the same sex or status) or simply widespread discrimination by society at large and researchers.

As already noted, some collectivities cannot usually be considered as vulnerable. Thus, the following Articles would not apply, for example, to an investigation of the advertising strategies of tobacco manufacturers or to research on political influence in judicial appointments. In cases where there is doubt as to whether the collectivity is a vulnerable research participant (e.g., a street gang from a disadvantaged minority group), researchers should consult their REBs.

Article 7.2

When dealing with vulnerable collectivities, researchers must satisfy REBs as to how they will deal with anticipated or actual disagreements between the researcher and the collectivity over ethically sensitive issues, including specifically:

(a) informed choice;

(b) privacy and confidentiality; and

(c) individual and collective harms.

Article 7.2 recognizes that there may be conflicts over fundamental ethical issues between researchers and the collectivities they study; indeed, it is possible that there are collectivities that will not accept the moral perspective that is operative throughout this Code. When such conflicts can be reasonably anticipated, the researcher must propose to the collectivity and to the REB a strategy for dealing with those differences.

F. COLLECTIVITIES AND THE INFORMED CHOICE PROCESS

In this Code, the agreement to participate in research involves a meeting of minds between the researcher and the prospective research participant. In the absence of such a meeting of minds, there would not be an informed choice with regard to research participation. Hence, if there is disagreement between the researcher and a collectivity over informed choice issues, fundamental questions must be addressed. These questions can arise especially when there is disagreement about the importance of individual, as compared to collective, informed choice. For instance, a collectivity may wish to veto research conducted on one of its sub-groups because it believes that the sub-group has no right to reveal information which is held confidential within the larger community; conversely, the sub-group may believe that it has been manipulated and oppressed and, therefore, that its choice should not be dictated by the group as a whole.

In working to seek informed choice from collectivities, two considerations are essential:

- informed choice needs to be obtained in a manner that is considered legitimate by the collectivity with respect both to process and to content; and
- normally the informed choice of all the collectivities engaged by the research is required.

Sometimes the consent of authorities is legally required for the conduct of research. Thus, even if permission is required or obtained from governmental authorities to undertake research with an Indigenous community, it is not ethical to do such research without seeking informed choice from that community itself. Under certain circumstances, for example in repressive regimes, seeking permission from authorities may insult or injure a collectivity.

From whom should a researcher seek informed consent on behalf of a collectivity? Certainly, where a collectivity has a leadership that is considered legitimate by its members and has the authority to consent on their behalf, consent from that leadership will likely suffice. There are some situations where the collectivity has no acknowledged leaders and other situations where the leadership is not vested by members with any delegated authority to decide for the group as a whole. In these situations, it is likely that the informed choice of individual members, especially when they are aware that others in the collectivity are also being approached, may well constitute the equivalence of informed consent from the collectivity as a whole.

However, in certain circumstances, addressing this question may be very difficult. [For example, there are many collectivities where the leadership, or its authority, is in such dispute that it is reasonable to conclude that there is no "legitimate" leadership.] There are other circumstances where leadership's acknowledged legitimate by only one segment in a collectivity as such by another. There are also situations where obtaining informed choice from one segment may result in reprisals within the collectivity.

In sum, the process of seeking informed choice from a collectivity may sometimes be difficult for every time a collectivity is implicated in a research project the possibility exists of a tension between individuals and the group or between sub-groups and collectivities.

As noted in Section I on naturalistic observation and in Section III on privacy, the researcher and the collectivity may have rival views of what is public or private and on the appropriate handling of information. Similarly, Article 7.2(c) deals with potential disputes about the relative importance of harms to the group as compared to harms to individuals within the group. This is especially important because the notion of a threshold for normally acceptable risk occupies a central part in determining what is or is not in accord with this Code (see Part 1).

Article 7.3

(a) Researchers must satisfy the REB that there will be a process of respectful negotiation where there is conflict with Article 7.2; and

(b) Should such negotiation prove unsuccessful or should researchers believe that such a process of negotiation is inappropriate, then researchers must demonstrate that:

(i) their research objectives cannot be reached if respectful negotiation takes place,

(ii) the research will produce more good than harm, and

(iii) the direct benefits and harms of the research will be fairly distributed among affected participants.

Article 7.3(a) expresses a strong preference for respectful resolution of differences between researchers and participants. Respect is an ethical principle that should lead to dialogue and a sincere will to negotiate. While this applies to all research participants, be they individuals or groups, it is applied in this case to groups as participants. As noted in Part 1, respect does not require the researcher to admire, endorse or tolerate the values of research participants. Rather, respect forbids over-riding the convictions of competent research participants.

Article 7.3(b) recognizes that there will be occasions in which respectful negotiation does not resolve differences satisfactorily or in which a process of negotiation would be ethically inappropriate (e.g., asking members of a violent criminal organization for permission to conduct interviews with defectors). In such circumstances, the REB may permit the research to go forward under Article 7.3(b). It should be noted that these conditions are applied elsewhere in this Code to research which may ethically problematic in other respects (Sections VI, VIII, IX, and X).

For all the Articles in this Section, but particularly Articles 7.2 and 7.3, it is essential that REBs be knowledgeable about the collectivities involved in the research. This can be achieved in a variety of ways, for example, by having academic or community members of the REB drawn from representative groups, using *ad hoc* community reviewers or by consulting with an advisory committee drawn from relevant communities - see Article 3.6(c).

G. GOOD PRACTICES

In addition to articles in this section, there are a number of ethical considerations in undertaking research with collectivities which are labeled "good practices." In general, these practices derive from guidelines for research in Indigenous communities and have been developed either by the communities themselves or in conjunction with researchers.[1] How well these guidelines apply to other situations must be judged on a case-by-case basis. However, experience indicates that researchers should consider these practices whenever undertaking research that implicates these collectivities.[2]

It is good ethical practice to conceptualize and realize research with collectivities as a partnership between the researcher and the collectivity. It is important that the researcher seek to work in partnership with those members of the collectivity who have expertise in the topic being researched. For example, it is a good practice to involve the collectivity in the design of the project. As researchers tend to define their problem orientation from the perspective of their discipline, it is often the case that the issue to be researched within a collectivity is external to the needs of that collectivity. Rather than advancing a research agenda that is imposed on the community, it is often helpful for researchers to examine the possibility that their research could be shaped in a manner that addresses matters relevant to the collectivity.

It is also good practice to provide the collectivity with information respecting the following questions:

- Will the collectivity's cultural estate and other property be protected?
- Will a preliminary report be made available for comment by the collectivity?
- Are researchers prepared to provide employment to members of the collectivity, where appropriate, without prejudice?
- Will researchers co-operate with institutions of the collectivity (such as a college)?
- Are researchers willing to deposit data as well as working papers and related materials in a repository of the collectivity (or one designated by the collectivity)?

Researchers should conduct their research in a manner that ensures that the various (and potentially conflicting) viewpoints held by the collectivity regarding the topics being researched are acknowledged in publications. Good practice generally necessitates that researchers make their 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.

It is often good practice, especially in the case of groups that are vulnerable, to provide the collectivity with an opportunity to react and respond to the findings before the completion of the final report, in the final report or even in all relevant publications that arise from the research (See Section I on information disclosure).

There are many situations where collectivities may wish to react to the findings, especially when shortcomings are perceived. It is usually inappropriate for the collectivity to seek (or to be

---

[1] See for example: American Anthropological Association (1991) "Statement on Ethics"
American Indian Law Center, Inc. (1994) "Model Tribal Research Code" (second edition)
Board of the Swiss Academy of Humanities and Social Sciences and of the Swiss-Liechtenstein Foundation for Archaeological Research Abroad (1994) "Principles for Partnership in Cross-Cultural Human Sciences Research with a Particular View to Archaeology". Canadian Archaeological Association/l'Association d'Archéologie Canadienne. (1996) "Statement of Principles for Ethical Conduct Pertaining to Aboriginal Peoples".

[2] Royal Commission on Aboriginal Peoples, Ethical Guidelines for Research. n.d.

given) a veto on the reporting findings. At the same time, it is inappropriate for researchers to dismiss matters of disagreement with the collectivity without giving them due consideration. It is hoped that there will be room for compromise. In cases where any disagreement persists, it is a minimal requirement that researchers provide the collectivity with an opportunity to make its views known. Failing agreement, researchers should accurately report any disagreement on interpretation of the data in the final report.

SECTION VIII

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 gene functions, and the characterization of normal and disease conditions in individuals, **biological relatives**, **families,** and groups. Allelic variation (that is, different forms of the gene) may be important among biological relatives and within and among different groups. For example, the characterization of mutations within the circular mitochondrial genome has been used to clarify migration patterns of early human populations.

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 this field of research is both exciting and rapidly changing, recently acquired knowledge regarding genes and their mutations is not yet matched with a full understanding of the implications for human beings.

In single gene disorders, for example, a mutation altering a biochemical pathway is directly related to disease. Yet even with such **Mendelian** inheritance, the presence of other genes or environmental factors will modulate expression. In disorders that are the consequence of multiple genes and environmental factors (i.e. multi-factorial 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 that other genetic and non-genetic factors may be necessary before disease develops (e.g., an inherited predisposition to breast cancer). Such factors mean that identifying a particular allele (e.g., by predictive testing) in individuals, biological relatives or a population may not mean 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 privacy and confidentiality issues may affect both the individual 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., and therefore, results, if revealed and publicized, may stigmatize the other individuals in that group.

Though not a new field, the development of new technologies to analyze genetic material is progressing 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 must be exercised. In addition, these rapid changes and the potential financial gain from marketing the technologies drive the need to be sensitive to ethical issues, especially as they apply to research.

The potential ability to identify all human genes and their mutations has profound social implications. The misunderstanding or the 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 in this Code and will require future deliberations by the research community and the public.

A. THE INDIVIDUAL, BIOLOGICAL RELATIVES, AND FAMILIES

Article 8.1

The genetics researcher must seek informed choice from the individual and report results to that individual. As genetic research involves the family and/or the community in terms of family history, linkage, and other studies, a potential tension exists between the individual, their families, and the group. Therefore, informed choice must 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 VII). 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 concede their position. 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 must ensure that the results of genetic testing and genetic counselling records are protected from access by third parties unless consent is given by the participant. Family information in databanks must be coded by number without the possibility of identification of participants within the bank itself.

Because the potential for gathering genetic knowledge of 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 testing on a parent or a child. As well, the knowledge by a third party (e.g., an employer or insurer) of a specific risk or diagnosis may lead to discrimination which could place the individual's job, career advancement, or insurability in jeopardy.

Unless special precautions are taken, databases containing genetic information may identify multiple biological relatives. Similarly, publications 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). This is important not only because an altered pedigree can target others, but also because such alteration may impair replication in future research or lead to flawed conclusions by other researchers, both of which are anathema to responsible science.

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 genotype/phenotype correlative studies, or to answer basic questions regarding human development. In the absence of guidelines, confidentiality may be compromised by DNA banking.

Accordingly, the researcher should be aware of these potential risks to privacy, 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 participants will be made aware of risks to their privacy.

Article 8.3

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

With the exception of gene therapy, physical risks in genetic research may not differ from 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 participant. For example, receiving information regarding genetic disease susceptibility or even carrier status may provoke anxiety, disrupt relationships or impacts negatively on an individual's life opportunities. Also, the individual's position within the family may be challenged by the decision of whether or not to participate. These problems are presently made more difficult in cases involving single gene disorders where confirmation of high risk or carrier status cannot be followed by any 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.

Children may be at particular risk for stigmatization both within and beyond the family because of knowledge gained through genetic studies. Therefore, generally speaking, children should not be tested unless harms are minimal, an intervention is available or useful information will be obtained. It may be appropriate, for example, to offer testing for an early onset condition such as polyposis coli to children in a family, but inappropriate to test for an adult onset condition for which no effective prevention exists.

C. GENETIC COUNSELLING

Article 8.4

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

Genetic counsellors are formally trained to impart genetic information and have two main roles 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 require that 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 makes an informed choice and after results are available. For example, in the Huntington Disease predictive testing endeavour, the use of pre- and post-test counselling was seen as 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 participants and the REB when results will be made available, and how counselling will be handled. As well, participants may need follow-up and the question will remain as to when follow-up should occur and where the researcher's obligation ends in this regard. 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, genetic developments and effective interventions occur at an unpredictable pace. It is, therefore, sometimes only practical to explain to research participants that they will need to contact their physician to keep informed (that is, that researchers are not able to maintain contact long after the research is completed).

In newer applications of predictive testing (e.g., inherited breast cancer), pre- and post-test counselling form an integral part of the testing project. Therefore, the researcher must recognize that educating the participants 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 in predictive testing projects should also be given to combining clinical (that is, counselling) expertise with that of the research geneticist.

At present, the geneticist or genetic counsellor 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 not be able to predict future consequences. The prudent researcher cannot assume she or he can anticipate all harms inherent in a particular project. One of the aims of the research project should be to assess the impact on human beings.

Families may define themselves in different ways in terms of biological, social, and cultural relationships. In addition, 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 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

Research on gene alteration must be limited to somatic cells and tissues. Neither research on germline gene alteration nor non-therapeutic use of gene alteration in humans is permitted.

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 (whereby the gene is introduced into the host genome) or plasmids (where integration does not occur, e.g., a method used with DNA vaccines). Alteration of human genes can be used to treat disease in an individual, alter germ cells to prevent the disease or alter for cosmetic "improvement." Gene alteration remains experimental and is not "therapy" in the accepted sense of the word and the use of animal models continues to be crucial in this area of incomplete knowledge. At present, the most common use of gene alteration is to treat serious single gene disorders (e.g., adenosine-deaminase deficiency, a subtype of an immune disorder, or life-threatening malignancies).

The timing of the gene alteration may be prenatal or postnatal. The use of germline alteration in the embryo or zygote implies alteration of cells not yet committed to specific organs, and therefore alters future reproductive cells. Accordingly, resulting changes could be transmitted to future generations. Two Canadian documents, the Medical Research Council Guidelines on Somatic Cell Gene Therapy in Humans (1990) and the Report of the Royal Commission on New Reproductive Technologies (1993), report that such germline therapy has serious ethical concerns and is not to be funded.

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 and 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 forever altered. Therefore, the circumstance exists (e.g., as a result of immune suppression in organ transplantation) where it becomes irrelevant if the research participant withdraws from the experiment. In addition, the need for lifetime follow-up is crucial to establish harms, benefits, and unrecognized concerns. While the autonomy of participants must be respected, the special circumstances of gene alteration must be clarified to potential participants and their families in advance of participation.

The following issues, articulated in the Medical Research Council's Guidelines on Somatic Cell Gene Therapy in Humans (1990), must 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 participant is less able to make an informed choice 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 participant from the research project makes early recognition of harms less likely and denies knowledge of such harms to future participants and researchers involved in gene alteration;
- in utero uses of somatic cell gene alteration may not involve the embryo or zygote 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; and
- in the case of rare genetic diseases, the survival and subsequent reproduction of treated participants 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 ameliorate 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 must 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 must also be maintained. The freedom of at risk couples to plan and carry potentially affected pregnancies, and the support of children and adults with handicapping conditions, must not be compromised.

It is difficult to offer pregnancy intervention as an option without implying that the genetic condition should result in termination. Researchers, genetic counsellers, and REBs should be aware that other groups carrying the same handicapping condition may view such judgement as disrespectful (see Article 8.4).

F. BANKING OF GENETIC MATERIAL

Article 8.7

Because the banking of genetic material poses potential harms to individuals, their families, and the collectivities to which they may belong, researchers must satisfy the REB and prospective research participants that they have addressed the issues involved in banking of genetic data including confidentiality, privacy, storage, use of the data, and results to come, withdrawal by the participant, and future contact of participants, families, and collectivities.

At present, no international consensus exists regarding the long-term banking of genetic material for the purposes of genetic research. A special concern (beyond those discussed in Sections VII and X) arises when it is difficult to separate genetic information on an individual from his or her biological relatives or community.

Although consensus has not been reached, a number of issues need to be considered by the researcher and clarified for the REB; in particular, issues around confidentiality, privacy of records, and information derived from stored genetic material. 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 participant. Similarly, unauthorized access to stored genetic material or results by third parties (e.g., insurance companies) must be prevented. Specifying whether banked genetic material will be non-nominative, that is, without identifiers, helps alleviate the concerns that other biological relatives may inadvertently be identified by linked data.

Storage of genetic material or research data 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, it should be explained 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 participant to choose from a number of options (e.g., the use of the material only in the present study, the use restricted to the condition, or the use in any genetic study) to a more limited consent form which specifies arrangements to maintain contact with the participant regarding future uses. Either method must be clearly explained during the informed choice process.

As stated previously, the biological aspects of genetic variability or disease 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 participant 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 participant wishes to receive results, gives the participant the right to make an informed choice.

The right to withdraw from a research study is a necessary component of the informed choice 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 participant.

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 considers all of the factors referred to herein in the description of the study and in the informed choice process. In projects involving already-stored genetic material, an REB should consider the importance of the factors on a project by project basis. Until consensus has been reached in the area of genetic banking, full disclosure to the research participant of the factors referred to herein would seem to be the prudent course, wherever possible.

G. COMMERCIAL USE OF GENETIC DATA

Article 8.8

At the outset of a research project, the researcher must discuss with the REB and the research participant the possibility that the genetic material and the information derived from its use could have potential commercial uses.

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. It is wrong for a researcher to claim ownership of genetic material by claiming that the concept of private ownership did not exist in the culture in issue. The researcher must seek further permission from the collectivity, if he or she plans another purpose for genetic material gathered during the course of research. Any plan to commercialize genetic material must be openly discussed with the family at the beginning of the project. Similarly, commercialization occurring after involvement in a research trial should be reviewed with the family, group, or collectivity, if possible.

SECTION IX

REPRODUCTION, INFERTILITY, EMBRYOS, AND FOETUSES

Research on reproductive technologies can cause deep divisions in society that are not likely to be resolved soon, especially since both biological knowledge and the responses of society to that knowledge continue to evolve. The Report of the Royal Commission on New Reproductive Technologies[1] represented the most authoritative and complete analysis of Canadian viewpoints in this broad area to its time and also reflects the divisions in public opinion.

Though informed by previously available extensive public and scholarly discussions of human reproduction, the position taken in this Code is basically a pragmatic one, recognizing the following issues that require attention:

- the present status of the law and of health care in Canada on interventions in human reproduction, though still controversial, is broadly consistent with an approach that correlates with permitted actions developmental stages; and
- it is preferable to develop a careful, moderate, and controlled approach to human reproductive research, rather than to introduce new practices under the relatively uncontrolled guise of diagnosis and therapy.

Legislation may in time address issues such as ectogenesis (use of an artificial womb), cloning, the age up to which zygotes or embryos can be used in research, issues of consent for the use of reproductive cells or tissues, and payment for reproductive cells and tissues. Researchers and REBs need to be aware of current legislation as they proceed in this area of research.

The considerations set out below are in addition to those described elsewhere in this Code. In applying the conditions for research in general to research on conception and the development of embryos and foetuses, particular regard must be paid to the following:

- it is not acceptable to study human reproductive tissues or cells that are intended to result in an ongoing pregnancy if the knowledge sought could be obtained by the use of other systems or models; and
- notwithstanding the many and complex concerns regarding research involving the human reproductive system, if all research in this area is precluded, there is a danger of inadequate care or a lack of knowledge in the future. (Many and complex concerns include possible physical harms to the embryo or foetus, the question of who can consent for the foetus, foetal interests versus maternal rights, and an overall concern of respect for the embryo or foetus.)

[1] Report of the Royal Commission on New Reproductive Technologies: Proceed with Caution. Ottawa, 1993.

A. RESEARCH INVOLVING GAMETES (OVA AND SPERM)

Article 9.1

The researcher must obtain informed consent from the individual from whom human reproductive cells were obtained for the research use of those cells and tissues.

Human reproductive cells (ova or sperm) are often obtained from a research participant as part of standard care or may be requested solely for research. Sperm is most commonly obtained as an ejaculated specimen, while ova can only be obtained by a surgical procedure (the exception would be washing the ova from the uterus). Informed choice and informed consent to obtain these cells must be sought from the individual providing them and must include the purpose of the proposed research (e.g., research involving infertility versus prevention of pregnancy). Researchers must pay close attention to the social sensitivity of their research.

Ova or sperm may be obtained from a cadaver for research purposes only if that individual had given prior informed consent. It is unacceptable to obtain ova from foetuses or from women unable to consent for themselves.

Article 9.2

No research will be carried out on ova or sperm that have been obtained through commercial transactions.

Only compensation for reasonable expenses actually incurred in donating the sperm or ova may be offered.

Article 9.3

Research must not be carried out with the intent of creating hybrid species which could survive by such means as mixing human gametes with cells or tissues of other species, or *vice versa*.

Human sperm and ova have the potential to create new life when fertilization occurs. The creation of hybrid species with intended survival, violates our basic norm of respect for human life.

However, research involving, for example, hamster cell/human sperm hybrids is acceptable for the purposes of evaluating aspects of human sperm function because such hybrids do not survive beyond the experiment.

B. RESEARCH INVOLVING HUMAN ZYGOTES OR EMBRYOS

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

Article 9.4

Human zygotes and embryos must not be specifically created for research purposes; however, research that involves human zygotes and embryos will be ethically acceptable if:

(a) the ova and sperm from which they were formed are obtained in accordance with articles 9.1, 9.2 and 9.3;

(b) the research does not involve the genetic alteration of human zygotes/embryos; and

(c) zygotes or embryos exposed to any manipulations not directed specifically to the ongoing normal development will not be transferred for continuing pregnancy.

Research potentially altering the zygote or embryo by chemical or physical manipulation must 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 on-going pregnancy.

On the other hand, pre-implantation diagnosis of a serious genetic disorder may involve testing of one cell of the early zygote, but not manipulation of the zygote itself ultimately destined for implantation (see Section VIII).

Article 9.5

In keeping with international consensus, the researcher must restrict research on human zygotes and embryos to the first 14 days of development.

The human zygote and embryo begins implantation at approximately six to seven days of development, and beyond the time of implantation (regarded as 14 days), cannot independently develop further; the embryo proper starts to develop at that time. Specifically, the embryo develops the primitive streak, or the first indication of neural development. The broad consensus restricting research on zygotes and embryos to the first 14 days of development is based on these stages of biological development. At present, commonly accepted contraceptive methods preventing implantation (not fertilization) may suggest a tolerance to research prior to implantation.

Article 9.6

Ectogenesis, cloning of human beings, formation of animal/human hybrids, or the transfer of zygotes/embryos between humans and other species are all unacceptable.

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 must be regarded as an intervention on the other. Research on methods of treatment of foetuses in utero poses no unique issues that are not addressed elsewhere in this Code. The decision of the woman is necessary and sufficient, and it is at the discretion of the woman whether the biological father is involved in the decision-making process.

D. RESEARCH INVOLVING FOETAL TISSUE

It is not acceptable to undertake research interventions that compromise the woman's decision on whether or not to continue her pregnancy. All research involving the use of foetal tissues must be guided by respect for the woman's integrity. To separate the decision to undergo an abortion from the decision to permit the use of the foetal tissue gives rise to a potential ethical dilemma: protecting the right of the woman to determine the outcome of her pregnancy versus the perceived potential to increase the number of abortions. The Royal Commission on Reproductive Technology concluded that prohibiting research in this area, with the possibility of alleviating suffering, would be uncaring.[1] As well, while women may consent to the use of their foetal tissue, they may not direct the use to particular individuals (e.g., a woman may not choose to have foetal tissue used for Parkinson disease research in a relative). This prohibition is based on concerns that the foetus not be used only as a source of tissue, but must also be recognized as a potential human.

[1] [1] Report of the Royal Commission on New Reproductive Technologies: Proceed with Caution. Ottawa, 1993.

SECTION X

HUMAN TISSUE

The use of **human tissue** for the purpose of research has proven to be of immense importance to the advancement of knowledge; it also, however, raises a fundamental question about the relationship that individuals have with their bodies. This question of self-identification is obviously personal but it also takes on cultural and religious dimensions. Thus, the ethical question is how can researchers respect an individual's sense of physical, spiritual, and cultural integrity when seeking to use their tissue.

The status that different people and peoples accord the human body and its parts is varied. For example, some people take little interest in tissue removed from their bodies; but in some cultures certain parts of the body (hair, placenta, blood) are regarded as sacred and, because of their significance and symbolic value, cannot be given away. 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 groups will regard as an invasive means to acquire tissue, others will not. Ordinarily, techniques for removing tissue such as biopsies or surgery are regarded as invasive. Drug administration or unusual dietary management associated with the acquisition of tissue or bodily waste products may also be regarded as invasive. The purpose of the research also plays a role in determining the invasiveness of the procedure. For example, in some cultures, the measurement of caffeine in hair might be considered non-invasive, but the measurement of cocaine in the same samples could be regarded as invasive. In other cultures, taking hair samples might be regarded as extremely invasive and a violation of physical integrity, regardless of what is being done with the samples.

In Canadian society, it is generally held that human tissue deserves some form of respect; for example, though their sale is prohibited, it is generally held that organs can be donated. Therefore, it is reasonable to draw the ethical conclusion that the use of tissue for research depends on an individual's altruistic gift — altruistic in the sense that the individual is 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 can reveal information about that person's current or future health as well as that of biological relatives (see Section VIII).

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**: identifiable tissue can be immediately linked to a specific individual (e.g., by way of an identifying tag or patient number).
- **traceable tissue**: 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**: 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**: anonymized tissue was originally identified but has been permanently stripped of identifiers.

To a considerable extent, genetic testing has greatly narrowed the concept of anonymous tissue (see Section VIII). Even more narrowed is the concept of traceable tissue, since it is now possible to identify biological relatives by using genetic markers.

A researcher may request REB approval for use of anonymous or anonymized 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 an informed choice in the new research project.

A researcher and the REB must 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 difficult 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, it is essential that the principles developed in Section I regarding harm and third party authorization be observed. For example, the post-mortem acquisition of brain tissue from a person suffering from dementia who had not consented in advance when competent would require third party authorization. Special care to avoid coercion or its appearance should also be shown when the participants are drawn from restricted or dependent groups, that is, those in the care, or under the authority, power or control, of others.

B. INFORMED CHOICE AND INFORMED CONSENT

It is essential to pay attention to the issues related to informed choice developed in Section I. Choice is expected to be adequately informed but individuals are free to forgo specific information and offer their tissue for research, the nature of which they may only understand in a general sense. Nonetheless, the participant must be informed of any reasonably anticipated harms (e.g., the possibility of future identification). Advance directives, for example, may include donations of tissue for non-specified research uses. In some provinces, however, the law may require that an individual make an informed choice with regard to specific uses of tissue in research.

Article 10.1

The informed choice of a living donor, or authorized third party in the case of incompetent individuals or, when the donor is deceased, a prior directive or third party authorization, must be sought and consent must be secured in order to acquire and use human tissue for research purposes.

This Article applies where tissue is to be recovered for research purposes, regardless of whether or not the tissue is also acquired for therapeutic purposes.

Many individuals will routinely give consent to the use of tissue, provided such tissue is obtained in non-harmful or non-invasive ways or in ways that are incidental to therapeutic procedures. Individuals who do not wish to contribute tissue to particular research projects for religious, cultural, or other reasons should be free to withhold consent without fear of penalty.

Article 10.2

In collecting tissue for research, the researcher must provide donors with information about the:

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

(b) potential uses for the tissue including any commercial uses;

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

(d) identifying information attached to specific tissue, and its potential traceability.

The researcher must propose to the REB appropriate measures to protect privacy and confidentiality when acquiring tissue from those who are unable to make an informed choice.

By providing individuals with information set out in Article 10.2 about the uses of their tissue, potential participants are then in a position to decide if their concerns about privacy and confidentiality are met.

The researcher must propose to the REB a method to ensure appropriate protection of donors' identities. It is important for researchers to understand that tissue gathered for one purpose (e.g., medical) may have serious implications from other perspectives (e.g., legal). Hair gathered to assess exposure to radiation may also reveal the use of illegal substances. It is also important to pay special attention to cultural or religious concerns regarding certain tissue or human products, such as embryos and fetuses (see Section IX), and concerns that some individuals may have about certain types or applications of research.

C. PREVIOUSLY COLLECTED TISSUE

Article 10.3

When identification is possible, researchers must seek permission from individuals, authorized third parties or, when appropriate, the collectivities in question for the use of their previously collected tissue. The provisions of article 10.2 also apply here.

Further, when the individuals who, after making an informed choice, provided previously collected tissue for research 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 legislation so requires.

Article 10.3 applies not only to research in the health sciences but also to anthropological, and genetic research (e.g., the Human Genome Project). Not only is individual identification a matter of sensitivity, but so is the identification of tissue belonging to families and to members of collectivities. Section VII details the ways in which permission should be sought from appropriate leaders of the collectivities.

When previously collected tissue is traceable only with extraordinary effort, the researcher and the REB must make a realistic assessment of the likelihood of such effort being undertaken in order to determine whether the risk of harm is negligible. If it appears probable that researchers will be able to identify or trace individuals or collectivities that provided the tissue, then the researcher should seek permission from the individuals or collectivities in question. Ideally, permission should be secured at the time the tissue is acquired and again if it is reasonably possible at the beginning of any subsequent research.

Even though it may not be possible to identify the individuals who provided the tissue, there still may be issues which must be addressed. For example, individuals may not want their tissue used for research purposes. The interests of biological relatives or members of collectivities, for instance, may be adversely affected though research uses of their anonymous tissue. Researchers must address issues of such harm to the satisfaction of the REB.