

Health Research Ethics Board

Policy Manual

Version March 27, 2012

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Introduction

The purpose of this manual is to provide the policies to be used by the Health Research Ethics Board (HREB) established under the Health Research Authority (HREA) Act of the Province of Newfoundland and Labrador.

Section 1, Background, provides the historical background to the legislation.

Section 2 describes the framework of the HREA, the Board of Directors and the relationship of HREA and the HREB and other research ethics bodies established in the province.

The remainder of this policy manual is specific to the HREB and will be used as the Policy Manual of the HREB.

Background Section 1

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The purpose of this section is to provide a brief background on the basis of ethics review and its importance and to provide background information on the establishment of the Health Research Ethics Authority Act.

1. Background on ethics review and its importance

Several sources describe the history of research ethics and the establishment of codes of conduct for research since World War II. The following descriptions are among the most well-known cases which have influenced the conduct of human research. The descriptions can be found at a number of other websites (e.g., Claremont Graduate University, <http://www.cgu.edu/pages/1722.asp>) and are cited by other Research Ethics Boards.

1948: *The Nuremberg Code.* The most dramatic and well-known chapter in the history of research with human subjects opened on December 9, 1946, when an American military tribunal initiated criminal proceedings against 23 leading German physicians and administrators for their willing participation in war crimes and crimes against humanity. Among the charges were that German physicians conducted medical experiments on thousands of concentration camp prisoners without their consent. Most of the subjects of these experiments died or were permanently crippled as a result.

Several German doctors had argued in their own defence that their experiments differed little from previous American or German ones. Furthermore, they showed that no international law or informal statement differentiated between legal and illegal human experimentation. As a direct result of the trial, the Nuremberg Code (1948) established the moral, ethical and legal requirements that must be met for humans to participate as subjects in research.

1950s: *Thalidomide.* In the late 1950s, thalidomide was approved as a sedative in Europe; it was *not* approved by the United States Federal Drug Administration (FDA). The drug was prescribed to control sleep and nausea throughout pregnancy, but it was soon found that taking this drug during pregnancy caused severe deformities in the fetus. Many patients did not know they were taking a drug that was not approved for use by the FDA, nor did they give informed consent to take an investigational drug. Some 12,000 babies were born with severe deformities due to thalidomide.

U.S. Senate hearings followed and in 1962 the so-called "Kefauver Harris Amendment" to the Food, Drug and Cosmetic Act were passed into law to ensure drug efficacy and greater drug safety. For the first time, drug manufacturers were required to prove to the FDA the effectiveness of their products before marketing them.

1964: *Declaration of Helsinki.* In 1964, the World Medical Association established recommendations guiding medical doctors in biomedical research involving human subjects. The

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Declaration governs international research ethics and defines rules for "research combined with clinical care" and "non-therapeutic research." The Declaration of Helsinki was revised in 1975, 1983, 1989, 1996, 2000, 2002, 2004 and 2008 and is the basis for the Good Clinical Practice guidelines used today.

Issues addressed in the Declaration of Helsinki include:
Research with humans should be based on the results from laboratory and animal experimentation
Research protocols should be reviewed by an independent committee prior to initiation
Informed consent from research participants is necessary
Research should be conducted by medically/scientifically qualified individuals
Risks should not exceed benefits
Research with human subjects is justified only when the degree of risk to subjects does not exceed the humanitarian importance of the knowledge to be gained.

1932-1972: Tuskegee Syphilis Study. During a research project conducted by the U.S. Public Health Service, 600 low-income African-American males, 400 of whom were infected with syphilis, were monitored for 40 years. Free medical examinations were given; however, subjects were not told about their disease. Even though a proven cure (penicillin) became available in the 1950s, the study continued until 1972 with participants being denied treatment. In some cases, when other physicians diagnosed subjects as having syphilis, researchers intervened to prevent treatment. Many subjects died of syphilis during the study. The study was stopped in 1973 by the U.S. Department of Health, Education, and Welfare only after its existence was publicized and it became a political embarrassment. In 1997 President Clinton apologized to the study subjects and their families. The study used disadvantaged, rural black men to study the untreated course of a disease that was not confined to that population. This placed the entire burden of risk on that population when a much broader population was to benefit from the findings. The Tuskegee Syphilis Study heightened awareness of the need to protect human subjects and to assure informed voluntary consent to participate in research involving human subjects.

The Belmont Report. In the U.S., The National Research Act of 1974, passed in response to the Tuskegee study, created the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research, which was charged to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. Carrying out its charge, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research prepared the Belmont Report in 1979. The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. The Report is a statement of basic ethical

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principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. The three basic ethical principles and their corresponding applications are:

Principle	Application
Respect for persons Individuals should be treated as autonomous agents Persons with diminished capacity are entitled to protection.	Informed consent Subjects, to the degree that they are capable, must be given the opportunity to choose what shall or shall not happen to them The consent process must include three elements: Information, Comprehension, and Voluntariness.
Beneficence Human subjects should not be harmed Research should maximize possible benefits and minimize possible harms.	Assessment of risks and benefits The nature and scope of risks and benefits must be disclosed in a systematic manner
Justice The benefits and risks of research must be distributed fairly.	Selection of subjects There must be fair procedures and outcomes in the selection of research subjects

1978: Medical Research Council (MRC) Guidelines. In Canada, other unethical human experiments occurred between the WWII years and the 1970s. Most notable were the brainwashing experiments conducted by Dr. Cameron and his colleagues at the Allen Memorial Institute of McGill University in the 1950s for the CIA, and the chemical warfare experiments performed on Canadian soldiers at Suffield, Alberta, in the 1940s.

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Canada's first attempt to introduce some control of research ethics occurred in 1978. Both the MRC and the Social Sciences and Humanities Research Council (SSHRC) issued guidelines which were based on the Belmont Report. MRC revised its guidelines in 1987.

The National Council on Bioethics in Human Research (NCBHR) was created in 1989 and began site visits of Research Ethics Boards (REBs). The primary purpose of these visits was to ascertain the extent of compliance between the activities of the REBs and MRC's guidelines. In 1995 the mandate was broadened to include all human research and the name was changed to the National Council on Ethics in Human Research (NCEHR).

In 1985 Dr. Roger Poisson, a Montreal Surgeon at Hôpital St-Luc, had received funding from the U.S. National Institutes of Health (NIH) for breast cancer research. The work was part of a larger study, the National Surgical Adjuvant Breast Project (NSABP), and the results were published in the New England Journal of Medicine suggesting that lumpectomy was as effective as full mastectomy. Investigations later found that Dr. Poisson had abused scientific integrity by falsifying patient records. In 1994 in response to this and other scandals, the three councils MRC, SSHRC, and the National Science and Engineering Research Council (NSERC) established a Tri-Council Working Group and in 1998 previous guidelines for research ethics integrity established by the MRC (*Guidelines on Research Involving Humans* and *Guidelines for Research on Somatic Cell Gene Therapy in Humans*) and SSHRC (*Ethics Guidelines for Research Involving Human Subjects*) were replaced by the Tri-Council Policy Statement (TCPS) *Ethical Conduct for Research Involving Humans*.

1998: Tri-Council Policy Statement (TCPS) Ethical Conduct for Research Involving Humans. In 1998, MRC, SSHRC and NSERC jointly published their guidelines as a single Canadian standard, the Tri-Council Policy Statement. The agencies have committed to keeping it a living or "evolving" document in order to respond to new developments and identified gaps. To this end, the Interagency Panel on Research Ethics (PRE) was established in 2001 by the three Canadian research agencies -- the Canadian Institutes of Health Research (CIHR) that replaced the MRC in 2000, NSERC and SSHRC who support the development and evolution of their joint research ethics policy. A revision of the TCPS was begun in 2008 and the 2nd edition of TCPS (TCPS2) became available December 2010.

Continuing Vigilance. Unfortunately, ethical controversies in research involving humans have not ceased. Most unethical behaviour results from a lack of awareness of ethical concerns and/or various pressures on researchers, REBs, and institutions. The insights gained from historical and more recent ethical controversies demonstrate why vigilant ethics review is necessary and appropriate. Research ethics policy must continue to evolve to protect research subjects and maintain trust between researchers and society as a whole.

2. Development and creation of the Health Research Ethics Authority



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The Human Investigation Committee (HIC) was created in the early 1970s as the biomedical research ethics board for Memorial University of Newfoundland (MUN) and over time gradually

replaced the hospital research ethics boards. By 2000, the HIC had become the joint research ethics board of MUN and the regional health authority Eastern Health.

During the late 1990s it became apparent that there existed a serious deficiency of the ethical review process, namely the HIC had little or no control over human health research conducted in the province that had not undergone local ethics review and approval. One incident in particular became the basis for a change in the policies for ethics review of health research in the province and the establishment of legislation for this review process. Specifically, in the 1980s and 1990s patients with a life-threatening cardiac condition and their families had been asked to take part in a genetics research study being conducted by researchers from out of province. There was inappropriate clinical follow-up and when enquiries were made of the local (provincial) genetics team no one had been involved in the study or had adequate knowledge of the study to provide follow up. The HIC had not been involved in the approval process of the study and therefore had no jurisdiction over the research study. Consequently, the Provincial Department of Health and Community Services (DHCS) commissioned a report by Dr. Verna Skanes to look at the conduct of genetics research in the province. The report was made available in May 2000 with the recommendation to establish a provincial health research ethics board.

In January 2000, the DHCS established two working groups: (1) the Provincial Health Research Ethics Board Working Group and (2) the Genetics Standards Development Working Group. Following extensive consultation [site visit from National Council on Ethics in Human Research (NCEHR): Klassen, McGillivray, Holmes and Dubois-Flynn); an experts panel review: McDonald, Kinsella and Caulfield; the report on genetics standards] and liaison with the working groups, the Health Research Ethics Authority Act was passed in November 2006.

The Act establishes a Health Research Ethics Authority (HREA) for the province of Newfoundland and Labrador. The HREA is charged with the general supervision of all health research involving human subjects conducted in the province and establishes the Health Research Ethics Board (HREB). In conjunction with the requirements of the relevant research ethics guidelines and regulations, all health research involving human subjects and conducted within the province must be reviewed and approved by the HREB. The HREA may also approve other not-for-profit, research ethics bodies (referred to in this policy manual as institutional research ethics boards, IREB) which meet the requirements of the TCPS2. This legislation mandates that no health research involving human subjects may be conducted in the province of Newfoundland and Labrador without receiving approval from the HREB or an IREB.

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3. Principles of Research Ethics

The standards and procedures by which the HREA and HREB operate and function are based on the guidelines provided in the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2nd edition*¹) and, where relevant, the *ICH-Good Clinical Practice*, the *Declaration of Helsinki*, the *Belmont Report (U.S.)* the *Code of Federal Regulations (CFR), Title 45, Part 46 (U.S.)* and *Health Canada, Food and Drugs Act, Food and Drugs Regulations Part C, Division 5*.

These guidelines embody the ethics principles of:

Respect for human dignity

Respect for free and informed consent

Respect for vulnerable persons

Respect for privacy and confidentiality

Respect for justice and inclusiveness

The responsibility for balancing harms and benefits

The responsibility for minimizing harm and maximizing benefit

¹ Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and the Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, December 2010. Referenced in this Policy Manual as TCPS2

Provincial Framework for Protecting Human Participants in Research

Section 2

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The Health Research Ethics Authority is established to oversee the administration and financial responsibilities of the organization. It is ultimately responsible for:

- ensuring that participants in human health research in the province are protected and to facilitate health research in the province and
- providing public awareness and education on ethics issues related to human health research.

To this end the Board of Directors has delegated to the Health Research Ethics Board (HREB) the responsibility to conduct review of research proposals and to provide continuing ethical oversight for human health research conducted under its authority, in particular, clinical trials and genetic studies. The HREA may also approve other not-for-profit research ethics boards (referred to in this manual as institutional research ethics boards, IREBs) which meet the requirements of the Tri-Council Policy Statement, 2nd edition (TCPS2).

In meeting this responsibility the HREB (and any approved IREB) shall require that Canadian and internationally accepted legal, ethical and regulatory principles affording protection of research participants shall govern the processes for review and continued oversight of human health research. The HREB shall evaluate a research proposal to ensure conformity with accepted scientific and ethical standards, and applicable regulations to promote the responsible conduct of research.

To this end the HREB shall review human health research protocols and related materials to ensure the following:

- Risks to subjects are reasonable in relation to anticipated benefits (if any), and the importance of the knowledge to be gained,
- Selection of subjects is equitable,
- Informed consent is sought from each prospective participant or substitute decision maker except in selected situations where consent may be waived,
- The consent is documented in accordance with, and to the extent required, by Tri-Council Policy Statement (TCPS2) guidelines and Good Clinical Practice (GCP) regulations and any other applicable guidelines and regulations,
- Provision is made for random and 'for cause' monitoring of implemented approved protocols to ensure the safety of subjects,
- The dignity and integrity of research participants is respected by protecting the privacy of research subjects and the confidentiality of private information collected in the context of the research study with appropriate additional safeguards to protect the rights and welfare of subjects who are members of a vulnerable group.

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Organizations requesting that the HREB or an IREB act as the Board of Record for a research study must document the roles and responsibilities of the members of the research team and any group involved in the research enterprise and demonstrate commitment to compliance with applicable research regulations and law.

Health Research Ethics Board Relationships

Section 3

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The purpose of this policy is to describe the roles of the HREB in relationship to the research community and how communication will be made with the research community.

1. Board of Record

For all research approved by the HREB, the HREB will serve as the board of record and as such will be responsible for continuing oversight and monitoring.

2. Other approvals required for conducting research

Research ethics approval by the HREB does not preclude the requirement for approval by the organization/institution in which the research will be conducted.

3. HREB notification of decisions

All decisions of the HREB are sent to the applicant.
The applicant is responsible for informing all other offices and organizations as appropriate.

4. Communicating with researchers

The staff of the Research Ethics Office (REO), the Ethics Officer (EO) and the Chair and Vice-Chair of the HREB communicate with the research community externally and in Newfoundland and Labrador through:

- Postings on the HREB website: <http://www.hrea.ca>
- Presentations and discussions with research groups

5. Public awareness

The staff of the REO, the EO and the Chair and Vice Chair of the HREB can provide educational sessions to the general public as requested.

Membership of Health Research Ethics Board (HREB)

Section 4

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The purpose of this policy is to describe the structure and membership of the HREB² and the duties and responsibilities of the members.

1. Committee Structure of the HREB

The HREB will have two subcommittees responsible for reviewing health research protocols:

- HREB-CT – A committee responsible for reviewing clinical trials of drugs and devices
- HREB-NCT – A committee responsible for reviewing all research other than clinical trials of drugs and devices

The chair and vice chair of the HREB will serve as the chairs of each of the sub-committees.

The membership of each sub-committee will be drawn from the membership of the HREB. The membership of each committee will be constituted based on TCPS2 guidelines as described below.

Each subcommittee will have a dedicated staff person (ethics coordinator) who will manage the business of the committee including receipt of applications, distribution of applications to review committee members, taking and transcribing minutes and attending to correspondence as required before and after review committee meetings. The ethics coordinators are directly responsible to the EO

2. HREB Chair

a. Appointment:

The chair of the HREB is appointed by the HREA from among the clinical researcher members of the HREB. To be eligible for appointment a candidate must have extensive research experience, expertise in clinical practice and pharmaceuticals and will normally have served at least three years on a TCPS-compliant research ethics board. The Chair will need to have completed any required ethics tutorials or any other requirements of national and international regulatory boards.

b. Duties and Responsibilities:

The Chair

² HREA Act ; Section 7 (7); The research ethics board may appoint one or more subcommittees composed of its members and those subcommittees have all the powers conferred on the board by this Act

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- presides at HREB-CT meetings and works with staff of the Research Ethics Office (REO) on HREB business and acts on behalf of the HREB to deliberate and adjudicate on research ethics issues between regular meetings of the HREB committees.
 - provides liaison, communicates and interacts with local, regional and national organizations and committees on research ethics initiatives, policies and standards to ensure that the HREB operates effectively at a high level of ethical standards.
 - participates in consultation, education and information to HREB and HREA members and to researchers, sponsors, research staff and research participants as required to ensure ethical standards are met
 - sits as an *ex-officio* member of the HREA

c. Accountability:

The Chair is accountable to the HREA to safeguard research participants through rigorous review, to lead and direct the HREB and to enhance through communication and education the ethical conduct of all research activity involving human subjects coming under the purview of the HREB.

3. HREB Vice Chair

a. Appointment:

The Vice Chair of the HREB is appointed by the HREA from among the researcher members of the HREB on the recommendation of the Chair and EO.

b. Duties and responsibilities:

The Vice Chair shares the duties of the Chair of the HREB and assumes the full responsibilities of the Chair in the Chair's absence. The Vice Chair serves as the chair of the HREB-NCT subcommittee.

c. Accountability:

The Vice Chair is accountable to the Chair of the HREB and through the Chair to the HREA.

4. Other Members of the HREB

The authority shall appoint the HREB members and the full HREB membership comprises the membership of the two research ethics review subcommittees: the HREB-CT and HREB-NCT.

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Each subcommittee is required to adhere to the guidelines for membership as provided in the TCPS2.

a. Voting members

Each subcommittee shall have:

- at least two persons who have experience in the conduct of the human health research covered by the HREB
- at least one person knowledgeable in ethics
- at least one person knowledgeable in the law related to health research involving human subjects
- at least one person to represent the general public
- at least one person whose primary experience and expertise are in a non-scientific discipline

The majority of HREB members will be Canadian citizens or permanent residents; both men and women must be represented.

Some members may represent more than one core constituency, e.g. a lawyer with non- science credentials. Members may be appointed to share a position. No more than two members with specific expertise may be appointed to share a position for alternate attendance at meetings.

b. Ex-officio Members

Ex-officio members attending meetings by virtue of their position may participate in discussion but do not vote.

Members of the HREA Board
Ethics Officer

c. Appointment

The HREA, following consultation with the Minister of Health and Community Services, the President of Memorial University and the Chief Executive Officer of the Eastern Regional Health Authority, shall appoint the full HREB comprising not fewer than 10 members.³

d. Term of appointment:

³ HREA Act; Section 7 (1) The authority, following consultation with the minister, the president of the Memorial University of Newfoundland and the chief executive officer of the Eastern Regional Health Authority, shall appoint the Health Research Ethics Board comprising not fewer than 10 members.

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The term of appointment for members, the Chair and Vice Chair will normally be not more than three years. Appointments may be renewed for one term. Initial appointments to the HREB will be for one, two or three years to ensure overlap of membership.

e. Responsibilities

Members of the HREB are expected to:

- attend orientation and information sessions.
- successfully complete the TCPS tutorial within three months of appointment
- sign an Oath of Confidentiality
- attend meetings regularly
- review all studies assigned to full review
- participate in functions related to the work of the HREB

Frequent unexplained absences from HREB meetings without prior notice to the staff of the REO or failure to meet the outlined responsibilities of an HREB member may be construed as a notice of resignation. If discussions with the member fail to resolve the issues outstanding, a letter of dismissal will be sent to the member by the Chair of the HREA.

5. Ad hoc advisors

Ad hoc advisors may be invited to attend HREB meetings to contribute specific expertise to meeting discussion. They do not vote. Their attendance will be noted in the minutes.

The research ethics review subcommittees of the HREB, at their discretion, may also co-opt persons on an *ad hoc* basis to review or provide scientific opinion or advice on specific applications requiring special expertise. These persons need not have experience on the HREB. These persons neither vote or participate in HREB deliberations. A list of persons co-opted on an *ad hoc* basis and the dates of meetings they attend will be retained in the REO.

6. Observers at Meetings

Observers may attend HREB meetings with the permission of the Chair but, normally, they may not attend more than six consecutive meetings. Observers do not vote or participate in HREB deliberations.

7. Working and Advisory Groups

The HREB may ask persons with special expertise and experience to serve on working or advisory groups to assist the Board. Current or past members of a TCPS2-compliant REB will form the majority of any such group. These groups will report in writing to the full HREB.

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8. Professional Development of HREB Members

The HREB Chair and EO provide orientation to HREB members. All members are required to successfully complete the TCPS training module and will be expected to attend seminars, workshops and educational sessions addressing relevant issues.

9. Oath of Confidentiality

All members of the HREB and any observers attending meetings are required to have a signed Oath of Confidentiality on file in the EO

10. Conflict of interest or bias

HREB members are in a clear conflict of interest or may have a bias when, for example, their own research projects are under review by the HREB or when they have been in direct academic conflict or collaboration with the researcher whose proposal is under review; REB members must withdraw from the committee meeting when such projects are under consideration⁴.

The minutes of the meeting must state that such a member was absent from the meeting for both the discussion and voting with respect to any relevant project.

11. Compensation of HREB members

The members of the HREB shall serve without remuneration but may be reimbursed for their travel and other expenses incurred as a member of the HREB on a scale approved by the minister.

The Chair of the HREB in addition to reimbursement of his or her travel and other expenses shall be compensated for carrying out his/her duties on a scale approved by the minister.

12. Liability of members

The members of the HREB are not personally liable for anything done or omitted to be done in good faith while carrying out his or her duties as a member of the HREB

⁴ TCPS Section 7

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HREB members are provided liability insurance through the HREA.

13. Resources

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS), 2nd edition.

ICH-Good Clinical Practice

Code of Federal Regulations (CFR) Title 45, Part 46

Health Canada, Food and Drug Act, Section C, Division 5.3

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The purpose of this policy is to describe the employees of the Research Ethics Office (REO) and the responsibilities and accountability of the Ethics Officer (EO) and staff. The Ethics Office is responsible for administrative support to the HREA Board of Directors and to the HREB.

1. Ethics Officer (EO)

a. Accountability:

The EO is accountable to the HREA

b. Duties and Responsibilities:

The EO is responsible for the management of the Research Ethics Office (REO).

The EO:

- Provides administrative support to the HREA and overall management of the staff of the REO
- Prepares an annual report for the HREA
- Prepares an annual budget for the HREA
- Provides liaison – information and assistance – with researchers, research staff, sponsors, regulators
- Manages the application process
- Coordinates orientation and educational activities (with Chair and Vice Chair)
- Coordinates monitoring activities (with Chair, Vice Chair and Monitor)
- Sits as a member of the Policy Advisory Group
- Sits as an *ex-officio* member of the HREB

The full description of the duties of the EO and qualifications are provided in Appendix 5.1

2. Administrative Support:

In addition to the EO the Office has three full time, permanent, administrative support staff: an ethics coordinator for each of the research ethics review subcommittees and a receptionist.

a. Ethics Coordinators

There are two ethics coordinators providing administrative support for the two research ethics review subcommittees: HREB-CT and HREB-NCT.

The ethics coordinators are accountable to the EO.

The duties of the ethics coordinators, for each of the HREB subcommittees, include

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- Coordinating daily activities, as necessary, with the EO

 - Coordinating daily activities, as necessary, with the appropriate chair of the HREB subcommittee
 - Providing administrative support for the chair of the HREB subcommittee including booking appointments, preparing correspondence, etc.
 - Attending and providing administrative support (clerical and hosting) to the bi-weekly meetings of the HREB subcommittee
 - Taking and transcribing minutes from the subcommittee meetings
 - Composing draft correspondence from minutes regarding decisions of the subcommittee meetings
 - Compiling the bi-weekly agenda packages for the subcommittee meeting
 - Responding to written, email, telephone and in-person inquiries regarding the subcommittee meeting
 - Providing liaison – information and assistance – with researchers, research staff, research offices (*e.g.* the Patient Research Centre of Eastern Health) sponsors, regulators
 - Coordinating information, orientation and educational sessions and workshops as requested
 - Updating the website as required

The full description of the duties of each of the ethics coordinators and qualifications are provided in Appendices 5.2 and 5.3

b. Receptionist

The receptionist is accountable to the EO.

Duties of the receptionist include

- Acknowledging receipt of applications from investigators and assigning reference numbers to applications.
- Maintaining a database of applications
- Distributing and tracking ethics renewals
- Preparing letters, memoranda and forms from rough draft and/or dictating equipment.
- Assisting in preparation of agenda packages for meetings
- Photocopying agenda items and other related documents for the HREB subcommittees.
- Answering and directing calls and enquiries made by phone, email or in-person.
- Maintaining the manual filing system.
- Ensuring delivery of meeting agenda packages.
- Ordering office supplies and catering items.
- Opening and distributing mail as appropriate.
- Attend meetings and take notes/minutes in the absence of either HREB subcommittee ethics coordinator.

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The description of the position of the receptionist and qualifications is provided in Appendix 5.4

Appendix 5.1 Position Description for Ethics Officer

Position - Ethics Officer

Based on the Eastern Health HL – 25 classification⁵

This position is responsible for the operations and management of the Research Ethics Office of the Health Research Ethics Authority and the Health Research Ethics Board. This position reports to the Chair of the Board of HREA.

Responsibilities

- Management of the Research Ethics Office (REO)
- Management of financial activities of the REO and the HREB including preparation of the annual budget; oversight of billing to Memorial University, Eastern Health, pharmaceutical companies; signing authority for the REO; management of monthly statements
- Provision of liaison – information, assistance - with researchers, research staff, sponsors, regulators
- Oversight of the management of application process
- Coordination and implementation of orientation and educational activities for HREB members including orientation sessions, seminars, workshops and any visiting-speakers
- Coordination of monitoring activities excluding those conducted through the Monitoring Program (see Section 10 of this policy manual)
- Drafting of annual report to HREA
- *Ex-officio* member of HREB
- Member of the Policy Advisory Group of the HREB

Qualifications

- Research based MSc or equivalent training and experience
- Excellent writing and presentation skills
- Excellent communication skills (telephone, email, paper)
- Excellent computer skills
- Extensive experience in financial record keeping
- Management experience

⁵ The current Ethics Officer was formerly employed by Eastern Health. In future, the EO may be employed by the HREA. The major elements of this job description will apply but there may be minor revisions.

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Preference will be given to persons with knowledge of research ethics and protection of privacy.

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Appendix 5.2 – Position Description for Ethics Coordinators to HREB-Clinical Trials subcommittee

Position - Secretary to HREB – Clinical Trial Subcommittee (HREB-CT)

Classification – Memorial University Intermediate Secretary ⁶

Job Duties:

- Coordinate daily activities, as necessary, with the Chair of the HREB (Chair of the HREB-CT) and the EO
- Attend bi-weekly HREB-CT meetings
- Take and transcribe minutes from the HREB-CT meetings
- Compose draft correspondence from minutes regarding decisions of the HREB-CT meetings
- Compile the bi-weekly agenda packages for HREB-CT
- Respond to written, email, telephone and in-person inquiries regarding HREB-CT
- Set up for bi-weekly meetings of HREB-CT
- Oversee hosting for the bi-weekly HREB-CT meeting, including ordering, placing and receiving food.
- Book rooms, send notices or invitations for orientation sessions, seminars, workshops and any visiting-speakers
- On the direction of the EO provide liaison with the Patient Research Centre, Research Nurse Coordinators and Principal Investigators as necessary
- Book appointments on behalf of the Chair of HREB-CT
- Query data base as required.
- File and access files as required
- Update website as required

Qualifications

- Considerable experience (3-5 years) in secretarial work
- Graduation from high school supplemented by courses in business education or secretarial science or any equivalent combination of experience and training
- Knowledge of Microsoft Office, in particular demonstrated ability to work in MS Access would be an asset
- Knowledge of web management software
- Shorthand and/or the ability to take minutes of meetings is **essential**
- Good oral and communication skills are **essential**
- Ability to work under strict deadlines

⁶ The current staff are employed by Memorial University. In future, staff may be employed directly by the HREA. The major elements of this job description will apply but there may be minor revisions.

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-
- Ability to work in a strictly confidential environment
 - Knowledge of Medical Terminology would be an asset

Appendix 5.3 – Position Description for Ethics Coordinators to HREB - Non Clinical Trials subcommittee

Position - Secretary to HREB – Non-Clinical Trial Subcommittee (HREB-NCT)

Classification – Memorial University Intermediate Secretary⁷

Job Duties:

- Coordinate daily activities, as necessary, with the Vice Chair of the HREB (chair of the HREB-NCT) and the EO
- Attend bi-weekly HREB-NCT Committee meetings
- Take and transcribe minutes from the HREB-NCT meetings
- Compose draft correspondence from minutes regarding decisions of the HREB-NCT meetings
- Compile the bi-weekly agenda packages for HREB-NCT
- Respond to written, email, telephone and in-person inquiries regarding HREB-NCT
- Set up for bi-weekly meetings of HREB-NCT
- Oversee hosting for the bi-weekly HREB-NCT meeting, including ordering, placing and receiving food
- On the direction of the EO provide liaison - information, assistance - with researchers and research staff
- Book appointments on behalf of the Chair of HREB-NCT committee
- Query data base as required.
- File and access files as required
- Update website as required

Qualifications

- Considerable experience (3-5 years) in secretarial work
- Graduation from high school supplemented by courses in business education or secretarial science or any equivalent combination of experience and training
- Knowledge of Microsoft Office, in particular demonstrated ability to work in MS Access would be an asset
- Knowledge of web management software
- Shorthand and/or the ability to take minutes of meetings is **essential**
- Good oral and communication skills are **essential**

⁷ The current staff is employed by Memorial University. In future, staff may be employed directly by the HREA. The major elements of this job description will apply but there may be minor revisions.

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-
- Ability to work under strict deadlines
 - Ability to work in strictly confidential environment
 - Knowledge of Medical Terminology would be an asset

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Appendix 5.4 – Position Description for Clerk Receptionist

Position - Clerk Receptionist

Classification – Memorial University Intermediate Clerk Stenographer⁸

Job Duties:

- Acknowledge receipt of applications from Investigators. Assign reference numbers to applications
- Maintain a database. Performing data entry duties regarding the inputting of information into the database
- Generate reports from the database on a monthly basis and as requested
- Distribute ethics renewal notifications to Investigators. Track ethics renewal applications for non-responders
- Prepare and type letters, memoranda, and other forms either from rough draft and/or dictating equipment
- Assist in preparation of bi-weekly agenda packages for meetings
- Photocopy agenda items/other related documents for the Health Research Ethics Authority.
- Answer telephone/in-person inquiries
- Maintain a manual filing system
- Ensure delivery of meeting agenda packages
- Order office supplies/catering items
- Open/distribute mail as appropriate
- Take minutes and transcribe oral dictation for the Appeals Panel
- Attend meetings and take notes/minutes in the absence of either HREB subcommittee Coordinator

Qualifications:

- Experience in moderately difficult and varied clerical work
- Graduation from high school, including and/or supplemented by courses in business education and computer skills
- Knowledge of Microsoft Office, in particular MS Access
- Demonstrated ability working with databases, in particular MS Access
- Ability to work in strictly confidential environment
- Ability to work under strict deadlines
- Require excellent oral communication skills

⁸ The current staff is employed by Memorial University. In future, staff may be employed directly by the HREA. The major elements of this job description will apply but there may be minor revisions.

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-
- Ability to take and transcribe oral dictation, if necessary
 - Ability to deal with the public tactfully and courteously
 - Knowledge of Medical Terminology would be an asset

Functions of the Health Research Ethics Board (HREB)

Section 6

Health Research Ethics Board
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The purpose of this policy is to describe the function of the HREB and the roles of the HREB research ethics review subcommittees⁹, HREB-CT and HREB-NCT.

1. Functions of the HREB

As described in Section 5 of this Policy Manual the HREB will have two subcommittees (HREB-CT and HREB-NCT) responsible for ethics review and continued oversight of health research protocols involving humans following provincial, national and international legal, ethical and regulatory standards as described in Sections 1 and 2 of this Policy Manual. The subcommittees are responsible to approve research applications, approve research applications subject to changes or refuse to approve research applications.

2. Review

Proportionate approach: The subcommittees will provide a proportionate approach to the review of research studies based on the general principle that the more invasive the research, the greater should be the care in assessing the research.

Regular meetings: The subcommittees shall meet regularly face to face, and on occasion include electronic conferencing.

Record keeping: Minutes of all meetings of the subcommittees shall be prepared and maintained by the REO staff. The minutes shall clearly document each committee's decisions and any dissents, and the reasons for them. In order to assist internal and external audits or research monitoring and to facilitate reconsideration or appeals, the minutes must be accessible to authorized representatives of the institution, researchers and funding agencies.

Decision making: The subcommittees will meet to review proposed research not delegated to expedited review. Each subcommittee shall function impartially, provide fair hearing and provide reasoned and appropriately documented opinions and decisions. Each subcommittee shall accommodate reasonable requests from researchers to participate in discussion of their studies. When considering a negative decision, the subcommittees shall provide the researcher with the reasons for doing so and give the researcher opportunity to respond before making a final decision.

Reconsidering a decision: Researchers have a right to request that the subcommittee reconsider a decision affecting the specified research project.

⁹ HREA Act; Section 7 (7) The research ethics board may appoint one or more subcommittees composed of its members and those subcommittees have all the powers conferred on the board by this Act

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Appeals: When researchers and the subcommittee cannot reach agreement through discussion and reconsideration, a decision may be reviewed by an Appeal Board (See Section 16 of this Policy Manual).

Conflicts of interest or bias: When reviewing research in which a member of the subcommittee has a personal interest or bias (as researcher or entrepreneur), the member may not be present when the subcommittee is discussing or making its decision (see Section 19 of this Policy Manual).

3. Continuing oversight

Annual ethics renewal Research studies are normally approved for one year and require annual verification that no changes have occurred since the previous annual review.

Approval of changes in research An investigator shall not make changes to a project in health research approved by one of the subcommittees without first submitting the proposed changes to the subcommittee and obtaining approval for the changes **except** where necessary to eliminate immediate hazards to the human subjects.

Audit of approved studies The HREB, through its Monitoring Program may conduct, at any time, a review of an approved study.

4. Review of serious concerns reported by investigator

Suspicion of wilful or voluntary scientific or ethical misconduct on the part of the principal investigator or a member of the study team will result in a report from the HREB to Health Canada in the case of a clinical trial and to all other appropriate organizational officials in the case of both clinical trials and non-clinical trial studies.

The subcommittee's approval shall be suspended until an investigation is completed. If a determination of scientific or ethical misconduct is made reports will be forwarded to appropriate organizational officials, research sponsors, research funding agencies, professional associations and regulatory bodies.

5. Suspension or termination of approval

The subcommittee may suspend a project when it is believed that

- the health research being conducted does not conform to the research project approved
- record keeping associated with the project is inadequate
- conduct towards human subjects involved in the research project is improper

The subcommittee may suspend the research project until the deficiencies identified have been corrected or the subcommittee may cancel the research project.

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Research cannot continue after suspension or termination of approval

References: TCPS2: Tri-Council Policy Statement: *Ethical Conduct for Research Involving Humans*, December 2010

Operations of the Health Research Ethics Board (HREB)

Section 7

Health Research Ethics Board
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The purpose of this policy is to describe the operational activities of the Health Research Ethics Board (HREB) and its research ethics review subcommittees, the HREB-CT and HREB-NCT. A list of Standard Operating Procedures (SOPs) of the REO is given on page xx of this manual and is available in the research ethics office (REO).

1. Submission of Applications

Persons intending to engage in health research involving human subjects shall submit an application for approval to the HREB

2. Assignment of Review Subcommittee and Reviewer

All clinical trial of drugs and devices applications shall be reviewed by the HREB-CT.

The Ethics Officer or designate will assign a reviewer for the application from among the committee membership.

3. Meetings

The members of the research ethics review subcommittees of the HREB meet face to face in regularly scheduled meetings which may occasionally include videoconferencing. These meetings occur every two weeks throughout the year.

4. Quorum

In order to achieve the meeting quorum, a majority of the appointed positions of the research ethics review subcommittees must be present. A position may be shared by more than one person. The core constituencies include research, legal, ethical, science and non-science, community and a person external to the organization or institution in which the research is being conducted. All constituencies must be represented and present at the meeting.

If a clinical trial is under review, the quorum for HREB-CT must include two clinicians.

5. Guidance for Applicants

- a. **Pre-application:** Information, guidelines and forms are available on the HREA website (<http://www.hrea.ca>) to help investigators prepare an application. The REO staff and HREB Chair and Vice Chair are available to answer questions regarding a proposed application.

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-
- b. **Screening and submission of applications:** Applications are screened by the staff of the REO and required revisions communicated to the investigator before acceptance of applications to be sent for review.

6. Determining level of review

All applications submitted are reviewed by the Chair of the HREB and/or the EO and assigned to one of three levels of review: **exempt, expedited, full review.**

- a. **Exempt:** Studies that meet the TCPS2 criteria for exemption will be classified as exempt from HREB review.³ *In general*, these are studies involving quality assurance or program evaluation, case studies, and publicly available data.
- b. **Expedited:** If, during the screening process, a research project is considered to be of no more than minimal risk the application may be sent for expedited review.
- c. **Full review:** The application is reviewed by committee at a regular meeting.

Regardless of the level of review, the ethical requirements for approval do not change; these requirements are applicable to all research involving human participants.

7. Determining requirement for written informed consent

The research ethics review subcommittee (HREB-CT or HREB-NCT) will be responsible for assessing the consent requirements.

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

The research ethics review subcommittee may waive the requirement to obtain informed consent based on the guidelines of the applicable regulations and guidance documents.

8. Approval

Applications which are reviewed by full subcommittee (HREB-CT or HREB-NCT) are granted approval by majority vote of the members present of a duly constituted meeting.

9. Appeal of HREB decisions

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Decisions of HREB to not approve or to rescind approval of research on ethical grounds can be appealed only on the basis of error of process, conflict of interest. (See Section 16 of the Policy Manual - Appeals)

10. Oversight and monitoring

Ongoing review of approved studies is provided for the protection of the rights and wellbeing of persons who volunteer as participants in research. Part of this oversight requires renewal of ethics approval at least annually.

Studies which have been approved by the HREB are subject to random auditing through the Monitoring Program. (See Section 10 of the Policy Manual)

11. Confidentiality of documents and materials

All materials and correspondence received and reviewed by the HREA/HREB and the research ethics review subcommittees and all documentation directly related to a research application will be maintained in strict confidence; held in a secure environment and shared only with those people that are required to have access to the materials in the performance of their duties or as may be required by law.

All persons having access to the confidential materials of the HREA/HREB will be required to sign an Undertaking of Confidentiality before such access can be provided.

Requirements for Documentation-Health Research Ethics Board

Section 8

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The purpose of this policy is to outline the requirements for the documentation of HREB activities, including the research ethics review subcommittees, HREB-CT and HREB-NCT.

1. Minutes

The HREB subcommittees shall prepare and maintain documentation of their activities including minutes of meetings which shall be in sufficient detail to show:

- Members voting and non-voting in attendance at meetings with times of late arrivals and early departures.
- Actions taken by the research ethics review subcommittees to recommend: approval, approval with modification, deferral pending revisions and refusal to approve and the vote on these actions including the number not voting for conflict of interest.
- The name of any member absenting him/herself from the protocol discussion and vote for conflict of interest.
- The name of any member wishing to have their dissenting vote recorded.
- The name of any member abstaining from the vote who wishes to have their abstention recorded.
- The basis for deferral, failure to approve or the requirement for changes.
- Any recommendation for more frequent than annual ethics renewal or progress reports.

2. Records

The staff of the EO shall prepare and maintain adequate documentation of HREB membership [HREB-CT and HREB-NCT] and activities for the periods specified in Health Canada and the US FDA regulations as well as any institutional policies.

The retention period will be set as the time from the completion of the research.¹ Records shall be accessible for inspection by the person implementing the HREB monitoring program or authorized representatives of the sponsor and federal agencies.

All correspondence and documentation except clinical trials shall be kept for a period of ten years. Documents relevant to clinical trials will be retained for a period of 25 years; only those documents not otherwise retained by the investigator will be archived.

In general, for each application reviewed by the HREB, retained records shall include:

- The full HREB application and consent documents, accompanying questionnaires, diaries, interview scripts, etc. where relevant;
- Copies of all correspondence between the HREB, the investigators, any external reviewers and sponsors, where applicable.
- Forms and notes concerning the initial and ongoing reviews, amendments, ethics renewals and the report from the Monitoring Program, where applicable.

Requirements for Documentation-Researcher/Applicant

Section 9

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The purpose of this policy is to describe the documentation required from the researcher/applicant to make application for ethics review and to maintain approval of health research.

Application for ethics review and approval is made by the **principal investigator (PI)** or by the industry **sponsor** (or designate) for industry-sponsored clinical trials. The applicant assumes responsibility for

- Submitting the Notification of Submission for Ethics Review form and the application package to the Ethics Office
- Responding to queries and corresponding in a timely manner
- Maintaining the project in good ethical standing
- Immediately reporting any unanticipated events

In the event of thesis research, the student will make application for the project and will serve as PI. It is required that the student's supervisor review the application with the student with regard to completeness, clarity, readability and editorial mistakes.

1. Application documentation

- a. The applicant will complete and forward directly to the HREA the Notification of Submission for Ethics Review form.
- b. Applicants must submit a complete application package as per the Application Guidelines found on the HREA website (<http://www.hrea.ca/>)
- c. Principal investigators who are making a *first time* submission to the HREB must include
 - a current *curriculum vitae*
 - TCPS tutorial certificate indicating successful completion or documented equivalent as indicated in Application Guidelines.

2. Post Approval Documentation

a. Ethics renewal

- Ethics renewal is required annually, on the anniversary of the date of the HREB notification of approval; it may be required more often.

Requirements for Documentation-Researcher/Applicant Section 9

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- Application for ethics renewal must be completed on the Ethics Renewal form (<http://www.hrea.ca/>)
 - For multi-site studies, the Ethics Renewal form is to be completed by the applicant (or designate) for each of the individual sites in NL.
 - Deviations and waivers in studies under the jurisdiction of Health Canada must be reported by the site investigator in the application for ethics renewal.

b. Protocol Amendments

Any proposed change in the conduct of a study **must** be submitted to the HREB office on the Amendment Form and approved, by the research ethics review subcommittee, **before** the change may be implemented. Such changes might include modification of recruitment procedures or inclusion or exclusion criteria, addition or deletion of study sites, changes to an intervention, consent forms, questionnaires or scripts (etc), and personnel. Amendments to the approved protocols which request major changes or contain new information that could increase the risk to participants are referred to the full research subcommittee (HREB-CT or HREB-NCT) that approved the original study, for review and vote.

c. Other reports required by the HREB

Serious and unanticipated adverse events that occur within NL are required to be reported to the HREB by the local investigator. Such an event may occur in both clinical trials and in other types of research, e.g. collapse during a rehabilitation program, emotional breakdown requiring follow up care during an interview, breach of privacy during correspondence in a genetics study.

For clinical trials the following additional reports are required¹⁰:

- *Safety reports* providing information on all serious adverse events (SAEs) occurring in a clinical trial of drugs and devices must be provided by the sponsor to the HREB normally on a three or six monthly basis.
- All *SAEs occurring at local sites* must be reported to the HREB by the site investigator
- *Deviations* from or *protocol changes* to eliminate immediate hazards to study participants do not require prior approval but must be reported to the HREB by the local site investigator as soon as reasonably possible. In the case of studies under the jurisdiction of Health Canada reporting must comply with ICH guidelines.

¹⁰ See Section 18 of this Policy Manual: Management of Serious Adverse Events and Safety Reports

Monitoring Section 10

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The purpose of this policy is to describe the terms of reference for the on-going review and monitoring of protocols approved by the HREB.

1. Responsibilities of the HREB and HREA

The HREB and the HREA are responsible for ensuring ongoing review (monitoring) of protocols approved by the research ethics review subcommittees. There are four categories of review:

2. Mandate

Monitoring provides both routine review of studies renewing ethics approval and detailed review of approved studies selected at random among protocols that are judged to impose participants to greater than minimal risk and for cause as requested by the HREB subcommittees.

Random audit or audit for cause does not include validation of research data records. It is focused on the review of documentation, the consent process, safety measures including laboratory requirements in relevant studies, protection of privacy, and, when appropriate, witnessing of the consent process and assessment of availability of the research team to subjects

Routine review by the subcommittees and the Research Ethics Office

- a. Routine review of non-clinical trial studies on at least an annual basis as part of the renewal of ethics approval. This review is the responsibility of the Chair or designate
- b. Routine review on at least an annual basis as part of the ethics renewal of clinical trials under the applicable regulations. This review is the responsibility of the full membership of the HREB-CT.

Random and for cause audit by the HREA monitor/s

- c. Review of a random sample of approved and implemented protocols that are judged to impose participants to greater than minimal risk.
- d. Review of approved and implemented protocols for cause as referred from the HREB subcommittees.

3. Appointment of the HREA monitor/s

The person(s) responsible for conducting the random and for cause audits is/are appointed by the HREA. Persons appointed to implement the HREA's Monitoring Program must have served at least one term on a TCPS-compliant REB.

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4. Accountability

The HREA monitor(s) will provide a preliminary report to the principal investigator of the study under review for feedback and discussion. A final written report on each case is provided to the investigator, the HREB subcommittees and the HREA Board of Directors.

Policy Advisory Group (PAG) to the Health Research Ethics Board
Section 11

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The purpose of this policy is to describe the terms of reference for the Policy Advisory Group (PAG) of the HREB.

1. Mandate

The PAG responds to requests from the staff of the Research Ethics Office and the Chair and Vice-Chair of the HREB. It also acts in response to new legislation, regulations and guidelines arising within federal and provincial jurisdictions, and international regulatory bodies. The Group regularly reviews previously approved HREB policies and Standard Operating Procedures.

The Chair of the HREB will approve and sign off on the policies developed by the PAG.

2. Appointment

The PAG is appointed by the HREB on the recommendation of the HREB Chair and Vice-Chair and the Ethics Officer (EO).

3. Membership

The PAG comprises the Chair (or Vice Chair) of the HREB, the EO and current or past members of the Human Investigations Committee (Memorial University)/HREB. All members must have had at least one year of experience on a TCPS-compliant REB or have equivalent research ethics experience.

Normally, membership shall not exceed eight members reflecting a diversity of background and experience.

4. Additional assistance to the Group.

The PAG may recruit or appoint groups to support its work.

The PAG, at its discretion, may co-opt or seek the opinion of persons on an *ad hoc* basis to help with specific tasks requiring special expertise. These persons need not have served on an REB.

5. Term of appointment

The term of appointment for members and for the Chair will normally be for three years but may be extended for an additional term.

6. Selection of Chair

Policy Advisory Group (PAG) to the Health Research Ethics Board
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The Chair of the PAG is chosen by the Chair of the HREB from among PAG members.

7. Meetings

The PAG meets regularly throughout the year. Special meetings may be called by the PAG Chair or the Chair of the HREB and may be requested by any member of PAG

8. Decisions

The decisions of PAG will be guided by the TCPS2 and GCP (or any guidance document superseding these) together with any federal or provincial legislation or regulations relevant to the work of the HREB. Decisions are normally by consensus. To ensure regular meetings despite the absence of one or more members, there shall be a quorum of four people. When fewer than 50% plus one of the members is present, minutes and pending decisions from the meeting will be circulated electronically among all members to obtain consensus.

9. Accountability

The PAG is accountable to the HREB.

A written report on the activities of the PAG is submitted annually to the Board of Directors of the HREA . Copies of all revised or new policies and procedures will be appended to this report.

Consent and Assent to Participate in Research

Section 12

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Revised: (v.2, March 27, 2012)

This policy provides direction on obtaining consent for research.

1. The consent process

Written voluntary and informed consent is required, prior to commencing the research, unless waived by the reviewing subcommittee of the HREB.

Informed consent must be voluntarily given, that is, without manipulation, undue influence or coercion. Evidence of consent should ordinarily be obtained in writing. In cases where verbal consent is being obtained as in telephone interviews, the date, time and place of consent must be documented. Where written consent is culturally unacceptable or where there are other good reasons for not recording consent in writing, the procedures used to seek consent must be provided to the HREB subcommittee responsible for reviewing the research protocol.

Research may begin only if prospective subjects or authorized third parties have been given the opportunity to give free and informed consent about participation and their consent has been given and is maintained throughout their participation in the research.

In the case of secondary use of data (part 7a of this section of the Policy Manual) letters requesting access to the data must be submitted with the application. If the data holder (custodian) requires ethics approval prior to release of the data, the researcher will submit the application to the HREB subcommittee for provisional review and, when approval from the data holder (custodian) is secured, will resubmit the application and accompanying documentation for final approval.

2. Responsibility to obtain consent

For clinical trials of drugs, devices or medical interventions, obtaining consent is the responsibility of the Principal (qualified) Investigator. .

For other research projects delegation of the responsibility to obtain consent must be identified in the application and approved by the HREB-NCT subcommittee.

3. The Consent Form Document

Researchers are required to use the appropriate consent template (clinical trials or general studies) as well as any standard wordings.

Researchers or their designated representatives shall provide the prospective participants with:

- a. information that the person is being invited to participate in a research study;

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- b.** an understandable statement of the research purpose, the identity of the researchers, the identity of any funder or sponsor, the expected duration and nature of participation, a description of research procedures, and an explanation of the responsibilities of the participant;
- c.** an understandable description of reasonably foreseeable harms and benefits;
- d.** an assurance that prospective participants are under no obligation to participate; have the right to withdraw at any time without prejudice to pre-existing entitlements; and throughout the course of the research will be given, in a timely manner, information that is relevant to their decision to continue or withdraw from participation;
- e.** information concerning 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;
- f.** the identity of the qualified designated representative who can explain scientific or scholarly aspects of the research;
- g.** the telephone number and email of the Ethics Office to provide for contact regarding possible ethical issues in the research;
- h.** an indication of who will have access to information collected on the identity of subjects, descriptions of how confidentiality will be protected, and anticipated uses of data;
- i.** information on the circumstances under which the researcher may terminate the subject's participation in the research;
- j.** information on any costs, payments, reimbursement for expenses or compensation for injury;
- k.** a statement to the effect that, by consenting, participants have not waived any legal rights
- l.** information on the assignment to a research intervention, for example, in the case of randomized trials, the probability of assignment to each option;
- m.** information about (i) foregoing alternative procedures that might be available to the subject, (ii) which aspects of the research involve the use of procedures that are not generally recognized or accepted; and, (iii) particularly in trials of therapeutic

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interventions, the care provided if the potential subject decides not to consent to participation in the study;

- n. the measures to be undertaken for dissemination of research results;
- o. information on participant identification whether direct or indirect;
- p. information that participants will not be identified except in extraordinary circumstances and then only with the express consent of the individual participants;
- q. how the participants will be informed of the results of the research;
- r. when applicable, information on the possibility of loss of confidentiality which could lead to psychological or legal consequences; and
- s. information about the researcher's plan for handling incidental findings which are not anticipated and may have important psychological, social, health-related or other implications for the participant but are not the focus of the research itself.

4. Reading level

The language used in the oral and written information about the research, including the written informed consent form, should be as non-technical as practical and should be understandable to the participant or the participant's legally acceptable representative and, where applicable, the impartial witness. Language will normally be at less than Grade 9 level. Aids to writing in plain language can be found on the HREA website (<http://www.hrea.ca>).

5. Research involving emergency health situations

Research involving emergency health situations shall be conducted only if it addresses the emergency needs of the participant and is in accordance with criteria established in advance by the HREB subcommittee. Research involving health emergencies can be carried out without the free and informed consent of the participant or the authorized third party if **ALL** of the following apply:

- a. a serious threat to the prospective subject requires immediate intervention;
- b. either no standard effective care exists or the research offers real possibility of direct benefit;

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- c. either the risk of harm is no greater than that of standard care or it is justified by the direct benefits to the subject;
 - d. the prospective subject is unconscious or lacks capacity to understand the risks, methods and purposes;
 - e. third party authorization cannot be secured in sufficient time despite diligent efforts and
 - f. no relevant prior directive is known to exist.

If the participant regains capacity or an authorized third party is found, free and informed consent shall be promptly sought.

6. Special populations

Special consideration must be given to the following populations when obtaining consent for participation in research. Ethical issues are to be addressed in the application and a detailed description of the proposed consent process must be submitted to the research ethics review subcommittee for consideration

a. Children

It is expected that any intervention to be tested in children will have been previously studied in adults and that the investigator will document that this is the case in the application. The committee will consider, on a case-by-case basis, the consent process proposed.

The rationale for considering the potential participant a ‘mature or emancipated’ minor must be provided by the investigator.

Mature minors: A mature minor¹¹ is defined as a child who is capable of giving consent to or refusing participation in research, and is able to appreciate the nature and consequences of the consent or refusal. Mature minors are considered to have the same capacity as competent adults and they can provide informed consent. In general, assent,

¹¹ In Newfoundland and Labrador, the official age of majority is established by statute to be 19 years of age. Persons below the age of majority are said to be “minors”. Just because an individual is a minor does not preclude that person from being able to provide consent to participate in research. In fact, individuals under the age of 19 are frequently considered to be able to give an informed consent. The age of consent for minor individuals is not dictated by statute.

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rather than consent, is required for research involving children up to age 19 (see Part 9 in this section of the Policy Manual: Assent for children). However, the “mature minor” principle may be followed and, in fact, may be more appropriate than assent, for low risk research involving older adolescents. Researchers wishing to obtain consent, rather than assent, from research participants who are mature minors must justify this request to the research ethics review committee.

Emancipated minors (e.g., by marriage or parenthood): Emancipated minors are considered to have the same capacity as competent adults and they can provide informed consent.

A description of assent/dissent for children is provided in Part 9 of this section of the Policy Manual.

b. Persons temporarily or permanently cognitively impaired

Individuals who are not legally competent shall only be asked to become research participants when:

- i. the research question can only be addressed using individuals within the group identified for study and there is potential benefit for these individuals
- ii. free and informed consent is obtained from their authorized representatives and
- iii. the research does not expose participants to more than minimal risks without the potential for direct benefits for individual participants

A description of the assent is provided in Part 10 of this section of the Policy Manual.

c. Persons in power relationships

The influence of power relationships on voluntary choice should be judged according to the particular context of prospective participants. The voluntariness of prisoners, members of organizations with authoritarian structures, employees or students may be restricted because their institutional context implies some constraint to follow the wishes of those who have some control over them. This control may be physical, financial or professional. There can be no voluntariness if consent is secured by the order of authorities, the most explicit exercise of undue influence. Particular attention should be paid to the elements of trust and dependency within doctor-patient or professor-student relationships.

d. Aboriginal communities

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There are special considerations of consent in studies involving aboriginal populations. It is expected that the investigator shall document his/her proposed adherence to the Canadian Institutes of Health Research (CIHR) guidelines for work with aboriginal persons/populations¹².

7. Clinical Trial Substudies

The following policies apply to clinical trial substudies involving genetic testing or biomarker research:

- a. Genetic testing and biomarker studies that are included in the purpose or the primary and/or secondary objectives of a study can be described in the main consent form (see template: *Consent to Take Part in a Clinical Trial*).
- b. A separate consent (see template: *Consent for Clinical Trial Substudies*) is required for participation in a clinical trial substudy; this consent will be optional for participants. Participation in a substudy cannot be a requirement for taking part in the main study.
- c. A separate consent (see template: *Consent for Clinical Trial Substudies*) is required for the release of anonymous study samples to a biobank for use in future studies. Such future studies will require approval by an REB.

8. Circumstances where the requirement for informed consent may be waived by the research ethics review committee of the HREB

In general, the HREB subcommittee may waive the requirement for informed consent if ALL of the following situations apply:

- a. the research involves no more than minimal risk to participants;
- b. the waiver is unlikely to adversely affect the rights and welfare of participants;
- c. the research could not practicably be carried out without the waiver;
- d. whenever possible and appropriate the participants will be provided with additional pertinent information after participation and
- e. the study does not involve a therapeutic intervention

¹² Canadian Institutes of Health Research. *CIHR Guidelines for Health Research Involving Aboriginal People*. May 2007. www.cihr-irsc.gc.ca/e/29134.html
TCPS2, Chapter 9, December 2010

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The most frequently granted waivers are for studies involving:

a. Secondary use of data

Many studies employ databases or records containing identifiers, collected for other purposes, to obtain lists of persons for recruitment or to access data to answer a research question without consent. These proposed uses of data with personal identifiers must be submitted to the HREB subcommittee and will be reviewed, on a case by case basis.

In its role of supporting the principles of privacy protection, the HREB requires, in all such cases, documentation of approval of access and of protection of data¹³ from the data guardian (custodian). Such documentation must include copies of the letters requesting data/records, including a list of the information requested or to be abstracted, and the data holder's (custodian's) approval of access to the data/records. These letters must be submitted with the application. If the data holder (custodian) requires ethics approval prior to release of the data, the researcher will submit the application to the HREB subcommittee for provisional review and, when approval from the data holder (custodian) is secured, will resubmit the application and accompanying documentation for final approval.

The investigator is required to put in place the normal protections for data¹⁴ including locked storage of paper files; password protected computer files and signed oaths of confidentiality of all members of the research team. More rigorous measures may be appropriate for more sensitive data or large databases.

b. Chart review

The HREB subcommittees generally waive written informed consent for chart review involving no contact with participants; for the secondary use of medical record databases such as admission/discharge or laboratory data; and for computerized medical records. However, the proposal for waiver must be fully justified by the investigator and the investigator must document the measures which will be taken to protect privacy.

c. Naturalistic observation

¹³ Personal health information as defined in Section 5(1) of the *Personal Health Information Act* refers to identifying information in oral or recorded form relating to physical or mental health of an individual or any of the transactions involving the provision of care.

¹⁴ Best Practices for Protecting Privacy in Health Research. <http://www.cihr-irsc.gc.ca/e/22085.html>

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Approval for naturalistic observation without consent may be granted on a case by case basis with attention given to the nature of the activities to be observed, the environment of the observation and the means of recording the observations and the planned privacy protections.

d. Research about organizations such as governments or corporations

Such institutions may refuse to cooperate or deny access to records but they need not be approached for consent. Individuals within these institutions who are approached to participate in a research project about their organizations must give individual consent.

9. Circumstances where an altered consent process may be approved by the HREB

The HREB subcommittees will review, on a case by case, basis, studies where the consent process may be altered. Such studies must be of minimal risk to the participant, unlikely to adversely affect the rights and welfare of participants, impracticable to carry out without the alteration and involving no therapeutic intervention. Such studies include:

- a.** research where full disclosure of information may influence the responses of the subject and thus invalidate the research. In such cases, debriefing should be proportionate to the sensitivity of the issue;
- b.** research in emergency health situations as noted previously;
- c.** anonymous surveys where completion and return of a survey in either hard copy or through an electronic format are considered to provide an implied consent;.
- d.** research involving telephone interviews where documented verbal consent may be acceptable.

10. Assent/dissent for children

Assent

It is essential that the researcher obtain the assent of the child and the consent of the parents before including a child in research. Assent depends on the child's age, maturity level, and developmental level. It is usually obtained after obtaining consent from the parents. However, the best moment to ask for assent will probably vary depending on the child's age and the family's style of communication.

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Like consent, assent is a process. Assent may vary over the course of the project; researchers should describe in the application the mechanisms they have put in place for ongoing confirmation of parental consent and participant assent.

Assent forms for children must be short, simple and separate from the main consent form and follow the general HREB guidelines for plain language¹⁵. The scope of the information to be communicated may vary depending on the child's maturity and the nature of the information, e.g. the social risks of research may be too complex to explain. However, collection of biological samples must be explained.

The person obtaining assent must be familiar with both the research project and the assent process. In the guardian's presence, that person may read the form out loud to the child; the information may be adapted, with more or less information provided, depending on the child's age, maturity and development¹⁶. If able to write, the child must write his/her name at bottom of the assent form; otherwise the form should indicate that the child has verbally assented. A copy of the assent form is given to the child and to the parent or guardian.

Dissent

In cases where parents consent but a child dissents verbally or by body language, the dissent must be respected to the extent that the child understands the nature and consequences of the research. It is possible to disregard a child's refusal if he/she is too young or immature or

¹⁵ Forms specific for age groups are being developed. Currently (April 2011) researchers are asked to use the assent template attached to the main consent form.

¹⁶ As a general rule of thumb, the age of the child can be used as the determinant of the type of information to provide, with information adapted to more or less information depending on the maturity of the child, as follows:

(Adapted from, Best Practices for Health Research Involving Children and Adolescents, Denise Avard et al, <http://www.pediagen.org/resources/BestPractices.pdf> <accessed April 1, 2011>)

Ages 0-5: There is no formal assent process, unless a mature pre-school age child can understand some information verbally and express verbal assent.

Ages 6 – 13: There is a specific assent form for this age range (under development). During the assent discussion adapt the information explained verbally to the child according to child's capacities. In general a Grade 3 reading level is appropriate for this age range.

Ages 14 – 19: There is a specific assent form for this age range (under development); it is probable that this assent form will be very similar to the adult consent form. In general a Grade 6 reading level is appropriate for this age range. During the assent discussion, adapt the information explained verbally to the child according to the child's capacities.

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otherwise incapable of understanding the research project or the risks and benefits of participating or in extraordinary circumstances where the investigator must provide a rationale for the exception.

11. Assent and dissent in other populations

In situations other than emergency room care, it is expected that persons cognitively impaired, temporarily or permanently, will be given the opportunity to assent. Participation, to the extent possible – supported decision making – is encouraged with participants unable to provide full consent but capable of understanding some aspects of the research. Formal consent should be obtained from the substitute decision maker acting on behalf of the potential participant. Dissent, either verbally or in body language, should be respected despite the consent of the substitute decision maker except in extraordinary circumstances where the investigator must provide a rationale for the exception.

Guidelines for obtaining consent and completing the consent template are available on the HREA website: <http://www.hrea.ca>

**Export of Personal Health Information (PHI) to Researchers
Outside Newfoundland and Labrador
Section 13**

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This policy addresses requests to allow Personal Health Information (PHI) to be sent to researchers outside the province of Newfoundland and Labrador.

PHI that is collected in the context of a research project will be retained by the local Principal Investigator and will not be sent outside the province without the express approval of the HREB subcommittee which originally approved it.

Such requests will be reviewed on a case by case basis and for approval, four conditions must be met:

1. the explicit consent of the participant to allow his or her PHI to be entered in a database held outside the province;
2. if relevant, an additional consent to provide personal identifiers for contact in future by the same or new investigators;
3. the approval by the HREB subcommittee of a completed checklist of privacy protections submitted provided by the recipient data guardian and
4. the approval by the HREB subcommittee of the recipient data guardian's plan for succession

Meaning of Signatures Section 14

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This policy provides guidance on the meaning of signatures on applications, annual ethics renewals, protocol amendments and adverse events reports.

1. Initial application

The principal investigator is the principal signing authority. One copy of the initial application must bear the signature of the principal investigator or, in the case of clinical trials, the applicant sponsor or designate.

This signature confirms that the applicant:

- a. agrees to comply with the TCPS2 and/or ICH guidelines and any other applicable document which guide the work of the HREB subcommittee;
- b. will inform the HREB subcommittee of any protocol changes;
- c. will inform the HREB subcommittee of any local serious adverse events considered to be related to an intervention;
- d. will submit, at least annually, application for ethics renewal
- e. understands and agrees to comply with HREB privacy policy (Section 15 of this Policy Manual) and applicable privacy legislation and with the safeguards stated in the application;
- f. understands that the HREB subcommittee may inform sponsors, granting agencies, parent institutions of findings of non-compliance with local and national research ethics policies and
- g. certifies that the information provided in the application is complete and accurate.

2. Documents submitted after initial approval

Normally, the principal investigator will sign all post approval documents such as annual ethics renewals and submissions of protocol amendments, deviations and serious adverse events. However, in the event that the principal investigator plans to be away from the research for more than a two week period, he/she must designate in writing *one* co-investigator who may sign in their absence. A copy of this designation must be sent to the Ethics Office prior to submission of any post-approval document.

Privacy Protection Section 15

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This policy provides the requirements for researchers for the collection, use and disclosure of personal health information (PHI) collected for research purposes. The collection, use and disclosure of PHI in research, under the PHI Act (PHIA) must be approved by the HREB or an approved research ethics body under the HREA Act¹⁷. The policy is guided by federal (PIPEDA) and provincial (ATIPPA, PHIA) legislation and national guidelines (TCPS, CIHR¹⁸).

This policy is based on the Canadian Standards Association (CSA) 10 fair information principles governing the access, use and disclosure of personal health information.

1. The CSA principles are:

- a. Being accountable for privacy protection
- b. Identifying the purposes for which the information will be used
- c. Ensuring consent for collection, use and disclosure of information
- d. Limiting the collection of data to only those elements needed to answer the research question
- e. Limiting the use, disclosure and retention of data to the original or a consistent purpose
- f. Ensuring the accuracy of the information collected, used and disclosed
- g. Implementing safeguards to ensure privacy protection
- h. Ensuring the openness of the policies and procedures implemented to protect privacy
- i. Allowing access to an individual research participant for the purpose of review
- j. Ensuring a mechanism for challenging compliance with privacy policies

2. Documentation required for compliance with the 10 fair information principles

¹⁷ PHIA Section 44: A custodian may disclose personal health information without the consent of the individual who is the subject of the information for research purposes but only where the research project has been approved by a research ethics board or research ethics body under the *Health Research Ethics Authority Act*

¹⁸ See Appendix 15.1: *CIHR Best Practices for Protecting Privacy in Health Research*

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- 1. Accountability:** The site principal investigator¹⁹ is accountable for documenting privacy protection for research participants and their information. The accountability of the principal investigator is evaluated in any monitoring after approval of the study. (See Section 10: Monitoring).
- 2. Identification of purposes:** For primary collection of information and secondary use of data, the principal investigator is required to specify the objectives of the research in his/her application to the HREB subcommittee. For secondary use of data these uses must be consistent with those documented in agreements with the data custodian.
- 3. Consent for collection, use and disclosure:** For most studies where research participants are asked to take part in an intervention, a written consent is required. Secondary use of data does not normally require written consent (see Section 12 of this Policy Manual). The consent will describe what information will be collected, who will be able to access the information, how the information will be used and how the information will be protected.
- 4. Limitation of the information to be collected:** Information to be collected by researchers from participants or from records must be provided to the HREB subcommittee in the application as part of the general summary of the project and must be limited to that required by the research question.
- 5. Limitation of use, disclosure and retention to the original or consistent purpose:** Information to be used, disclosed or retained by the researcher must be limited to that described in the application approved by the HREB subcommittee. Participants are informed of these limitations in the consent form and must indicate permission for any potential future uses of the data. (See Section 12: Consent)
- 6. Assurance of accuracy of data.** Every effort must be made to collect accurate data and to confirm its accuracy if there seem to be inconsistencies.
- 7. Safeguards.** The principal investigator must ensure compliance with the privacy protections required by the HREB subcommittee. These include organizational, technological and physical safeguards.

¹⁹ The site principal investigator is the researcher named as the principal investigator for each NL site in a clinical trial; in other studies there is a single principal investigator responsible for ensuring the protection of the privacy of participants.

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- 8. Transparency.** Transparency is an important component of the protection of personal health information of research participants. The measures taken by the study team to protect privacy must be detailed in the consent process.
- 9. Access to study information by participants.** Research participants who have participated personally in a project are able to access the information collected from them within the time frame for retention of records imposed by agencies and institutions and if the data has not been anonymized for sending to an outside agency.
- 10. Challenging compliance.** Any research participant taking part in a research study may **challenge** any perceived non-compliance with the researcher's stated privacy protections. This challenge would normally go first to the principal investigator of the study as well as to the HREB subcommittee. The HREB subcommittee would request the Monitoring Program to review the study for cause.
- 3. Protection of research participants is addressed in the following HREB documents:**
- Application Form: Multisite Clinical Trials
 - Application Form: General Research
 - Application Form: Secondary Use of Data
 - Consent Template: Multisite Clinical Trials
 - Consent Template: General Research
 - Consent Template: Pharmacogenetic add-on
 - Consent Template: Tissue Banking add-on

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Appendix 15.1: Guidance Document

CIHR Best Practices for Protecting Privacy in Health Research²⁰ in Summary Form

These Privacy Best Practices are intended to provide guidance for the health research community in Canada on the application of fair information principles to research involving personal information, and to assist in the interpretation of the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS) by offering additional detail and practicality.

These Privacy Best Practices do not replace existing laws, policies and professional codes of conduct that apply to certain types of personal information, designated organizations and/or specific kinds of activity.

Privacy Best Practices

The Elements are presented in summary in this section to provide a quick reference for the reader. Full descriptions of each Element along with links to selected excerpts from the TCPS are in the main body of this document as referenced below. .

ELEMENT #1: Determining the research objectives and justifying the data needed to fulfill these objectives

At the outset of the research design process, and as thoroughly as possible given the proposed research method, researchers should:

- identify and document research objectives and questions as a basis for determining what data will be needed;
- anticipate and document research questions related to the primary research objective, which might become relevant after the initial data analyses; and
- anticipate and document likely future uses of the data, including possible collaborations with other researchers or possible commercial uses.

In the case of a *database created for general research purposes*, researchers should define the scope and purpose in a way that will be meaningful for research ethics boards (REBs) and any prospective research participants, even if the boundaries are at a relatively general level. This is an opportunity to be as open and transparent as possible about the proposed research, and to reassure research participants and REBs that although future research purposes are not specified in detail, data management, storage and use will occur within a defined framework, including review and approval by an REB.

If appropriate, setting up an *advisory committee* drawn from the scientific community, other relevant areas (such as ethics, policy, or information technology) and those affected by the condition or health

²⁰ *Best Practices for Protecting Privacy in Health Research (2005) CIHR*
http://www.cihr-irsc.gc.ca/e/documents/et_pbp_nov05_sept2005_e.pdf

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event under study, can assist in defining the scope and strategic priorities for a research project in the context of both short and long-term initiatives.

All potential relevant and useful research questions cannot always be foreseen at the outset of a research project. For example, researchers using *inductive methods* of research may discover an "emergent" research approach through encounters with and in collaboration with research participants. In such research, the development of research questions and procedures is an ongoing process. While planning their research, researchers should attempt to foresee both obvious and emerging issues related to privacy. These should be included in the submission to an REB. Researchers should also document for an REB any amendments to the protocol and consequent privacy protection strategies emerging over the course of the study.

ELEMENT #2: Limiting the collection of personal data

Researchers should plan to collect personal data only as necessary for the research. The amount of personal information collected and the level of identifiability and sensitivity of this information should be restricted to what is necessary to achieve the research objectives.

Consider first whether individually identifiable data are needed, or whether non-identifiable data or aggregate data would serve the research objectives (e.g. data on individuals grouped by age or some other meaningful variable).

For research involving *secondary use of data* for research, if identifiable data are required for the research, direct identifiers should be avoided or concealed, to the extent that is reasonably practical (e.g. as soon as a data linkage has been completed). Data without direct identifiers can be:

- *coded* to allow a trace-back to individuals, by means of:
 - *single-coding* (the researcher has the key to the code to link the research data back to direct identifiers, which are held separately); or
 - *double-coding* (an increased level of confidentiality protection over single coding because the data holder does not give the researcher the key to re-identify individuals); or
- *without a code*, if the capacity to trace the research data or results back to individuals is not required for the research purpose.

Even if the direct identifiers in shared data have been removed or coded, consider how to *minimize the collection or sharing of potentially identifying data elements*.

For *inductive data collection*, for example where open-ended interview techniques are used, the extent of personal data to be collected may not always be foreseeable in detail at the outset of the interview. In these cases, the ongoing negotiation of consent with research participants is the best way to ensure that the privacy of individuals and the community is being appropriately protected.

ELEMENT #3: Determining whether consent from individuals is required

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Voluntary and informed consent from legally competent individuals or authorized third parties is a fundamental principle in research involving humans, and specifically for the use of their personal data.

Under specified circumstances, given a satisfactory rationale by the researcher, an REB may approve the waiver of a consent requirement, or a partial waiver of some elements of a consent requirement. According to TCPS Article 2.1(c), the REB must find and document that:

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

In addition to REB approval, access to personal data for research without consent will be subject to specific legal requirements in relevant jurisdictions.

When a research objective requires the *collection of personal information directly from individuals to whom the data belong and linking to other sources to form a combined file*, consent should be sought for both types of data collection at the time of direct contact with prospective research participants.

For secondary use of data for research, an REB should consider the following factors in determining whether a research proposal meets the requirements for waiver of consent:

- necessity of personal data for the research purposes;
- potential harms and benefits of the research;
- inappropriateness or impracticability of consent;
- expectations of individuals;
- views of relevant groups;
- legal requirements; and
- openness (informing the public).

These factors, and the description in the Elements, expand on TCPS Article 2.1(c)(i)- (iii).

An REB may determine that seeking consent from individuals is *inappropriate* because there is potential harm to individuals from direct contact, or contact with individuals is not permitted under a previous data-sharing agreement, law or policy.

Seeking consent from individuals for the use of their personal data may be considered *impracticable* when there are difficulties in contacting or notifying individuals for reasons such as:

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- the size of the population being researched;
 - the proportion of prospective participants likely to have relocated or died since the time the personal information was originally collected; or
 - the lack of an existing or continuing relationship between prospective participants and the data holder who would need to contact them (e.g. a patient database that does not have a regular follow-up program to maintain a complete and accurate record of changes in registrants' contact information over time); such that:
 - there is a risk of introducing bias into the research because of the loss of data from segments of the population that cannot be contacted to seek their consent, thereby affecting the validity of results and/or defeating the purpose of the study; or
 - the additional financial, material, human, organizational and other resources needed to obtain consent could impose a hardship or burden on the researchers or organization so burdensome that the research could not be done.

ELEMENT # 4: Managing and documenting consent

Consent is an ongoing process that begins upon first contact with prospective participants or authorized third parties, and ends only with the conclusion of their participation in the research or use of their information. Participants should understand that their consent is voluntary, to be obtained without manipulation, undue influence or coercion, and can be withdrawn at any time.

Evidence of initial and ongoing consent and the withdrawal of consent should be *documented* as appropriate for audit and legal purposes.

The majority of research studies use an *opt-in consent*. Opting-in means that prior to the start of the research or data collection, informed individuals give clear indication that they voluntarily agree to participate in the research.

Presumed consent with an opt-out mechanism should be used only when an REB considers prior opt-in consent to be inappropriate or impracticable. A valid opt-out mechanism means that individuals have the opportunity at some time during the research or data collection process to give a clear indication (in writing or orally) that they do not want to be participants in the research or to have their data used in the research. If individuals do not choose to opt-out of the research, their consent is presumed as long as they were given reasonable notice of the research and meaningful opportunity to opt-out.

Collection of data without direct personal identifiers may be necessary or proposed when the research deals with highly sensitive conditions or activities. In such circumstances, consent should be documented but the identity of research participants should not be linkable to their data or to results of analyses.

The researcher may need *information on who does not want to participate in research or who withdraws from research*, for example to document who is not to be included in follow-up research activities; and/or to take into consideration relevant characteristics of the population not included in the study, when

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reporting possible bias in research results. In these circumstances, researchers may obtain information about non-participants or those withdrawing consent only with individuals' consent or the approval of an REB to waive the consent requirement in the particular circumstances.

Participants in *qualitative studies* are especially vulnerable to unintended identification. For example, in quoting interviewees, biographical details may be revealed that make protecting identities difficult. Therefore, paying attention to the trust relationship between researcher and participant, and obtaining ongoing consent, are very important.

ELEMENT #5: Informing prospective research participants about the research

Researchers should provide to prospective participants or to authorized third parties disclosure of all information relevant to voluntary and informed consent.

Information should be communicated to prospective participants in *plain language*, in oral and/or written form, so that it is easily understood.

The *amount of time* taken to communicate information to prospective participants should be appropriate to the need, not excessive nor too brief. For example, the information could be layered, with a one-page summary of the research, a short consent form, an appendix with more detailed information and instructions on how to obtain more information.

During the consent process, the researcher should determine whether the participant wishes to be *informed of any meaningful research results* that specifically relate to them.

Researchers, particularly those in the areas of health services, population and public health, and genetics/genomic research who study whole populations, should strive to *communicate with the relevant population and governmental authorities regarding results* that are pertinent to the improvement of health and/or the prevention of disease. The population studied should be made aware of possible socio-economic discrimination or group stigmatization as a result of the research results, such as because of perceptions of genetic risks. In the context of genetic research, the population should also be informed of the means taken to minimize the risks.

In the consent process and discussion, researchers using *qualitative methods* may consider involving participants in the writing and reporting process, depending on the circumstances.

For a hybrid project involving the *direct collection of data from individuals and secondary use of data from other sources*, the prospective research participant should also be informed of all expected types and sources of personal data to be used, any expected linkages and the expected purposes for which data will be used.

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When personal data are to be entered into a *database for multiple research uses* over an extended period, research participants should also be informed of such things as: expected types of studies, expected data types and purposes, expected commercial uses, data retention period, and the process for overseeing the use and security of data. Participants may also be given the opportunity to provide *authorization for future uses*, with or without re-contact, including the opportunity to withdraw consent (and any identifying information) in the future. Additional options may include:

- to be re-contacted on a regular (or as needed basis) to seek consent for new research uses of the data, if desired and practicable; and/or
- to not be re-contacted, but to authorize the researchers to use the data only in certain ways in the future (e.g. with or without direct identifiers, coded or in non-identifiable form; or for certain areas of research).

ELEMENT #6: Recruiting prospective research participants

The proposed recruitment procedure and materials should be included in the submission for *REB approval*. The procedure and materials should *foster the conditions for voluntary consent*, and not exert undue influence on prospective participants to agree to take part in research.

Initial contact with individuals about a research project should be made by someone that individuals would expect to have relevant information about them, or in other ways that do not inappropriately intrude on their life or privacy.

Wherever possible, the researcher should *anticipate at the time of the original collection* the future uses of personal information for further recruitment purposes, and seek consent from individuals for these purposes.

The REB will need to determine if consent is required for the *secondary use of personal information for recruitment purposes*. Researchers and REBs should be aware of any legal restrictions on contacting individuals in these circumstances.

When a researcher is making a *request for access to data* to recruit participants, the preferred option is for the data holder to determine eligibility of individuals for the research on the basis of criteria provided by the researchers, and to make the initial contact to:

- inform eligible individuals about the research so that they can contact the researcher, if interested, or
- to seek consent from individuals to release their nominal information to the researcher who will contact them to inform them about the research.

When the preferred option is impracticable or inappropriate, an REB may consider whether a researcher should be permitted access to minimal personal data only for the purposes of determining eligibility for the research or contacting individuals to invite them to join the study. If it is legally permissible and the

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REB considers it appropriate, personal information may be released with appropriate confidentiality protection such as a signed confidentiality agreement with access restricted to the data holder's site and use limited to the stated purpose.

Researchers should avoid situations where eligible individuals are not aware, prior to being contacted, of information about themselves that makes them eligible for participation in the research, such as a cancer diagnosis.

Typical *scenarios* for recruiting participants, including *community-based research* and *genetics research*, and preferred approaches are briefly described.

ELEMENT #7: Safeguarding personal data

Institutions or organizations where research data are held have a responsibility to establish appropriate institutional security safeguards. Data security safeguards should include organizational, technological and physical measures.

Researchers should take a risk assessment and management approach to protecting research data from loss, corruption, theft or unauthorized disclosure, as appropriate for the sensitivity and identifiability of the data.

REBs should review and approve researchers' proposed measures for safeguarding any personal data to be collected.

ELEMENT #8: Controlling access and disclosure of personal data

Data sharing for research purposes - whether of linked or unlinked data sets - is an important way of enabling socially valuable research. It avoids unnecessary duplication of data collection, which reduces the burden on research participants and permits researchers to use limited or scarce resources more productively.

However, once approved by an REB, there should be strict limits on access to data and secure procedures for data linkage, subject to data-sharing agreements.

When personal data are essential to research objectives and questions, researchers need a plan for making public the results of research in ways that do not permit tracing back to individuals if they do not wish their identities to be known.

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The most secure way of conducting *data linkages* requested by external researchers is for the data holder to conduct the linkage and provide linked data sets to the researcher without direct identifiers and at the minimum level of identifiability necessary for the research purpose. If that is not practicable, a trusted third party may conduct the linkage or the researcher may conduct the linkage on the data holder's site. As a last option, a researcher may be permitted to conduct the linkage at a secure site but under strict controls, as specified in a data-sharing agreement. Following the linkage of datasets, the person doing the data linkage should reduce datasets to the lowest level of identifiability needed to accomplish the research objectives.

Data-sharing agreements bind data providers and researchers to their respective responsibilities and obligations for protecting personal data. Data-sharing agreements should set out the terms and conditions under which data providers will allow researchers to access personal data for research purposes.

In assessing the privacy aspects of research, researchers and REBs should also be aware of the possibility that in some instances *individuals may want their identities to be known*-for example, when individuals

want their contribution to research as participants to be recognized, or where they want to help others afflicted with a similar condition. In some *qualitative research*, individual participants may understand and willingly accept the possibility that their identities may be revealed in the public reporting of research results.

ELEMENT #9: Setting reasonable limits on retention of personal data

Personal data should be retained as long as is necessary to fulfill the research purposes. Personal data may then be destroyed or returned to the data provider, if appropriate, as set out in the terms of the original collection, data-sharing agreement, institutional policies, and legal requirements.

Retention periods for personal data should be defined in writing. Researchers should be explicit about what they plan to do with the data they collect and have storage, management and access policies in place.

When personal data are collected in a *database to support general health research purposes* in the future, personal data may be retained for the general purposes originally consented to, subject to security safeguards proportionate to the identifiability and sensitivity of the data.

Administrative databases such as hospital discharge records and vital statistics registries, which may be used to support health research, may retain personal data over the long-term, provided that this is permitted according to legislation or the mandate of a public body such as a government health department.

Any long-term retention of personal data established for general health research purposes should be subject to periodic audits and effective oversight by independent third parties including REBs.

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ELEMENT #10: Ensuring accountability and transparency in the management of personal data

Individuals and organizations engaged in health research involving personal data are accountable for the proper conduct of such research in accordance with applicable funding policies, privacy principles and/or legislation. Processes and practices must be clearly established and implemented in order to give meaningful effect to these policies, principles or laws. Proper accountability and transparency practices require adequate resources for such things as communication, education and training relating to privacy.

Roles and responsibilities of all those involved in the conduct and evaluation of research should be clearly defined and understood, including those of researchers, their employing institutions, REBs, any data stewardship committees, Privacy Commissioners and other legally-designated privacy oversight agencies. Their concerted efforts should aim to provide a coherent governance structure for effective and efficient data stewardship.

Recognizing that transparency may enhance public support for, and interest in, socially valuable research, individuals and organizations engaged in the conduct and evaluation of health research should:

- be open to the public with respect to the objectives of the research;
- be open about the policies and practices relating to the protection of personal data used in the research;
- promote ongoing dialogue between the research community and privacy oversight agencies; and
- promote ongoing dialogue between the research community and the community at large (the public).

When a *database is created for multiple research purposes, or across multiple sites or jurisdictions*, researchers and institutional data holders should promote coordinated and streamlined approaches to the review of privacy and confidentiality concerns, and to data stewardship over the long term.

A *centralized data stewardship committee* could be put in place to authorize future uses of the database in accordance with the research objectives and, where applicable, within the parameters set by the consent obtained from participants. The responsibilities of this committee could include the review of data access requests; long-term management of the database; coordination of reviews by local REBs (e.g. by means of agreements between REBs, institutions and researchers, as appropriate); and provision of information to the public (e.g. on a web site).

Appeals Section 16

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This policy applies to all appeals from decisions of the HREB. It is guided by national guidelines and all applicable legislation and regulations.

1. Reconsideration of an HREB subcommittee decisions

Informal resolution of disagreement concerning decisions of an HREB subcommittee is sought first through meetings of the investigator and the chair of the subcommittee that reviewed the study. If issues are not resolved, the investigator may be invited to address the subcommittee. If the matter is not resolved, the investigator is informed in writing by the HREB subcommittee chair and informed that they may appeal the decision to the standing Appeal Panel of the HREA.

2. The Appeal Panel and Appeal Board

The Appeal Panel is a standing committee appointed by the HREA following consultation with the Minister of Health and Community Services, the president of Memorial University and the chief executive officer of the Eastern Health Authority. It is constituted according to applicable guidelines, regulations and legislation. Members of the Appeal Panel exclude current members of the HREA, HREB or any other approved Research Ethics Body.

3. Grounds for appeal

Decisions of the HREB subcommittee to not approve or to rescind approval of research on ethical grounds can be appealed only on the basis of error of process, conflict of interest or bias. All researchers have the right to request, and the HREB subcommittee has an obligation to provide, reconsideration of decisions affecting a research project.

4. Initiating an appeal

Investigators wishing to lodge an appeal against a decision of the HREB subcommittee must submit a letter to the Chair of the HREA Appeal Panel within 90 calendar days of notification of the HREB subcommittee decision. The Chair of the Appeal Panel will then appoint five of the members of the Panel to an Appeal Board; members of the Appeal Board will be selected with regard to the subject matter of the appeal. Members of the HREB subcommittee will be informed that an appeal has been made and notified of the Appeal Board's final decision. The HREB subcommittee has no involvement in the appeal process. Anyone wishing to make an appeal should contact the HREA office at 709-777-6974.

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5. Consideration of the appeal

The Chair of the Appeal Panel will convene a meeting of the Appeal Board to consider the appeal. All documentation concerning the application and review process as well as any correspondence will be provided to the Appeal Board. Normally the principal investigator as well as representatives of the HREB subcommittee which reviewed the study will be given opportunity to present to the Appeal Board.

6. The decision of the Appeal Board

The Appeal Board may uphold the appeal and substitute the decision it considers appropriate or it may dismiss the appeal.

The decision of the Appeal Board is binding on the principal investigator and the HREB subcommittee. The decision shall be given in writing to the HREB and subcommittee chair (s) and the principal investigator and include the reasons for the Appeal Board's decision. An appeal of the Appeal Board decision must be heard through the justice system.

References

TCPS2 Chapter 6C (Reconsideration and Appeals)

Health Research Ethics Authority Act; Sections 15 - 18

Review Fees Section 17

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The purpose of this policy is to define the guidelines for payment of fees by sponsors for review of research projects by the Health Research Ethics Board [HREB-CT]. In order to manage its responsibilities in the protection of human participants in research, sufficient resources need to be available to assure human research participant protection.

1. Background

Effective the date of proclamation of the HREA Act the HREB will implement a review fee for all industry-sponsored protocols. This practice is consistent with practices of research ethics boards, both institution-based and private, that review such protocols.

Fees will be used to offset administrative costs associated with support and enhancement of the basic HREA activities including education and training of staff and HREB members. The fee structure will be reviewed annually.

2. Policy

This fee applies only to *industry-funded* contract research sponsored by pharmaceutical and other for-profit entities and reviewed by the HREB-CT. This refers to sponsor-initiated studies designed to evaluate the safety, efficacy, benefits, adverse reactions, and/or other outcomes of drugs, devices, diagnostics, treatments, procedures, medical evaluations, monitoring or preventive measures or other related industry-sponsored studies. Human research protocols funded by federal, provincial, local or public agencies, non-for-profit foundations and grants in aid of research awarded by for-profit entities are excluded from the HREB review fee. Student and trainee initiated studies are also excluded from the review fee.

3. Applicability

The invoice for this fee will be issued directly to the sponsor/Contract Research Organization (CRO) after first review by the committee. Payment is due upon review by the committee for services rendered and is not contingent upon securing approval by the HREB or executing a contract with the PI and/or institution.

Management of Serious Adverse Events and Safety Reports Section 18

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This policy defines the receipt and management by the HREB of Serious Adverse Events (SAEs) and safety reports related to health research involving human subjects.

The HREB will accept and review only the following

1. Reports of individual local SAEs occurring at sites for which the HREB serves as the board of record. SAEs are to be submitted on the *Serious Adverse Event Report Form LOCAL EVENT* available at <http://www.hrea.ca>.
2. Industry sponsored clinical trial summary safety reports from the sponsor, i.e. Data Safety Monitoring Board (DSMB) reports and/or quarterly, biannual or annual safety reports.. Such reports, whenever possible, should provide an overview of the analysis of events, assessment of the risk /benefit ratio and any actions required as a result of the safety review. Line listings of safety events may be provided as part of the summary safety report.

Note: Researchers are not required to submit nor will the HREB accept or review individual SAEs occurring at sites outside the jurisdiction of the HREB.

Responsibility

- Local SAEs and summary reports will be reviewed by the Chair or Vice-Chair of the HREB and followed up as necessary.
- Summary safety reports from industry-sponsored clinical trials will be added to the file and will be reviewed as part of the ethics renewal process.
- Amendments and actions resulting from a safety review by the sponsor of an industry-sponsored clinical trial will be reviewed and approved by the full Committee as required.

APPENDIX 18: Guidance Documents

18.1 Health Canada - Food & Drug Act; Division 5; Part C

Serious Unexpected Adverse Drug Reaction Reporting
C.05.014.

(1) During the course of a clinical trial, the sponsor shall inform the Minister of any serious unexpected adverse drug reaction in respect of the drug that has occurred inside or outside Canada as follows:

- (a) if it is neither fatal nor life threatening, within 15 days after becoming aware of the information; and

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(b) if it is fatal or life threatening, within seven days after becoming aware of the information.

(2) The sponsor shall, within eight days after having informed the Minister under paragraph (1) (b), submit to the Minister a complete report in respect of that information that includes an assessment of the importance and implication of any findings made.

18.2 . FDA (USA) - Title 21--Food And Drugs; Chapter I-- Subchapter D--Drugs For Human Use - PART 312 -- INVESTIGATIONAL NEW DRUG APPLICATION

Subpart D--Responsibilities of Sponsors and Investigators; Sec. 312.66

Assurance of Institutional Review Board (IRB) review.

An investigator shall assure that an IRB that complies with the requirements set forth in part 56 will be responsible for the initial and continuing review and approval of the proposed clinical study. The investigator shall also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

18.3. ICH –GCP

3.3 Procedures

The IRB/IEC (Institutional Ethics Committee) should establish, document in writing, and follow its procedures, which should include:

3.3.8 Specifying that the investigator should promptly report to the IRB/IEC:

- a. Deviations from, or changes of, the protocol to eliminate immediate hazards to the trial subjects (see 3.3.7, 4.5.2, 4.5.4).
- b. Changes increasing the risk to subjects and/or affecting significantly the conduct of the trial (see 4.10.2).
- c. All adverse drug reactions (ADRs) that are both serious and unexpected.

New information that may affect adversely the safety of the subjects or the conduct of the trial.

4.11 Safety Reporting

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4.11.1 All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique

code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the IRB/IEC.

4.11.2 Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.

4.11.3 For reported deaths, the investigator should supply the sponsor and the IRB/IEC with any additional requested information (e.g., autopsy reports and terminal medical reports).

Conflict of Interest

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The purpose of this policy is to provide guidelines for HREB members and researchers for disclosure of any real, perceived or potential conflict of interest (COI) in relation to the review of a research protocol or the conduct of a research project.

1. Definition of conflict of interest (COI):

A COI exists when there is an incompatibility of two or more duties, responsibilities, or interests (personal or professional) of an individual or institution as they relate to the ethical conduct of research, such that one cannot be fulfilled without compromising another²¹. A COI may be real, perceived or potential.

Real conflict: At least three prerequisites have to be established before it can be said that there is a real COI:

- the existence of a private interest
- that the COI is known to the researcher/HREB member
- that the COI is sufficient to influence the exercise of the researcher's/HREB member's duties or responsibilities related to the ethical conduct of research

Perceived conflict: A perceived COI exists when a reasonably well informed person could have a reasonable belief that a COI exists.

Potential conflict: A potential COI is one that may develop into an actual conflict. The potential exists as soon as the researcher/HREB member can foresee that he/she has a private interest that may be sufficient to influence a public duty or responsibility. It may be real or perceived.

A real, perceived or potential conflict of interest does not preclude the involvement of the researcher in the research project or the involvement of the HREB member in review of the project but it does mean that the conflict shall be disclosed. The conflict may then be disallowed or allowed and managed with the decision recorded appropriately.

2. Management of COI

Management of conflict of interest is a process. The first step is disclosure. The steps taken by the HREB will be context-based and proportionate to potential harms. When disclosure is not enough to manage the COI given the information provided by the researcher, the HREB will withhold approval of the project

²¹ TCPS2, 2010

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until steps are taken to address the issues of concern to the HREB. These steps may require the researcher to withdraw from the research or allow others to make research-related decisions.

3. HREB members and COI

HREB members must disclose real, perceived or potential COI to the HREB and, where necessary, members must withdraw from HREB deliberations and decisions. This would be the case when an HREB member

- is or has been in direct conflict with researchers on academic or scientific issues
- has collaborated with the researcher whose research is under review

An HREB member in a COI should disclose and fully explain to the HREB the COI. A researcher in a COI with a member of the HREB may raise with the HREB any concerns with respect to the COI. An HREB member in a COI should withdraw from the committee when such projects are under consideration where the Committee feels this is the most appropriate management of the conflict.

4. Researchers and COI

Researchers should disclose to the HREB real, perceived or potential personal or professional COI of which they are aware that may have an impact on their research. COI may arise from:

- interpersonal relationships – family or community
- financial partnerships
- other economic interests or incentives
- involvement in dual or multiple roles within or outside an institution

As part of the research protocol submitted for HREB review, researchers should provide details on the research project, budgets, commercial interests, consultative relationships and other relevant information and documentation and identify strategies to prevent, disclose and properly manage conflicts.²²

²² Disclosure of COI to the HREB is also a requirement for any MUN faculty or staff member under its COI policy. HREB will review the disclosed COI and send a written decision to the researcher with a

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copy to the Office of Research Services and the MUN COI Committee, setting out the issues reviewed, the reasons for the decision, and (where the decision is to manage the conflict) the process agreed upon.