

TCPS2 2014

TRI-COUNCIL POLICY STATEMENT

Ethical Conduct for Research Involving Humans

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Canadian Institutes of Health Research
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the expansion of knowledge. Given the fundamental importance of research and of human participation in research, we must do all that we can as a society to ensure that research is conducted in an ethical manner so as to build public confidence and trust. By promoting and guiding the ethical conduct of research involving humans, this Policy seeks to contribute tangibly to these goals.

No single document can provide definitive answers to all ethical issues that may arise in an undertaking as complex as research involving humans. This Policy aims to assist those who use it – researchers, sponsors, members of research ethics boards (REBs), participants, and the public – to identify ethical issues in the design, conduct and oversight of research and to point the way to arriving at reasoned and ethical responses to these issues.

B. Core Principles

Respect for human dignity has been an underlying value of the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS or the Policy) since its inception. Despite clear recognition of its centrality in research ethics, the term lends itself to a variety of definitions and interpretations that make it challenging to apply.

Respect for human dignity requires that research involving humans be conducted in a manner that is sensitive to the inherent worth of all human beings and the respect and consideration that they are due. In this Policy, respect for human dignity is expressed through three core principles – Respect for Persons, Concern for Welfare, and Justice. These core principles transcend disciplinary boundaries and, therefore, are relevant to the full range of research covered by this Policy.¹

Article 1.1 The guidelines in this Policy are based on the following three core principles:

- Respect for Persons
- Concern for Welfare
- Justice

These principles are complementary and interdependent. How they apply and the weight accorded to each will depend on the nature and context of the research being undertaken. Specific applications are addressed in the following chapters.

Respect for Persons

Respect for Persons recognizes the intrinsic value of human beings and the respect and consideration that they are due. It encompasses the treatment of persons involved in research directly as participants and those who are participants because their data or human biological materials, which for the purposes of this Policy include materials related to human reproduction, are used in research. Respect for Persons incorporates the dual moral obligations to respect autonomy and to protect those with developing, impaired or diminished autonomy.

Autonomy includes the ability to deliberate about a decision and to act based on that deliberation. Respecting autonomy means giving due deference to a person's judgment and ensuring that the person is free to choose without interference. Autonomy is not exercised in isolation but is influenced by a person's various connections to family, to community, and to cultural, social, linguistic, religious and other groups. Likewise, a person's decisions can have an impact on any of these connections.

An important mechanism for respecting participants' autonomy in research is the requirement to seek their free, informed and ongoing consent. This requirement reflects the commitment that participation in research, including participation through the use of one's data or biological materials, should be a matter of choice and that, to be meaningful, the choice must be informed. An informed choice is one that is based on as complete an understanding as is reasonably possible of the purpose of the research, what it entails, and its foreseeable risks and potential benefits, both to the participant and to others. Respect for Persons also includes a commitment to accountability and transparency in the ethical conduct of research.

Certain factors may diminish a person's ability to exercise their autonomy, such as inadequate information or understanding for deliberation, or a lack of freedom to act due to controlling influences or coercion. Such constraints may include the fear of alienating those in positions of authority, such as professional or personal caregivers, researchers, leaders, larger groups, or a community to which one belongs. Other constraints may consist of barriers to accessing resources or knowledge outside the research context. These factors and constraints should be addressed prior to any research being carried out, so as to ensure participants are sufficiently protected.

Some people may be incapable of exercising autonomy because of youth, cognitive impairment, other mental health issues or illness. While autonomy may be considered a necessary condition for participation in research, involving those who lack capacity to make their own decisions to participate can be valuable, just and even necessary. For those prospective participants, additional measures are needed to protect their interests and to ensure that their wishes (to the extent that these are known) are respected. These measures will generally include seeking consent from an authorized third party who is entrusted to make decisions on behalf of the prospective participant, based on knowledge of that person and that person's wishes or, if such wishes are unknown, on consideration of that person's welfare. Even when the requirements of free, informed and ongoing consent cannot be met, Respect for Persons requires involving individuals in circumstances of vulnerability in decision making where possible. This may include asking about their feelings regarding participation and/or for their assent.

Where it is foreseeable that a participant may lose decision-making capacity during a research project, for example in studies of cognitive impairment, it may be appropriate to ask participants to express their preferences and ensure that they have authorized a trusted person to make decisions on their behalf should they lose the capacity to decide whether or not to continue their research participation (see Article 3.11 for guidance on research directives for individuals who lack decision-making capacity).

Concern for Welfare

The welfare of a person is the quality of that person's experience of life in all its aspects. Welfare consists of the impact on individuals of factors such as their physical, mental and spiritual health, as well as their physical, economic and social circumstances. Thus, determinants of welfare can include housing, employment, security, family life, community membership, and social participation, among other aspects of life. Other contributing factors to welfare are privacy and the control of information about the person, and the treatment of human biological materials according to the free, informed and ongoing consent of the person who was the source of the

information or materials. A person's or group's welfare is also affected by the welfare of those who are important to them. Harm includes any negative effects on welfare, broadly construed (for the relationship between risk and harm, see Chapter 2, Section B). Note that, for the purposes of this Policy, "group" and "community" are used in their ordinary sense. More detailed types of community as defined in Chapter 9 are specific to Aboriginal contexts.

Concern for Welfare means that researchers and REBs should aim to protect the welfare of participants, and, in some circumstances, to promote that welfare in view of any foreseeable risks associated with the research. They are to provide participants with enough information to be able to adequately assess risks and potential benefits associated with their participation in the research. To do so, researchers and REBs must ensure that participants are not exposed to unnecessary risks. Researchers and REBs must attempt to minimize the risks associated with answering any given research question. They should attempt to achieve the most favourable balance of risks and potential benefits in a research proposal. Then, in keeping with the principle of Respect for Persons, participants or authorized third parties, make the final judgment about the acceptability of this balance to them.

The welfare of groups can also be affected by research. Groups may benefit from the knowledge gained from the research, but they may also suffer from stigmatization, discrimination or damage to reputation. Engagement during the design process with groups whose welfare may be affected by the research can help to clarify the potential impact of the research and indicate where any negative impact on welfare can be minimized. Researchers must also consider the risks and potential benefits of their research and the knowledge it might generate for the welfare of society as a whole. Where research on individuals may affect the welfare of a group(s), the weight given to the group's welfare will depend on the nature of the research being undertaken, and the individuals or group in question. This consideration does not imply, however, that the welfare of a group should be given priority over the welfare of individuals.

Justice

Justice refers to the obligation to treat people fairly and equitably. Fairness entails treating all people with equal respect and concern. Equity requires distributing the benefits and burdens of research participation in such a way that no segment of the population is unduly burdened by the harms of research or denied the benefits of the knowledge generated from it.

Treating people fairly and equitably does not always mean treating people in the same way. Differences in treatment or distribution are justified when failures to take differences into account may result in the creation or reinforcement of inequities. One important difference that must be considered for fairness and equity is vulnerability. Vulnerability is often caused by limited decision-making capacity, or limited access to social goods, such as rights, opportunities and power. Individuals or groups in vulnerable circumstances have historically included children, the elderly, women, prisoners, those with mental health issues and those with diminished capacity for self-determination. Ethnocultural minorities and those who are institutionalized are other examples of groups who have, at times, been treated unfairly and inequitably in research, or have been excluded from research opportunities. People or groups whose circumstances cause them to be vulnerable or marginalized may need to be afforded special attention in order to be treated justly in research.

The recruitment process, both of participants who may become directly involved in research and those who participate as the source of information or biological materials to be used in research, is an important component of the fair and equitable conduct of research. Participation should be based on inclusion criteria that are justified by the research question. Inequity is created when particular groups fail to receive fair benefits of research or when groups, or their data or their biological materials, are excluded from research arbitrarily or for reasons unrelated to the research question.

An important threat to Justice is the imbalance of power that may exist in the relationship between researcher and participant. Participants will generally not understand the research in the same way and in the same depth as does the researcher. Historically, there have been instances in which this power imbalance has been abused, with resulting harm to participants.

The Core Principles – Conclusion

The importance of research and the need to ensure the ethical conduct of research requires both researchers and REB members to navigate a sometimes difficult course between the two main goals of providing the necessary protection of participants and serving the legitimate requirements of research. The three core principles that express the value of human dignity provide the compass for that journey. Their application will help ensure that a balance between these two goals is maintained. Applying the core principles will also maintain free, informed and ongoing consent throughout the research process and lead to sharing the benefits of the research. These results will help to build and maintain the trust of participants and the public in the research process.

C. How to Apply This Policy

Proportionate Approach to REB Review

This Policy aims to strike an appropriate balance between recognition of the potential benefits of research, and protection of participants from research-related harms, including injustices and breaches of Respect for Persons. Given that research involving humans spans the full spectrum of risk, from minimal to significant, a crucial element of REB review is to ensure that the level of scrutiny of a research project is determined by the level of risk it poses to participants (see Article 6.12). A reduced level of scrutiny applied to a research project assessed as minimal risk does not imply a lower level of adherence to the core principles. Rather, the intention is to ensure adequate protection of participants is maintained while reducing unnecessary impediments to, and facilitating the progress of, ethical research. This approach is in keeping with the need to respect academic freedom and not to place unwarranted constraints upon it.

In the context of both initial and continuing research ethics review, the REB assesses the ethical acceptability of a research project through consideration of the foreseeable risks, the potential benefits and the ethical implications of the project (see Article 2.9). These two steps constitute the proportionate approach to REB review that is recommended throughout the Policy.

Research Ethics and Law

In addition to the principles and guidelines in this Policy, researchers are responsible for ascertaining and complying with all applicable legal and regulatory requirements with respect to consent and the protection of privacy of participants (see Chapter 5). These legal and regulatory requirements may vary depending on the jurisdiction in Canada in which the research is being conducted, and who is funding and/or conducting the research, and they may comprise constitutional, statutory, regulatory, common law, and/or international or legal requirements of jurisdictions outside of Canada. Where the research is considered to be a governmental activity, for example, standards for protecting privacy flowing from the *Canadian Charter of Rights and Freedoms*, federal privacy legislation and regulatory requirements would apply.

The law affects and regulates the standards and conduct of research involving humans in a variety of areas, including, but not limited to privacy, confidentiality, intellectual property and the decision-making capacity of participants. In addition, human rights legislation and most documents on research ethics prohibit discrimination on a variety of grounds and recognize equal treatment as fundamental. REBs and researchers should also respect the spirit of the *Canadian Charter of Rights and Freedoms*, particularly the sections dealing with life, liberty and security of the person, as well as those involving equality and discrimination.

Researchers may face situations where they experience a tension between the requirements of the law and the guidance of the ethical principles in this Policy. In such situations, researchers should strive to comply with the law in the application of ethical principles. Researchers should consult with colleagues, the REB or any relevant professional body, and if necessary, seek independent legal advice to help resolve any conflicts between law and ethics, and guide an appropriate course of action.

This legal context for research involving humans is constantly evolving and varies from jurisdiction to jurisdiction. For this reason, REBs and researchers should be aware of applicable laws so they can identify legal issues that may occur in the conduct of research. REBs may satisfy this obligation through expertise among their members or through wider consultation. The researcher may seek independent legal advice when necessary.

The Perspective of the Participant

In designing and conducting research or reviewing the ethics of research, researchers and REBs must be mindful of the perspective of the participant. It may be necessary to consider the various contexts (e.g., social, economic, cultural) that shape the participant's life, to properly evaluate the implications of the research in terms of the core principles.

Appropriate Expertise for Review

It is also important that research ethics review be appropriate to the disciplines, fields of research, and methods of the research being reviewed. This means that REBs must understand the discipline and method under review and be able to assess the research on its own terms. This Policy provides more direction concerning appropriate expertise in Articles 6.4 and 6.5.

Interpreting This Policy

This Policy contains both guidance for the interpretation of the principles of research ethics, as well as a number of mandatory requirements for researchers, institutions and members of REBs. Mandatory provisions are signalled by the use of the term “shall.” Guidance for the interpretation of the core principles is generally indicated by use of the term “should.”

Evaluating the ethics of research involving humans is not, and cannot be, an exact science. The interpretation and application of the articles and principles to particular circumstances will always be a part of the exercise. The articles in this Policy are intended to provide guidance, and in some cases, to set out certain requirements. The application sections are intended to supplement the articles with further explanation and examples. Although they cannot guarantee identical decisions across REBs, they can ensure that researchers and REBs employing this Policy are operating within the same parameters and taking into account the same considerations as they design and evaluate research involving humans.

At the end of some chapters, a section entitled “References” provides links to documents that contain further guidance on specific topics addressed in the chapter. These references are not meant to be exhaustive, but are offered to assist the reader who wishes to explore certain topics in greater detail.

This Policy will continue to evolve in response to the emerging needs and suggestions of all those whom this Policy is intended to serve, including the research community, participants and the public.

Definitions

The definitions provided in this Policy are intended specifically and solely for the purposes of this Policy.

Endnote

¹ The three core principles incorporate within them the eight guiding ethical principles set out in the 1998 TCPS. Respect for Human Dignity is expressed through the three core principles. Respect for Free and Informed Consent and Respect for Vulnerable Persons are both reflected in the principle of Respect for Persons, while Respect for Vulnerable Persons is also reflected in the principle of Justice. Respect for Privacy and Confidentiality is an element of Concern for Welfare. Respect for Justice and Inclusiveness is covered in the core principle of Justice. Balancing Harms and Benefits, Minimizing Harm and Maximizing Benefit are, in fact, not principles, but are the means by which the principle of Concern for Welfare is put into effect. Each of these elements is addressed in greater detail in a chapter or section of this Policy.

By using these broader and more encompassing core principles, this Policy seeks to provide a more focused framework for the ethical guidance that follows. It is also a framework that harmonizes with other national and international ethics policies.

have further legal obligations that may be determined in part by the nature of the research and the jurisdiction in which the research is being conducted.¹

A. General Principles

Consent Shall Be Given Voluntarily

- Article 3.1**
- (a) Consent shall be given voluntarily.
 - (b) Consent can be withdrawn at any time.
 - (c) If a participant withdraws consent, the participant can also request the withdrawal of their data or human biological materials.

- Application**
- (a) The voluntariness of consent is important because it respects human dignity and means that individuals have chosen to participate in research according to their own values, preferences and wishes.

The approach to recruitment is an important element in assuring voluntariness. In particular, how, when and where participants are approached, and who recruits them are important elements in assuring (or undermining) voluntariness. In considering the voluntariness of consent, REBs and researchers should be cognizant of situations where undue influence, coercion or the offer of incentives may undermine the voluntariness of a participant's consent to participate in research.

Undue Influence

Undue influence and manipulation may arise when prospective participants are recruited by individuals in a position of authority. The influence of power relationships (e.g., employers and employees, teachers and students, commanding officers and members of the military or correctional officers and prisoners) on the voluntariness of consent should be judged from the perspective of prospective participants, since the individuals being recruited may feel constrained to follow the wishes of those who have some form of control over them. This control may be physical, psychological, financial or professional, for example, and may involve offering some form of inducement or threatening some form of deprivation. In such situations, the control exerted in a power relationship may place undue pressure on the prospective participants. At the extreme, there can be no voluntariness if consent is secured by the order of authorities.

REBs and researchers should also pay particular attention to elements of trust and dependency in relationships (e.g., between physician and patient or between professor and student). These relationships can impose undue influence on the individual in the position of dependence to participate in research projects. Any relationship of dependency, even a nurturing one, may give rise to undue

influence even if it is not applied overtly. There may be a greater risk of undue influence in situations of ongoing or significant dependency.

Pre-existing entitlements to care, education and other services should not be prejudiced by the decision of whether or not to participate in, or to withdraw from, a research project. Accordingly, for example, a physician should ensure that continued clinical care is not linked to research participation. Similarly, where students do not wish to participate in research studies for course credits, they should be offered a comparable alternative.

Coercion

Coercion is a more extreme form of undue influence, involving a threat of harm or punishment for failure to participate. Coercion would negate the voluntariness of a decision to participate, or to remain, in a research project.

Incentives

Incentives are anything offered to participants, monetary or otherwise, for participation in research (incentives differ from reimbursements and compensation for injury, which are discussed in Article 3.2[j]). Because incentives are used to encourage participation in a research project, they are an important consideration in assessing voluntariness. Where incentives are offered to participants, they should not be so large or attractive as to encourage reckless disregard of risks. This is a particular consideration in the case of healthy volunteers for the early phases of clinical trials, as discussed in Article 11.1. The offer of incentives in some contexts may be perceived by prospective participants as a way for them to gain favour or improve their situation. This may amount to undue inducement and thus negate the voluntariness of participants' consent.

This Policy neither recommends nor discourages the use of incentives. The onus is on the researcher to justify to the REB the use of a particular model and the level of incentives. In considering the possibility of undue influence in research involving financial or other incentives, researchers and REBs should be sensitive to issues such as the economic circumstances of those in the pool of prospective participants, the age and decision-making capacity of participants, the customs and practices of the community, and the magnitude and probability of harms (see Chapter 4, Section B). Guardians and authorized third parties should not receive incentives for arranging the involvement in research of the individual they represent. However, they may accept reasonable incentives or compensation on behalf of that individual, as long as these are suitable to the circumstances.

- (b) To maintain the element of voluntariness, participants shall be free to withdraw their consent to participate in the research at any time, and need not offer any reason for doing so. In some cases, however, the physical practicalities of the

project may prevent the actual withdrawal of the participant partway through, for example, if the project involves only a single intervention, or if the termination of a medical research procedure may compromise the safety of the participant.

The participant should not suffer any disadvantage or reprisal for withdrawing nor should any payment due prior to the point of withdrawal be withheld. If the research project used a lump-sum incentive for participation, the participant is entitled to the entire amount. If a payment schedule is used, participants shall be paid in proportion to their participation.

- (c) The consent process should set out any circumstances that do not allow withdrawal of data or human biological materials once collected. In some research projects, the withdrawal of data or human biological materials may not be feasible (e.g., when personal information has been anonymized and added to a data pool). Researchers must provide a rationale to the REB for using collection methods that do not permit subsequent withdrawal of data or human biological materials. Where the terms of the research do not allow for withdrawal of their data or human biological materials, the identity of the participants shall be protected at all times during the project and after its completion. Participants shall also be informed that it is difficult, if not impossible, to withdraw results once they have been published or otherwise disseminated.

Consent Shall Be Informed

Article 3.2 Researchers shall provide to prospective participants, or authorized third parties, full disclosure of all information necessary for making an informed decision to participate in a research project.

Application At the commencement of any process of consent, researchers (or their qualified representatives) shall provide prospective participants with the information set out in the following list, as appropriate to the particular research project. Not all the listed elements are required for all research. However, additional information may be required in particular types of research or under particular circumstances.

If a researcher does not include some of the listed disclosure requirements, they should explain to the REB why these requirements do not apply to that particular project. It is also up to the REB to consider whether all elements listed, or additional elements, are necessary to the consent process of the research project.

The information generally required for informed consent includes:

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

Chapter 4

FAIRNESS AND EQUITY IN RESEARCH PARTICIPATION

Introduction

The principle of Justice holds that particular individuals, groups or communities should neither bear an unfair share of the direct burdens of participating in research, nor should they be unfairly excluded from the potential benefits of research participation. Inclusiveness in research and fair distribution of benefits and burdens should be important considerations for researchers, research ethics boards (REBs), research institutions and sponsors. Issues of fair and equitable treatment arise in deciding whether and how to include individuals, groups or communities in research, and the basis for the exclusion of some.

This chapter addresses inclusion in research of individuals and groups that might be inappropriately excluded on the basis of attributes such as culture, language, gender, race, ethnicity, age and disability. It provides guidance relevant to inclusion in research of specific groups such as women, children, the elderly and those who lack the capacity to decide whether or not to participate in research. Historically, these groups have often been inappropriately excluded from research.

This chapter also addresses the fair inclusion and equitable treatment of individuals, groups and communities whose situation or circumstances make them vulnerable in the context of a specific research project. These individuals run the risk of being included in research in ways that may be unfair and inequitable. This chapter provides guidance relevant to the equitable distribution of the risks and benefits of research.

Over-protectionist attitudes or practices of researchers or REBs, whether intentional or inadvertent, can exclude some members of society from participating in research. The exclusion of individuals, groups or communities may constitute a failure to treat them justly. For example, age has been used to exclude individuals from participation in research, particularly health research (e.g., studies that only accept participants between the ages of 18 to 35). As a result, sufficient research may not be done on groups that fall outside of narrow age criteria. The inclusion of the young and the elderly in research, for example, ensures that treatments frequently given to these populations are effective and safe.

Researchers, institutions and REBs all have important roles to play in advancing that societal commitment, and ensuring a fair distribution of the benefits and burdens of research. Researchers and REBs must navigate between the dangers of imposing unfair burdens on particular participants, groups and communities, and overprotecting them. In assessing fairness and equity issues in the research ethics process, REBs should not intervene in the choice of research topics.

A. Appropriate Inclusion

Article 4.1 Taking into account the scope and objectives of their research, researchers should be inclusive in selecting participants. Researchers shall not exclude individuals from the opportunity to participate in research on the basis of attributes such as culture, language, religion, race, disability, sexual orientation, ethnicity, linguistic proficiency, gender or age, unless there is a valid reason for the exclusion.

Application Article 4.1 is based on the principle of Justice. It imposes a duty on researchers not to exclude individuals or groups from participation for reasons that are unrelated to the research. This duty is explicitly stated because groups have been inappropriately excluded from participation in research on the basis of attributes such as gender, race, ethnicity, age and disability.

The focus, objective, nature of research and context in which the research is conducted inform the inclusion and exclusion criteria for a specific research project. Some research may be focused on a certain individual (such as in a biography), or a group of individuals who share a specific characteristic (e.g., an identifiable group of painters who happen to be all of one sex; a religious order that is restricted to one sex). Other examples include research that is focused on specific cultural traditions or languages, or on one age group (e.g., a biomechanical modeling study of posture corrections in adolescents). Such research should not be precluded so long as the selection criteria for those to be included in the research are germane to answering the research question. Researchers who plan to actively exclude particular groups should clarify to their REBs the grounds for the exclusion.

Where a language barrier exists between the researcher and the prospective participant, various measures may be used to ensure effective communication in recruitment and consent discussions. For example, an intermediary who may not be part of the research project or team, but who is competent in the language used by the researchers, as well as that preferred by the participant, may assist with communication between prospective participants and researchers. The selection of an intermediary and their activities will depend on the nature, context and risks of the research.

B. Inappropriate Exclusion

Research Involving Women

Women have historically been inappropriately excluded from participating in some research. This exclusion of women, where unwarranted, has delayed the advancement of knowledge, denied potential benefits to women, and exposed women to harm when research findings from male-only research projects were generalized inappropriately to women, as has often been the case in clinical drug trials. The inclusion of women in research advances the commitment to Justice, improves the generalizability of research findings to women where that is a goal of the research, and is essential to ensure that women and men benefit equally from research.

Article 4.2 Women shall not be inappropriately excluded from research solely on the basis of gender or sex.

Application Researchers should not exclude women from research unless there is a valid reason for doing so. While some research is properly focused on particular research populations that do not include women, or include very few women, women should generally be represented where there is a reasonable expectation that the results of the research will be generalized to women.

Article 4.2 rejects discriminatory and unethical use of inclusion or exclusion criteria that presumptively or inappropriately exclude women because of their gender or sex.

Article 4.3 Women shall not be inappropriately excluded from research solely on the basis of their reproductive capacity, or because they are pregnant or breastfeeding.

Application Researchers should not exclude women from research on the basis of their reproductive capacity, or their pregnancy, or because they are breastfeeding, unless there is a valid reason for doing so.

Subjecting women of childbearing potential to inappropriate requirements precludes their participation in research. Exclusions should be made on the basis of clear criteria that reflect balanced attention to the potential benefits as well as the foreseeable risks of the research that may affect the welfare of women. For example, researchers should not require participants to use oral contraception, unless there is a valid reason for doing so.

In considering research on pregnant or breastfeeding women, researchers and REBs shall take into account foreseeable risks and potential benefits for the woman and her embryo, fetus or infant, as well as the foreseeable risks and potential benefits of excluding pregnant or breastfeeding women from the research.

Research Involving Children

Children have varying degrees of maturity – metabolically, immunologically and cognitively – that may present important challenges for research design and the consent process, depending on the nature and complexity of the research. In addition to the vulnerability that arises from their developmental stage, children may also lack the decision-making capacity to decide whether or not to participate in research (see Article 4.6). As well, physical or psychological harms a child may experience in a research setting may have long-lasting consequences. As a result, researchers have often avoided the inclusion of children in some research, especially in clinical trials testing new treatments, so as to eliminate any risks. Clinical trials conducted only with adults yield a generally poor understanding of the results that apply to children.

As is the case with women, the inclusion of children in research advances the commitment to justice in research by improving our knowledge of, and ability to respond to, the unique needs of children throughout their development.

Article 4.4 Children shall not be inappropriately excluded from research solely on the basis of their age or developmental stage. The inclusion of children in research is subject to Article 4.6.

Application Researchers should not exclude children from research unless there is a valid reason for doing so. Participation of children in research is justifiable when the research objective cannot be achieved with adult participants only. When considering the inclusion of children in research, researchers and REBs shall consider a child's stage of physical, physiological, psychological, and social development to ensure adequate protections for the child's welfare. Where children have not yet attained the capacity to decide for themselves whether or not to participate in research, researchers shall seek consent from an authorized third party while ascertaining the child's assent or dissent, as outlined in Chapter 3. Note that Article 4.6 equally applies to children.

Research Involving the Elderly

As the population ages, the proportion of elderly people is increasing, and so is their life expectancy. Research designed to improve our understanding of a wide range of aspects of aging and the lives of elderly people is important for ensuring that they stay fully integrated into society and maintain a continuing high quality of life. Medically, elderly patients are the highest consumers of drugs, yet many of these treatments have not been tested adequately on elderly patients. Research that takes into account the differential effects on the elderly and how best to accommodate their needs provides scientific evidence that can inform changes to policies and standards of care for the elderly.

Article 4.5 Elderly people shall not be inappropriately excluded from research solely on the basis of their age.

Application Researchers should not exclude elderly people from research unless there is a valid reason for doing so. When considering the inclusion of elderly people in research, researchers and REBs shall consider their physical and social needs to ensure adequate protections. Depending on their social circumstances, elderly people may require some reasonable accommodation for mobility, transportation support and other types of assistance to facilitate their participation in research. The principle of Justice requires that such accommodations for the natural processes of aging be considered by REBs and researchers. Exclusion of the elderly shall not be based on easily remediable issues that are not germane to the research question.

Research Involving Participants Who Lack the Capacity to Consent for Themselves

The core principles of Justice and Concern for Welfare entail special ethical obligations toward individuals who lack capacity to consent to participate in research. This section sets out conditions that apply to research involving those who cannot consent for themselves. It should be read in conjunction with Section C of Chapter 3.

Article 4.6 Subject to applicable legal requirements, individuals who lack capacity to decide whether or not to participate in research shall not be inappropriately excluded from research. Where a researcher seeks to involve individuals in research who do not have decision-making capacity, the researcher shall, in addition to fulfilling the conditions in Articles 3.9 and 3.10, satisfy the REB that:

- (a) the research question can be addressed only with participants within the identified group; and
- (b) the research does not expose the participants to more than minimal risk without the prospect of direct benefits for them; or
- (c) where the research entails only minimal risk, it should at least have the prospect of providing benefits to participants or to a group that is the focus of the research and to which the participants belong.

Application Children, and individuals with cognitive impairments or intellectual disabilities may lack the capacity to decide whether or not to participate in particular research initiatives. As a result, they have, historically, experienced both over-inclusion as populations of convenience for some research and unjustified exclusion from other research. Yet the advancement of knowledge about their social, psychological, and health experiences and needs may depend on their appropriate participation in research. Their inclusion in research requires special considerations as outlined in this article.

To be ethically acceptable, the participation of those who lack the capacity to decide for themselves shall be necessary and appropriate to address the research question. Researchers and REBs shall consider the level of risk to which participants who lack decision-making capacity are exposed, and the prospect of direct benefits to accruing to the participants. Their participation should generally be limited to research of minimal risk as defined in this Policy (see Chapter 2 for the definition of minimal risk).

Where the research presents more than minimal risk, it should have appropriate justification aimed at generating knowledge of sufficient importance to addressing the participants' disorder, condition, interest or situation. Such research should have the prospect of direct benefits for the participants themselves commensurate with the level of foreseeable risk to participants. The relation of the potential benefit to the foreseeable risk presented by the research should be at least as favourable to the participants as that provided by available alternative approaches.

Where the research entails only minimal risk, it is sufficient if the research presents the prospect of benefits to participants or to a group that is the focus of the research and to which the participants belong.

The research design should take into account factors that may affect the decision-making capacity of prospective participants to receive information, to consent to

the research at some stage, or to participate in it. These factors may be permanent or may vary over time (e.g., the participant’s decision-making capacity may fluctuate over time). Articles 3.9 and 3.10 in Chapter 3 establish other conditions regarding research that involve individuals who lack decision-making capacity. This includes the involvement of an authorized third party to consent on their behalf, and adequate provisions to ascertain the wishes of the individuals concerning their participation.

Participants’ Vulnerability and Research

Article 4.7 Individuals or groups whose circumstances may make them vulnerable in the context of research should not be inappropriately included or automatically excluded from participation in research on the basis of their circumstances.

Application The core principles of Respect for Persons, Concern for Welfare, and Justice entail special ethical obligations toward individuals or groups whose circumstances may lead to their vulnerability in the context of a specific research project and limit their ability to fully safeguard their own interests. Those who are owed special ethical obligations may include individuals who are institutionalized, those in dependent situations, or those whose circumstances (e.g., poverty or poor health status) may render even modest participation incentives so attractive as to constitute an inducement to take risks they would otherwise not take. Their situation may also compromise the voluntariness of consent in other ways. However, individuals should not automatically be considered vulnerable simply because of assumptions made about the vulnerability of the group to which they belong. Their particular circumstances shall be considered in the context of the proposed research project.

REBs and researchers shall carefully examine the relationship between the circumstances of the individuals and groups they aim to recruit, and the proposed research question. They should not presume that these circumstances will automatically result in the inclusion or exclusion of individuals or groups as prospective participants. Participation should be based on inclusion or exclusion criteria that are justified by the research question. Researchers and REBs should recognize and address changes in a participant’s circumstances that may create, heighten, or attenuate their vulnerability, and provide special protections or consideration.

In general, researchers should be familiar with the cultural, social and economic circumstances of prospective participants, groups or communities. Researchers should anticipate, to the best of their ability, needs of participants, groups and their communities that might arise in any given research project. Especially when groups, and their communities, have a wide range of pressing needs due to their low socioeconomic circumstances, these needs can present significant ethical challenges for researchers. An equitable distribution of research benefits (discussed below) can help ensure that individuals, groups and communities whose circumstances may make them vulnerable in the context of research are not inappropriately included in research based on these circumstances.

Equitable Distribution of Research Benefits

Researchers should consider ways to ensure the equitable distribution of any benefits of participation in research. Benefits of research participation may be direct, where, for example, an individual participant experiences amelioration of a health condition as a result of an experimental therapy, or learns new information about social issues as a result of participation in a research focus group. In a community hosting research, benefits may take the form of information sharing, training for local personnel, the establishment of health care or similar services. Benefits may be indirect, where the participation in research of an individual or group, or in a research project involving a community contributes to the advancement of knowledge that may lead to improved conditions for a group to which the participant belongs. Such knowledge may also inform other communities or society in general.

Researchers should also be sensitive to the expectations and opinions of participants regarding potential benefits of the research. Prior to the commencement of the research, researchers should formally or informally discuss these expectations with individuals and/or groups, and outline the scope and nature of potential benefits that may accrue to participants during and after the research (see Article 9.13). REBs should be vigilant to ensure that the proposed distribution of benefits is fair, without imposing undue burdens on the researcher that would make it too difficult or costly to complete research.

Researchers should normally provide copies of publications, or other research reports or products, arising from the research to the institution or organization – normally the host institution – that is best suited to act as a repository and disseminator of the results within the participating communities. This may not be necessary in jurisdictions where the results are readily available in print or electronically. In general, researchers should ensure that participating individuals, groups and communities are informed of how to access the results of the research. Results of the research should be made available to them in a culturally appropriate and meaningful format, such as reports in plain language in addition to technical reports.

References

Best Practices for Health Research Involving Children and Adolescents, Center of Genomics and Policy, 2012.

superstitious; violation of community norms regarding the use of human tissue and remains; failure to share data and resulting benefits; and dissemination of information that has misrepresented or stigmatized entire communities.

Where the social, cultural or linguistic distance between the community and researchers from outside the community is significant, the potential for misunderstanding is likewise significant. Engagement between the community involved and researchers, initiated prior to recruiting participants and maintained over the course of the research, can enhance ethical practice and the quality of research. Taking time to establish a relationship can promote mutual trust and communication, identify mutually beneficial research goals, define appropriate research collaborations or partnerships, and ensure that the conduct of research adheres to the core principles of Respect for Persons, Concern for Welfare – which in this context includes welfare of the collective, as understood by all parties involved – and Justice.

Research Involving Indigenous Peoples in Other Countries

Although the present chapter addresses research involving Aboriginal peoples in Canada, researchers, REBs, participants and the research community at large may find the guidance articulated here useful when undertaking research or reviewing a proposal involving Indigenous peoples in other countries who endorse collective decision making as a complement to individual consent. It is critically important, however, to seek local guidance in the application or adaptation of this Policy to Indigenous peoples outside of Canada.

For considerations that apply to research conducted in another country, see Chapter 8, Section B.

C. Applying Provisions of This Policy in Aboriginal Contexts

Requirement of Community Engagement in Aboriginal Research

Article 9.1 Where the research is likely to affect the welfare of an Aboriginal community, or communities, to which prospective participants belong, researchers shall seek engagement with the relevant community. The conditions under which engagement is required include, but are not limited to:

- (a) research conducted on First Nations, Inuit or Métis lands;
- (b) recruitment criteria that include Aboriginal identity as a factor for the entire study or for a subgroup in the study;
- (c) research that seeks input from participants regarding a community's cultural heritage, artefacts, traditional knowledge or unique characteristics;
- (d) research in which Aboriginal identity or membership in an Aboriginal community is used as a variable for the purpose of analysis of the research data; and
- (e) interpretation of research results that will refer to Aboriginal communities, peoples, language, history or culture.

Application Paragraph (a) refers to First Nations, Inuit and Métis lands that include Indian reserves, Métis settlements and lands governed under a self-government agreement or an Inuit or First Nations land claim agreement. Researchers should become informed about formal rules or oral customs that may apply in accordance with a particular First Nations, Inuit or Métis authority. In different jurisdictions, research activities may be regulated in various ways.

Paragraph (c) refers to cultural heritage, which includes, but is not limited to, First Nations, Inuit and Métis peoples' relations with particular territories, material objects, traditional knowledge and skills, and intangibles that are transmitted from one generation to the next (e.g., sacred narratives, customs, representations or practices). Cultural heritage is a dynamic concept, in that materials, knowledge and practices are continuously adapted to the realities of current experience.

Cultural heritage research such as archaeological research involving burial sites or sacred landscapes and handling of artefacts may raise ethical obligations important to the Aboriginal community that may not be addressed in academic research proposals. Researchers and communities should agree in advance on how to reconcile or address these divergent perspectives (see Articles 9.8 and 9.12).

Appropriation of collective knowledge, treatment of such knowledge as a commodity to be traded, or making unauthorized adaptations for commercial purposes, may cause offence or harm to communities from which the knowledge originates. Such conduct has prompted initiatives in various countries and international agencies to address unethical, unfair, and inequitable treatment of traditional knowledge and knowledge holders (see Article 9.18).

Paragraph (e) refers to both primary collection of research data and secondary use of information collected originally for a purpose other than the current research purpose (see Article 2.4 and Chapter 5, Section D). Articles 9.20 to 9.22 address community engagement and individual consent for secondary use of identifiable information and human biological material for research purposes.

Nature and Extent of Community Engagement

Article 9.2 The nature and extent of community engagement in a project shall be determined jointly by the researcher and the relevant community, and shall be appropriate to community characteristics and the nature of the research.

Application Diversity among and within communities makes generalizations about the form of community engagement inappropriate. Diversity within Aboriginal communities may encompass differences in levels of formal education and employment, mobility, generational differences and intermarriage with non-Aboriginal persons. This diversity increases the importance of clarifying mutual expectations and obligations with the community, and incorporating them into a research agreement.

Chapter 13

HUMAN GENETIC RESEARCH

Introduction

Human genetic research involves the study of genetic factors responsible for human traits and the interaction of those factors with each other, and with the environment. Research in this area includes the identification of genes that comprise the human genome; functions of genes; the characterization of normal and disease conditions in individuals, biological relatives, families, communities and groups; and studies involving gene therapy. Participants in clinical trials are increasingly being asked to participate in genetic studies in addition to the primary clinical trial. With the growth of genetic research, especially whole-genome research, researchers, research ethics boards (REBs) and participants should be aware of the ethical issues that this research raises.

Genetic research may have profound social impacts, both positive and negative. As genetic research advances, genes and their alleles (versions) are being identified, but the function of each gene and its relationship to disease conditions, or other characteristics may not be clear. In single-gene disorders, for example, an allele of a single gene is directly related to a hereditary disease. More commonly, diseases or personal characteristics are influenced by multiple genes, as well as environmental factors.

Research may help us better understand the human genome, and genetic contributions to health and disease. It may lead to new approaches to preventing and treating disease. Individuals may benefit from learning about their genetic predispositions, if intervention strategies are available to prevent or minimize disease onset and mitigate symptoms, or to otherwise promote health. Genetic research also has the potential, however, to stigmatize individuals, communities or groups, who may experience discrimination or other harms because of their genetic status, or may be treated unfairly or inequitably.

A. Application of Core Principles to Genetic Research

Genetic information has implications beyond the individual because it may reveal information about biological relatives and others with whom the individual shares genetic ancestry. The participation of an individual in genetic research may therefore have ramifications for these other persons, communities or groups. In some cases, researchers specifically seek to conduct genetic research with members of families, communities or groups that requires particular attention to the social and cultural contexts in which participants live. Research with families, communities or groups may raise special considerations regarding recruitment of participants, consent processes, privacy and confidentiality.

Article 13.1 Guidance regarding a proportionate approach to research ethics review, consent, privacy, confidentiality, research with human biological materials and other ethical guidance described in earlier chapters of this Policy apply equally to human genetic research.

Application In developing and reviewing proposals involving genetic research, researchers and REBs should refer to earlier chapters in this Policy, including consent in Chapter 3, privacy and confidentiality in Chapter 5, and human biological materials and materials related to human reproduction in Chapter 12. Other chapters relevant to the specific research proposal should also be consulted, such as Chapter 9 concerning research involving Aboriginal peoples or Chapter 11 on clinical trials. This chapter does not reiterate guidance set out in earlier chapters. Rather, it focuses on issues that arise specifically in the context of human genetic research and provides guidance for managing information revealed through genetic research, provision of genetic counselling, participation of families, communities and groups in genetic research, banking of human biological materials, and research involving gene transfer.

B. Plans for Managing Information Revealed through Genetic Research

Article 13.2 Researchers conducting genetic research shall:

- (a) in their research proposal, develop a plan for managing information that may be revealed through their genetic research;
- (b) submit their plan to the REB; and
- (c) advise prospective participants of the plan for managing information revealed through the research.

Application The types of information that may be revealed through genetic research – and the implications of this information for participants and their biological relatives – require that researchers and REBs ensure that an appropriate plan is in place for managing information. In some cases, genetic research may reveal known gene-disease associations or other information, including incidental findings, that may be clinically relevant for individuals (or their biological relatives) in treating or alleviating health conditions or risks. In other cases, research may reveal information that is inconclusive in its scientific, clinical or other implications. Genetic research may also reveal information about family relationships, including adoption and non-paternity.

This range of information varies in its possible implications for individuals. In some cases, follow-up clinical testing and counselling may be recommended. Information may also have implications for biological relatives and may raise disclosure considerations, as discussed in Article 13.3(b). Genetic information may also affect eligibility for employment or insurance if, for example, an individual who acquires genetic information is required to disclose disease predisposition risks to employers or insurers.