HRSO
Human Research Standards Organization

CAN/HRSO - 300.01 - 2022

CONDUCT OF HUMAN RESEARCH

SCC CCN

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Foreword

Human Research Standards Organization (HRSO) is a Canadian, not-for-profit, standards development organization accredited by the Standards Council of Canada (SCC).

HRSO's mandate is to unite progressive, insightful Canadian visionaries to collectively interpret, reform, and frame the national human research landscape through the development of National Standards of Canada (NSCs).

HRSO develops NSCs of relevance to Canadians conducting, overseeing and participating in human research. The adoption of NSCs ensures harmonization, partnership, and economic growth of this activity within Canada and internationally.

HRSO's NSCs are developed in accordance with the current *Requirements & Guidance - Accreditation Standards Development Organizations* established by SCC.

The timeline for development of NSC CAN/HRSO-300.01-2022 "Conduct of Human Research" was as follows:

Notice of Intent Publication: 2020/02/25
First Meeting of Technical Committee: 2021/03/29
Public Consultation Period: 2022/02/11 – 2022/04/12
Final Meeting of Technical Committee: 2022/04/21

HRSO will ensure that this NSC remains current and relevant by maintaining it on a continual basis through ongoing Technical Committee review.

A NSC is a standard developed by a Standards Council of Canada (SCC) accredited Standards Development Organizations, in compliance with requirements and guidance set out by SCC. More information on NSCs can be found at www.scc.ca.

SCC is a Crown corporation within the portfolio of Innovation, Science and Economic Development (ISED) Canada. With the goal of enhancing Canada's economic competitiveness and social well-being, SCC leads and facilitates the development and use of national and International Standards. SCC also coordinates Canadian participation in standards development and identifies strategies to advance Canadian standardization efforts.

Accreditation services are provided by SCC to various customers, including product certifiers, testing laboratories, and standards development organizations. A list of SCC programs and accredited bodies is publicly available at www.scc.ca.

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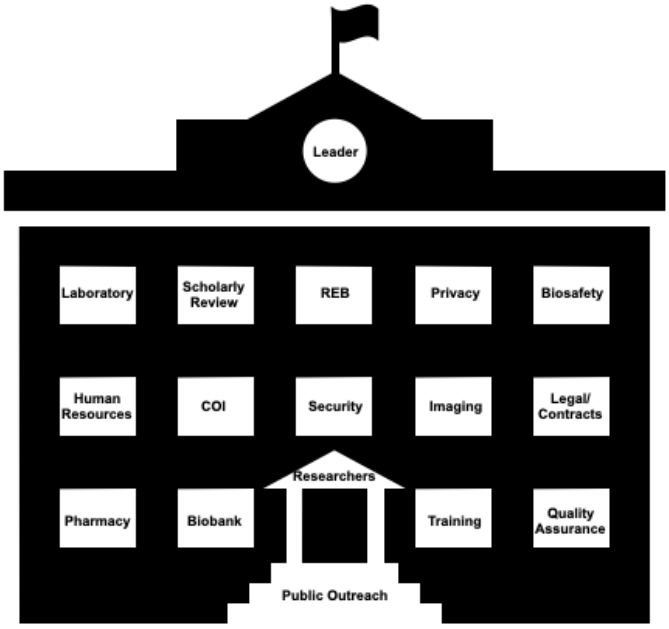
Introduction

Human research can provide knowledge that assists society in many ways, including through the production of socially beneficial goods, services, and improved insights into human behaviour. Achieving these benefits in an ethical way requires respect for the dignity and rights of those whose data and participation make these benefits possible. It is incumbent on organizations conducting human research to govern themselves accordingly.

Effective governance of human research takes into consideration that Research Participant protection is a shared responsibility. Included in this are the individuals or entities whose actions affect research data integrity, and the health, welfare, interests, and rights of Research Participants. All of these interdependent entities interact in a system to promote a culture of research safety, integrity, quality, efficiency, and accountability. Additionally, they inform human research policy and practice.

A Research Enterprise (RE) may possess some or all of the examples of interdependent entities and third parties illustrated below in Figures 1 and 2. On the one hand, a RE's structure may include all of the entities required for effective governance under a unified leadership within a single organization. This type of governance structure is called a Human Research Protection Program (HRPP), and is depicted below:

Figure 1:

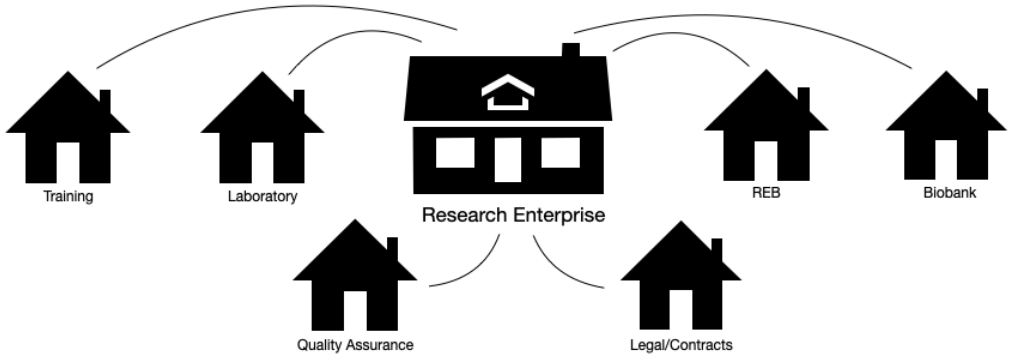


On the other hand, a RE may concentrate on a sub-set of the above-stated governance components under its auspices, as illustrated in Figure 2. To fulfill its governance obligations, the RE may sub-contract some of these functions to other entities. One

example of a RE could be a research site or series of research sites, linked to an independent REB, biobank, laboratory, etc.

Another example could be a Contract Research Organization (CRO) or Academic Research Organization (ARO). Here, a number of functions are carried out within the CRO or ARO, with the remainder achieved through collaboration or agreement.

Figure 2:



Adherence to this NSC ensures that a RE has access to the necessary structural components, oversight capabilities, and procedural documents to safeguard the rights and welfare of Research Participants, safely conduct research, and produce reliable, verifiable, and credible research data in an environment that promotes efficiencies and mitigates risks.

Consistent application of this NSC will ensure that human research is conducted uniformly from one organization to another, and from one province or territory to another, enabling harmonization, collaboration, and economic growth of this activity within Canada and internationally.

This NSC outlines the requirements for the ethical conduct of human research by a RE, either as a stand-alone organization, or as a functional entity within a HRPP. NSC CAN/HRSO-100.01-2020 “Development of a Human Research Protection Program (HRPP)” is referenced throughout this NSC for REs that are functioning within a HRPP.

HRSO intends to expand relevant topics within this NSC, and other NSCs that it has already developed, as it advances the development of new standards for human research in Canada.

It is the responsibility of the user of this NSC to judge its suitability for the user’s intended purpose. This NSC may be used for conformity assessment.

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ICS Code 03.100.40

1. Scope

This NSC applies to all individuals, as well as all for-profit and not-for-profit, public and private organizations engaged in the conduct of human research. By reducing the variability of interpretation of regulations, policies, and guidelines, this NSC provides a basis for the establishment of unambiguous procedural documents that adhere to Canadian and international normative references.

Human research incorporates various types of qualitative and quantitative methods, disciplines (eg, health, social sciences and humanities, arts, engineering), and approaches (eg, interventional, observational) conducted in a variety of domains (eg, biomedical, social, legal, behavioural). Human research may involve the use of existing or prospectively collected data or specimens.

“Shall” vs “Should”

In this NSC, “shall” indicates that the requirement is mandatory and is supported by normative references, whereas “should” indicates that the requirement is recommended, or a best practice statement.

2. Normative References

This NSC was developed in accordance with the normative documents listed below, all of which are publicly available. The user of this NSC should refer to the latest edition or revision of the normative documents.

Canadian Legislation

Health Canada Food and Drugs Act
https://laws-lois.justice.gc.ca/eng/acts/F-27/page-1.html

Personal Information Protection and Electronic Documents Act (PIPEDA)
https://laws-lois.justice.gc.ca/ENG/ACTS/P-8.6/page-1.html

Canadian Regulations

Health Canada Food and Drugs Regulations, Part C, Division 5
https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices/guidance-documents/guidance-drugs-clinical-trials-human-subjects-gui-0100.html

Health Canada Natural Health Products Regulations, Part 4
https://laws-lois.justice.gc.ca/eng/regulations/SOR-2003-196/page-7.html

Health Canada Medical Device Regulations, Part 3

https://laws-lois.justice.gc.ca/eng/regulations/sor-98-282/page-9.html#h-1021976

Policies and Guidelines

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2018) https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2018.html

Interpretations - Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2018) Interpretations https://ethics.gc.ca/eng/policy-politique_interpretations.html

Material Incidental Findings - Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2018)
https://ethics.gc.ca/eng/incidental_findings.html

Tri-Agency Research Data Management Policy (2021)
https://www.ic.gc.ca/eic/site/063.nsf/eng/h_97610.html

International Council for Harmonization (ICH) of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice Guideline
https://www.ich.org/page/efficacy-guidelines

Good Clinical Data Management Practices (GCDMP) https://scdm.org/gcdmp/

The First Nations Principles of Ownership, Control, Access, and Possession OCAP®
https://fnigc.ca/ocap-training/

Other Regulations

US Code of Federal Regulations Title 21
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

US Code of Federal Regulations Title 45
https://www.ecfr.gov/current/title-45

3. Terms and Definitions

Biological Materials: These include tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, and other body fluids. These also include materials related to human reproduction, including embryos, fetuses, fetal tissues, and human reproductive materials. Biological materials are also referred to as biological samples.

Collective/Community Consent: An agreement that is achieved through adherence to the governance structure of the Community in question. In the absence of a governance

structure, an agreement is achieved through consultation with groups of individuals reflecting the diversity of the Community in question.

Community: A group of people with a shared identity or interest that has the capacity to act or express itself as a collective. A Community may be territorial, organizational, or defined by a shared interest. A Community may have governance processes that affect human research such as leadership engagement, recruitment, consent, and dissemination and ownership of research results.

Community and Research Participant Engagement: A process that establishes an interaction between an Investigator/Researcher, or a Research Team, and a Community or individual participants. It signifies the intent of forming a collaborative relationship between them, although the degree of collaboration may vary depending on the Community context and the nature of the research.

Compensation: Something given or received as an equivalent for services, debt, loss, injury, suffering, lack, etc.; an indemnity.

Concluding Review of Research: A review conducted by the REB that occurs when research activities have concluded, in order to ensure that ethical oversight is no longer required.

Conflicts of Interest: A set of conditions or factors (such as money, friendship, reputation) in which professional judgment concerning a primary interest (such as the welfare of a Research Participant) is unduly influenced by a secondary interest (such as financial gain). Conflicts of interest have the following components:

- a relationship - one party (the trustor) is entitled to trust that the other (the trustee) will promote or protect their interests in relation to matters within that relationship
- a conflicting interest - an influence that tends to make the trustee’s judgment on a given decision less reliable in promoting or protecting the trustor’s interests than it would normally be
- an exercise of judgment - the trustee must be able to make a decision that affects the trustor’s interests.

Conflicts of Roles: A situation that occurs when incompatible demands are placed on an individual relating to their job or position, such as conflicting fiduciary responsibilities (eg, an Investigator/Researcher reviewing her own research while serving on an REB).

Conformity Assessment: Processes used to demonstrate that a product, service, management system or body meets specified procedures or requirements.

Continuing Review of Research: A review conducted by the REB of the ethical acceptability of research that occurs while the research is ongoing, but prior to the expiration of ethical oversight set by the REB.

Data: Any set of values of qualitative or quantitative variables. Data may be recorded in any format (eg, electronic, paper) and include *de novo* collections or secondary use of existing data.

Data and Safety Monitoring Board (DSMB): A multidisciplinary, expert advisory group established by a research sponsor, that is responsible for safeguarding the interests of Research Participants by reviewing emerging data, assessing the safety and efficacy of research procedures, and monitoring the overall conduct of research. A DSMB is also referred to as a Data and Safety Monitoring Committee (DSMC).

Deviations from Approved Research: Any alteration to the REB-approved research without prospective REB approval.

Essential Documents: A term usually associated with clinical research, essential documents are those documents which individually and collectively permit evaluation of the conduct of research and the quality of the research data produced.

Equity, Diversity, and Inclusion (EDI): Criteria implemented to remove barriers to the recruitment and full participation of Research Participants and development of research teams. These terms are described individually as follows:

- Equity - The removal of systemic and other barriers and biases enabling all individuals to have equal opportunity and access.
- Diversity - The demographic mix of the community (eg, race, colour, place of origin, religion, immigrant and newcomer status, ethnic origin, ability, sex, sexual orientation, gender identity, gender expression, age), with a focus on the representation of equity-deserving groups.
- Inclusion - The practice of ensuring that all individuals are welcomed, valued, and respected for their contributions, and are able to fully participate.

Human Research: A systematic, rigorous investigation involving human beings that includes, but is not limited to, the following disciplines: health research, social sciences and humanities research, creative and arts-based research, and engineering research, and includes, but is not limited to, the following methods:

- interventional research, observational research
- qualitative research, quantitative research
- social and behavioural research, health services research, public health research, educational research
- research involving existing human data and human biological materials and their derivatives
- research involving living or deceased individuals.

Human Research Protection Program (HRPP): An organization-wide program composed of a network of interdependent entities that share the responsibility for Research Participant protection and interact in a system that promotes a culture of research integrity, quality, efficiency, accountability, and evidenced-based practices. A HRPP can exist in any for-profit or not-for-profit, public or private organization where human research is conducted and/or overseen.

Incentive: Anything offered, monetary or otherwise, to encourage participation in research.

Incidental Findings: A discovery concerning Research Participants or prospective Research Participants that is made in the course of research but is outside the objectives of the research study. Incidental findings are material incidental findings if they are reasonably determined to have significant welfare implications for the Research Participant or prospective Research Participant.

Indigenous Peoples: In the context of Canada, persons of First Nations, Inuit, or Métis descent, regardless of where they reside and whether their names appear on an official register.

Individuals who Play a Role in the RE: Any individual or entity within an organization whose actions directly or indirectly affect research data integrity and the welfare, interests, or rights of Research Participants, such as Investigators/Researchers, Administrative Personnel, Student Researchers, Research Coordinators, Research Monitors, Research Associates, and Community or Patient Partners.

Initial Review of Research: A review conducted by the REB of the ethical acceptability of research that occurs prior to the initiation of any research activities.

Investigational Product: An unlicensed product or a licensed product when used or assembled (formulated or packaged) differently from the approved form, when used for an unapproved indication, or when used to gain further information about an approved use, including a preventative (vaccine), a therapeutic (drug, biologic, natural health product), device, diagnostic, or palliative used in clinical human research.

Investigator/Researcher: In the context of a RE or HRPP, an individual who carries out human research.

Knowledge Mobilization (KM): An umbrella term encompassing a wide range of activities relating to the production and use of research results, including knowledge synthesis, dissemination, transfer, exchange, and co-creation or co-production by researchers and knowledge users.

Knowledge Translation and Exchange (KTE): A process of exchange between researchers and knowledge users designed to make relevant research information

available and accessible to stakeholders for use in decision-making about practices, programs and policies.

Meta-data: Data that describe the data collected.

Modifications to Approved Research: Proposed changes to previously REB-approved human research. Once human research has received REB approval, any subsequent changes must be reviewed and approved by the REB prior to implementation, except when necessary to prevent or alleviate immediate and serious negative impacts to Research Participants. Modifications are also referred to as amendments to approved research.

National Standard of Canada (NSC): A standard developed by a Standards Council of Canada (SCC) accredited Standards Development Organization, in compliance with requirements and guidance set out by SCC.

Negative Impact: Any event, whether anticipated or not, that does or could adversely affect research data integrity, the health, welfare, interests or rights of Research Participants, Investigators/Researchers, and third parties such as families and communities, or the conduct of the research. Examples include, but are not limited to, breaches of privacy, incidental findings, adverse events, serious adverse events, and unanticipated problems.

Ongoing Review of Research: A review conducted by the REB of the ethical acceptability of research that occurs on a continuous basis following the Initial Review of research until the Concluding Review of research.

Privacy Rights: An individual's right to be free from intrusion or interference by others. Individuals have privacy interests in relation to their bodies, personal information, expressed thoughts and opinions, personal communications with others, and spaces they occupy.

Procedural Documents: A collective term used to describe policies, procedures (such as standard operating procedures), and guidelines.

Protocol Waiver: REB approval of a prospective request by an Investigator/ Researcher or research sponsor to permit modifications, on a case-by-case basis, to the approved research protocol.

Publicly Accessible Registry: In the context of clinical research, the publication of an internationally agreed set of information about the design, conduct and administration of clinical trials. These details are published on a publicly accessible website managed by a registry conforming to World Health Organization standards (eg, www.clinicaltrials.gov).

Publicly Declared Emergency: A situation that has been proclaimed an emergency due to the extraordinary risks it presents, by an authorized public official in accordance with legislation and/or public policy. Publicly declared emergencies arise suddenly or unexpectedly and require urgent or quick responses to minimize devastation. Examples include, but are not limited to, natural disasters, large communicable disease outbreaks, catastrophic civil disorders, bio-hazardous releases, environmental disasters, and humanitarian emergencies.

Quality Management System (QMS): A formalized system that documents processes, procedures, and responsibilities for achieving quality policies, standards, and objectives. A QMS helps coordinate and direct an organization's activities to meet regulatory requirements and improve its effectiveness and efficiency on a continuous basis.

Research Data: Data used for research purposes. For this NSC, the term "research data" is restricted to data about humans, including their biological materials.

Research Enterprise (RE): An entity, such as an institution or corporation that, as part or all of its activities, conducts or facilitates human research. A RE can exist as a component of a HRPP.

Research Ethics Board (REB): An appropriately constituted group that applies ethics principles in its review and ongoing evaluation of research involving humans. A REB is also known as an independent or institutional review board (IRB), independent ethics committee (IEC), a research ethics review committee (RERC), a research ethics committee (REC), or ethics review board (ERB).

Research Participant: An individual whose data, biological materials, or responses to interventions, stimuli, or questions may be used to answer one or more research questions.

Research Team: A group of individuals working together in a committed way towards a common research goal.

Restitution: Compensation offered to Research Participants for injuries or losses that arise as a result of their participation in human research.

Secondary Use: The use of information or human biological materials for a purpose other than the original purpose for which it was collected.

Vendors and Sub-Contractors: Entities that sell products and services to the Research Enterprise or HRPP (Vendors) or provide services under contract to the Research Enterprise or HRPP (Sub-Contractors). Some important examples of Sub-Contractors include, but are not limited to, external REBs, external Investigators/ Researchers, external biobanks, and contract research organizations.

4. Technical Requirements

4.1 Research Enterprise (RE)

The following sections set out the technical requirements for a RE that is not an entity within a HRPP. NSC CAN/HRSO-100.01-2020 shall apply to any RE that exists within a HRPP.

4.1.1 Mandate

The RE shall have a written mandate that describes, but is not limited to, the following:

4.1.1.1 the scope of the human research advanced by the RE.

4.1.1.2 the organizational structure of the RE.

4.1.1.3 the desired organizational culture of the RE

4.1.1.4 the relevant laws, normative texts, and NSCs governing the RE.

4.1.1.5 the source of the mandate, and the processes for its approval, updates, and revisions.

4.1.1.6 the commitment to proper functioning of the RE commensurate with the volume and complexity of the human research. (Examples of various elements associated with the proper functioning of a RE can be found in Annex A.)

4.1.2 Qualifications and Training of Individuals who Play a Role in the RE

The RE shall ensure that individuals who play a role within it are qualified and trained for their roles and participate in ongoing training.

Procedural documents shall:

4.1.2.1 ensure that, prior to interacting with Research Participants and/or engaging in human research activities, all individuals are trained for their roles within the RE, and in human research protection.

4.1.2.2 ensure that all Individuals who Play a Role in the RE have relevant and valid credentials, certification, education, and experience.

4.1.2.3 ensure that Investigators/Researchers will only be approved to conduct human research in their specific areas of expertise for which they have relevant and valid credentials, certification, education, and experience.

4.1.2.4 describe the plan for ensuring ongoing training and continuing education for all Individuals who Play a Role in the RE, including training and continuing education from external sources.

4.1.2.5 outline the process for the creation and maintenance of training records or files for all Individuals who Play a Role in the RE.

Examples of acceptable training, credentials, certification, education, and experience for Individuals who Play a Role in the RE can be found in Annex B.

4.1.3 Public and Community Engagement

Where there is a NSC for engaging the public in human research, the RE shall recognize and follow it. If a NSC does not exist, the RE shall ensure that it has procedural documents to support a program(s) that engages the public and specific Communities in the RE. Engagement may include, but is not limited to, knowledge mobilization, research consultation, stakeholder committee participation, and active involvement in the research.

Procedural documents should:

4.1.3.1 describe the elements and tools of a program(s) designed to engage the public and specific Communities in the RE in a manner that recognizes the importance of equity, diversity, and inclusion.

4.1.3.2 describe the process for implementation of the program(s).

4.1.3.3 ensure that the program(s) involves all stages of research and all Individuals who Play a Role in the RE.

4.1.3.4 describe the plan for communicating and publicizing the program(s) to the public and specific Communities, including the method of accessing the program.

4.1.4 Conflicts of Interest and Conflicts of Roles

The RE shall have procedural documents to identify, disclose, review, and manage conflicts of interest and conflicts of roles of Individuals who Play a Role in the RE and their personal associates.

Procedural documents shall:

4.1.4.1 identify which aspects of conflicts of interest (eg, monetary, reputational, or institutional) and conflicts of roles (eg, having a care role as well as a research role) are relevant to the RE (eg, situational and structural), in particular, those that involve conflicts with the fiduciary or trust responsibilities

of the Individuals who Play a Role in the RE with respect to Research Participants and the achievement and communication of research results.

4.1.4.2 outline the process for Individuals who Play a Role in the RE, as well as Vendors and Sub-Contractors, to delineate their responsibilities in the RE and disclose conflicts of interest and conflicts of roles that may affect meeting those responsibilities.

4.1.4.3 describe how, on a continuing basis, the identification and disclosure of conflicts of interest and conflicts of roles will be documented, managed, and reported.

4.1.4.4 ensure that Individuals who Play a Role in the RE are trained on how to identify and disclose conflicts of interest and conflicts of roles.

4.1.5 Undue Influence

The RE shall have procedural documents to ensure that Individuals who Play a Role in the RE, as well as Vendors and Sub-Contractors, function independently and free from undue influence.

Procedural documents shall:

4.1.5.1 include a definition of undue influence as it pertains to Individuals who Play a Role in the RE, as well as Vendors and Sub-Contractors, and their human research responsibilities and activities. The definition shall describe the various threats of undue pressure such as those that may be perceived from owners, shareholders, board members, Community members, institutional officials or other Individuals who Play a Role in the RE, study sponsors, or government, and what safeguards are in place to mitigate those threats.

4.1.5.2 ensure that Individuals who Play a Role in the RE, as well as Vendors and Sub-Contractors, shall function free from any undue influence that may affect their human research responsibilities.

4.1.5.3 describe the process for Individuals who Play a Role in the RE, as well as Vendors and Sub-Contractors, to identify and disclose incidents of undue influence.

4.1.5.4 describe how the identification and disclosure of incidents of undue influence will be documented, managed, and reported.

4.1.5.5 describe how the RE will protect individuals who disclose incidents of undue influence from reprisal and how information about the protections offered will be disseminated to those that play a role in the RE, as well as Vendors and Sub-Contractors, in order to promote a culture of responsible research.

4.1.6 Shared and Delegated Responsibilities

REs have a variety of governance arrangements and work in varying contexts, therefore, the RE shall have procedural documents to establish the shared and delegated responsibilities for each human research project, including individuals within and outside the RE.

Procedural documents shall outline the process for:

4.1.6.1 ensuring that all individuals involved in a human research project are aware of their responsibilities and understand that the protection of Research Participants is a shared responsibility, even if particular responsibilities are delegated.

4.1.6.2 creating and updating a list or log for each human research project of the individuals within and outside the RE and their respective responsibilities.

4.1.7 Compliance and Quality Improvement

The RE is responsible for promoting a culture of responsible conduct of research and continuous quality improvement. Therefore, the RE shall have procedural documents for assessing compliance with RE procedures, managing incidents of non-compliance, and improving the quality of its research operations.

<u>Compliance with RE Procedures</u>

Procedural documents shall describe the:

4.1.7.1 qualifications, training, and responsibilities of individuals assessing compliance of the RE, and ensure that the individual(s) (i) have a direct line of report to the highest authority of the RE, and (ii) are assessed, on a continual basis, for potential conflicts of interest and conflicts of roles (see section 4.1.4 Conflicts of Interest and Conflicts of Roles).

4.1.7.2 process for assessing compliance with RE procedures, including, but not limited to:

(a) the frequency, number, and level of scrutiny of compliance assessments commensurate with the size of the RE, and the complexities and risks associated with the human research;

(b) the methods for data collection; and

(c) the metrics employed in order to conduct an analysis of compliance.

Procedural documents should:

4.1.7.3 ensure that a report will be prepared at least annually that summarizes all of the compliance assessment findings, including incidents of non-compliance, for presentation to the highest authority of the RE.

Managing Incidents of Non-Compliance

Procedural documents shall:

4.1.7.4 include definitions of non-compliance, serious non-compliance, and continuing non-compliance within the RE.

4.1.7.5 outline the process for managing incidents of non-compliance including, but not limited to, how they are identified, reported, received, reviewed, and investigated.

4.1.7.6 outline the process for reporting incidents of non-compliance, serious non-compliance, and continuing non-compliance including, but not limited to, the following:

(a) the timeline for reporting;

(b) the format for reporting; and

(c) to whom the incidents of non-compliance shall be reported (eg, appropriate Individuals who Play a Role in the RE, the REB, research sponsors, regulatory authorities, Research Participants).

4.1.7.7 outline the ways that Individuals who Play a Role in the RE shall mitigate future incidents of non-compliance, serious non-compliance, and continuing non-compliance.

Continuous Quality Improvement of Research Operations of the RE

Procedural documents should:

4.1.7.8 describe the process for continuous quality improvement of research operations of the RE that includes, but is not limited to, the following:

(a) the individual(s) responsible for continuous quality improvement and a delineation of tasks for which this individual(s) is responsible;

(b) a plan to assess performance;

(c) a schedule of the performance indicators that will be monitored in order to routinely evaluate improvement efforts and outcomes;

(d) the methods for assessing, measuring, monitoring, and analyzing the performance indicators;

(e) an evaluation of the results and determination of subsequent actions; and

(f) a process by which to improve on items that emerge from (e).

4.1.7.9 ensure that individuals involved in research operations of the RE understand the performance indicators and are empowered to improve efforts and results.

4.1.7.10 ensure that stakeholders outside the RE, especially Research Participants, are involved in and apprised of continuous quality improvement activities.

4.1.7.11 outline the process for receiving, assessing, and addressing complaints, including anonymous complaints, from Individuals who Play a Role in the RE, Research Participants (see section 4.5.8 Research Participants' Inquiries and Concerns), and from stakeholders outside the RE.

4.1.7.12 describe how the RE will protect complainants from reprisal and how information about this protection will be disseminated to those that play a role in the RE and stakeholders outside it.

4.1.7.13 include a process to report on the results of the performance of the RE, and what, if any, procedures or changes in practice emerge due to the continuous quality improvement activities.

4.1.8 Selection of Vendors and Sub-Contractors

The RE shall have procedural documents for selecting Vendors and Sub-Contractors to ensure that their operations are compliant with relevant laws, normative texts, and NSCs pertaining to the conduct of human research and its oversight.

Procedural documents shall describe the process for:

4.1.8.1 the selection of Vendors and Sub-Contractors engaged to fulfill a role(s) on behalf of the RE. The process should prioritize selection of Vendors and Sub-Contractors that hold proof of relevant third-party conformity assessments such as certification, qualification or accreditation.

4.1.8.2 assessing the procedural documents of Vendors and Sub-Contractors that do not hold proof of third-party conformity assessments. The process shall include the criteria upon which the selection decision is made and any training or other measures that are required.

Procedural documents should describe the process for:

4.1.8.3 overseeing and managing Vendors and Sub-Contractors engaged to fulfill a role(s) on behalf of the RE.

4.1.8.4 conducting for-cause and random audits of all Vendors and Sub-Contractors engaged to fulfill a role(s) on behalf of the RE.

4.1.9 Operations during Disruptive Events and Publicly Declared Emergencies

Where there is a NSC for operations during disruptive events and publicly declared emergencies, the RE shall recognize and follow it. If a NSC does not exist, the RE shall ensure that it has procedural documents for research operations during disruptive events and publicly declared emergencies.

Procedural documents shall:

4.1.9.1 define disruptive events, publicly declared emergencies, and essential activities.

4.1.9.2 describe how essential activities will be maintained during disruptive events and publicly declared emergencies.

4.1.9.3 outline the process for ensuring the safety and wellbeing of:

(a) Research Participants; and

(b) Individuals who Play a Role in the RE

during disruptive events and publicly declared emergencies, including the plan for communication.

4.1.9.4 outline the process for ensuring the integrity of the following during disruptive events and publicly declared emergencies:

(a) the informed consent process;

(b) communications with Research Participants;

(c) essential documents;

(d) human research data;

(e) biological materials, if applicable; and

(f) investigational products, if applicable.

4.1.9.5 describe the process for resuming research operations as the disruptive event or publicly declared emergency subsides.

4.1.9.6 describe the process for assessing and documenting the response to the disruptive event or publicly declared emergency and any lessons learned for the future.

4.2 Development of a Human Research Protocol

The RE shall have procedural documents for the development of a human research protocol. Examples of the types of information contained in a human research protocol can be found in Annex C.

Procedural documents for the development of a human research protocol shall include:

4.2.1 a description of the background and rationale of the human research, including, but not limited to:

(a) factual information related to the research topic, including a listing of the literature cited;

(b) prior research in the area under investigation;

(c) the reason for conducting the human research in the context of the background information; and

(d) the value that the proposed human research adds to the current knowledge of the research area.

4.2.2 a statement of the objectives of the human research, including, but not limited to:

(a) the purpose of the human research;

(b) the question that the proposed human research addresses; and

(c) the approach that the Investigators/Researchers will take to address the question or objective identified in the human research protocol.

4.2.3 identification of the human research population under study, including, but not limited to:

(a) a description of eligibility, such as inclusion and exclusion criteria;

(b) a justification for the selection of Research Participants including equity, diversity, and inclusion; and

(c) other relevant characteristics such as potential vulnerabilities, accessibility, and willingness to engage in research.

4.2.4 a description of the human research methods, including, but not limited to:

(a) study design;

(b) engagement with Community or Patient Partners, as appropriate;

(c) chronology and timelines of what is to be accomplished;

(d) workflow and/or schedule of assessments;

(e) intervention, if applicable, including allocation;

(f) population sampling techniques;

(g) process for recruiting Research Participants;

(h) process for re-contacting Research Participants for future related research projects, if applicable;

(i) process of soliciting consent from Research Participants;

(j) process for safeguarding the vital interests of Research Participants, including, but not limited to, privacy, reputation, Community standing, and bodily and mental integrity;

(k) elements of partial or full deception, if any, and plan to debrief;

(l) elements of blinding and unblinding, if any, and plan to debrief;

(m) process for data collection, including the types of research data that will be collected;

(n) who will be granted direct access to Research Participants' information and for what purpose;

(o) plan for data governance and management (see Section 4.9 Data Governance in Human Research);

(p) anticipated future uses of research data, if applicable;

(q) whether participation in the research is contingent on consenting to future, unspecified uses of research data, if applicable;

(r) management of Research Participants' withdrawal of consent regarding their participation;

(s) management of Research Participants' requests for withdrawal of research data and biological materials;

(t) plan for data and safety monitoring, if required;

(u) plan for data analysis;

(v) plan for dissemination of research results; and

(w) plan for termination of the research, including early termination.

4.2.5 an outline of how the risks associated with the human research will be managed, including the processes for:

(a) assessing, minimizing, and mitigating foreseeable risks to Research Participants involved in the human research and to the research study; and

(b) communicating negative impacts and follow-up actions to Research Participants and appropriate stakeholders, including, but not limited to, study sponsors, regulators, institution, and the REB.

4.2.6 a description of the ethical considerations related to the human research, including, but not limited to:

(a) the REB of record, and process for reporting to the REB; and

(b) issues that may raise ethical concerns, such as:

- Research Participant compensation, restitution, and incentives
- individuals in situations of vulnerability including threats to the physical, mental, and social integrity of Research Participants
- conflicts of interest or conflicts of roles
- financial disclosure
- undue influence
- misconception regarding the personal benefits of the research (eg, therapeutic misconception)
- withdrawal of Research Participants
- privacy and confidentiality
- research data integrity
- incidental findings.

4.2.7 a description of the roles and responsibilities of each member of the Research Team.

4.2.8 a description of the quality management systems for the conduct of the study.

4.3 Approvals of Human Research

4.3.1 Obtaining Approvals to Conduct Human Research

The RE shall have procedural documents to ensure that proposed human research attains all levels of approval that are required prior to the commencement of any human research activities. Examples of research activities that require approval prior to their commencement can be found in Annex D.

Procedural documents shall ensure that, before the commencement of any human research activities:

4.3.1.1 a review(s) will be conducted, as appropriate, within or external to the RE, to determine whether the proposed human research is scientifically valid and has value to affected individuals, communities, and society at large.

4.3.1.2 where required, approval(s) from committees or individuals within or external to the RE will be received for the proposed human research.

4.3.1.3 the proposed human research receives approval by a properly constituted REB.

4.3.1.4 where required, written authorization from the appropriate regulatory authorities will be received for the proposed human research for investigative sites within the RE.

4.3.1.5 where required, approval from the appropriate Community or external organization will be received for the proposed human research.

Procedural documents shall ensure that:

4.3.1.6 for applicable research, the proposed human research will be entered into a publicly accessible registry, external to the RE, after receiving all required approvals, and maintained thereafter.

Procedural documents should ensure that:

4.3.1.7 a registry of the RE’s human research studies will be created, maintained, and be publicly available.

4.3.2 Deviations from Approved Human Research

The RE shall have procedural documents for managing deviations to approved human research.

Procedural documents shall:

4.3.2.1 describe the criteria for classifying deviations from approved human research (eg, minor and major based on Research Participant safety or scientific validity) and criteria for reporting them.

4.3.2.2 outline the management and reporting, including the timeline for reporting, of deviations from the REB-approved human research including:

(a) those done to eliminate an immediate and serious negative impact to a Research Participant and for which a waiver from the REB cannot be requested beforehand; and

(b) all other reportable deviations.

4.3.2.3 describe the circumstances under which a waiver would be requested from the REB that would allow a prospective deviation from the REB-approved human research to proceed.

4.3.3 Modifications to Approved Human Research

The RE shall have procedural documents for modifying or amending approved human research.

Procedural documents shall describe which modifications to approved research:

4.3.3.1 require approval from the REB, or any other approvals (see section 4.3.1 Obtaining Approvals to Conduct Human Research), prior to their implementation.

4.3.3.2 can be implemented prior to approval in order to prevent or alleviate immediate and serious negative impacts to Research Participants.

4.3.3.3 are administrative in nature and or do not require approval prior to their implementation.

Procedural documents should:

4.3.3.4 describe the process for ensuring that modifications to approved human research are applied consistently across affected research documentation and communicated to the Research Team.

4.4 Interactions with the REB

The RE shall have procedural documents for interacting with the REB.

Procedural documents shall:

4.4.1 state that only the REB has the authority to determine what constitutes human research that falls under its auspices.

4.4.2 outline the process for consulting the REB prior to the commencement of research.

4.4.3 describe the requirements for submission to the REB for Initial Review, Ongoing Review, Continuing Review, and Concluding Review.

4.4.4 outline the process for submitting new information to the REB that affects the safety, welfare or consent of Research Participants.

4.4.5 outline the process for submitting modifications to, and deviations from the research to the REB, including waivers to approved research (see sections 4.3.2 Deviations from Approved Human Research, and 4.3.3 Modifications to Approved Human Research).

4.4.6 outline the process for requesting reconsideration of REB decisions, including decisions that affect the termination or suspension of research activity, and the assurance that research will only be conducted when REB approval is active and continuous.

4.4.7 include a provision for the REB to observe the informed consent process and monitor the research.

4.5 Research Participants

4.5.1 Research Participant Recruitment

The RE shall have procedural documents for the recruitment of potential Research Participants.

Procedural documents shall:

4.5.1.1 outline the general expectations for Research Participant recruitment for human research including:

(a) how, when, and where Research Participants may be approached;

(b) the qualifications and training of the individuals responsible for recruiting Research Participants, and guidance to minimize conflicts of interest or conflicts of roles;

(c) the content of all participant-facing materials, methods, and media designed to recruit Research Participants for human research, such as advertisements, scripts, and social media postings;

(d) the measures that may be taken to eliminate or minimize therapeutic or other misconceptions with respect to Research Participant recruitment; and

(e) the measures that may be taken to eliminate or minimize undue influence or coercion with respect to Research Participant recruitment.

4.5.1.2 state that the recruitment of Research Participants will not be initiated until after:

(a) receiving all necessary approvals for the human research including ethical acceptability from an REB (see section 4.3.1 Obtaining Approvals to Conduct Human Research); and

(b) the research has been entered into a publicly accessible registry, if required.

4.5.1.3 state that Investigators/Researchers, recruiters, and third parties will not be incentivized to recruit Research Participants, such as finders' and referral fees, or non-monetary incentives.

4.5.2 Informed Consent Documents

The RE shall have procedural documents for the development of Informed Consent Documents.

Procedural documents shall describe the information contained in the Informed Consent Documents whether generated by the RE or from an external source. Annex E outlines the essential elements of an Informed Consent Document.

4.5.3 Process of Obtaining Informed Consent

The RE shall have procedural documents for obtaining informed consent, or waivers or alterations to consent requirements, from Research Participants or their legally authorized representatives.

Procedural documents shall outline the process for:

4.5.3.1 obtaining informed consent and assent, if applicable, prior to the initiation of human research, including, but not limited to:

(a) verifying the appropriate individual from whom informed consent will be obtained;

(b) determining the acceptable settings wherein consent may be obtained, and the justification for the mode of consent (eg, oral, written, collective, e-consent);

(c) assessing and accommodating the diverse needs of the individuals from whom consent is solicited, such as age, gender, culture, language, (dis)ability, and decision-making capacity;

(d) where applicable, soliciting consent from Research Participants, and the qualifications and training of the individuals involved;

(e) verifying and documenting consent from Research Participants;

(f) determining the steps that may be taken to minimize and conflicts of roles, coercion, and undue influence in the solicitation of consent from Research Participants;

(g) ensuring the involvement of a witness, if any, in the informed consent process;

(h) ensuring the allowance of time for Research Participants to ask questions and make a decision concerning participation; and

(i) assessing the resources available to Research Participants to support informed consent.

4.5.3.2 ensuring that the Research Participant’s consent is an ongoing process.

4.5.3.3 re-soliciting consent from Research Participants when amendments are made to the Informed Consent Documents, where applicable.

4.5.3.4 re-soliciting consent when there is a significant change in decision-making capacity of the Research Participant.

4.5.4 Withdrawal of Research Participation

The RE shall have procedural documents for managing the withdrawal of Research Participants whether voluntary or for other reasons.

Procedural documents shall outline the:

4.5.4.1 criteria for premature withdrawal of Research Participants (eg, safety concerns, withdrawal of research sponsorship, decision of the Research Participant, request from the Investigator/Researcher, REB or other regulatory authority).

4.5.4.2 process for communicating with Research Participants the rationale and implications of premature withdrawal from research and alternate options available.

4.5.4.3 process for safety monitoring of Research Participants withdrawn from research, if applicable.

4.5.4.4 process for Research Participants to withdraw their research data and biological materials including an indication of when research data and biological materials can be withdrawn.

4.5.5 Negative Impacts of Research

The RE shall have procedural documents for monitoring and reporting negative impacts of research.

Procedural documents shall outline the:

4.5.5.1 process for monitoring negative impacts of research on Research Participants and others.

4.5.5.2 process for reporting negative impacts to relevant groups such as Research Participants, the RE, REB, research sponsors, and regulatory authorities, as appropriate.

4.5.5.3 process for addressing and mitigating negative impacts including provision of care or support, indemnification, and other support, if applicable.

4.5.5.4 process for ensuring that Research Participants have the necessary tools to inform care providers of their participation in research, where applicable.

4.5.5.5 circumstances that would lead to the premature termination of research including stopping rules.

4.5.6 Research Participant Compensation, Restitution, and Incentives

The RE shall have procedural documents for the compensation of Research Participants' time, effort, and expenses, restitution for research related injury or loss,

and incentives designed to encourage their participation in human research. Annex F outlines the various elements to consider regarding Research Participant compensation, restitution, and incentives.

Procedural documents shall:

4.5.6.1 describe whether and under what conditions Research Participants may be compensated for:

(a) direct expenses incurred during their participation in human research (eg, reimbursement for transportation, childcare, lodging, meals); and

(b) indirect expenses incurred during their participation in human research (eg, time, unpaid leave from work), and the schedule of such reimbursements in proportion to the duration of their participation.

4.5.6.2 describe the provisions, if any, that should be made for restitution to Research Participants for injuries or losses that arise as a result of their participation in human research.

4.5.6.3 describe the conditions and justification wherein Research Participants may be offered incentives, monetary or otherwise (eg, gift cards, raffle tickets), in order to encourage their participation in human research, and the schedule of such incentives.

4.5.6.4 describe the requirement for informing Research Participants of the details concerning compensation, restitution for research related injury or loss, and incentives.

4.5.7 Respecting Research Participants' Cultures, Beliefs, and Social Identity

The RE shall document how it will ensure that the culture, beliefs, and social identity of Research Participants and their communities will be respected.

4.5.7.1 Procedural documents shall describe the process for ensuring that the culture, beliefs and social identity of Research Participants will be respected by all Individuals who Play a Role in the RE, and applied throughout the entire human research process. This includes, but is not limited to, the building and fostering of relationships with, and inclusion of, culturally- and socially-identifiable individuals and their communities in the entire human research process.

4.5.8 Research Participants' Inquiries and Concerns

The RE shall have procedural documents to address inquiries and concerns of Research Participants.

Procedural documents shall describe:

4.5.8.1 who, in general, within the RE is responsible for addressing and directing inquiries and concerns of Research Participants, and describe how their contact information will be conveyed to Research Participants.

Procedural documents should describe:

4.5.8.2 a plan to communicate to Research Participants that a process is in place to address their inquiries and concerns.

4.5.8.3 the process for addressing inquiries and concerns of Research Participants in a manner that is inclusive, accessible, and respectful of their rights and privacy.

4.5.8.4 the process to ensure that Research Participants' inquiries and concerns will be addressed in a timely and efficient manner.

4.5.9 Privacy Considerations

Where there is a NSC dealing with privacy as it relates to human research, the RE shall recognize and follow it. If a NSC does not exist, the RE shall ensure that it has procedural documents consistent with applicable privacy laws that protect the privacy interests of Research Participants and maintain the confidentiality and security of Research Participants' personal information throughout the lifecycle of the research.

Research Objectives

4.5.9.1 Procedural documents shall limit the research data to be collected to those required to accomplish the research objectives.

Recruitment

Where individuals are being identified from a list that is not in the public domain, then procedural documents shall outline the acceptable options for ensuring that:

4.5.9.2 either the data custodian of the list or their delegate screens for potential Research Participants.

4.5.9.3 only individuals with a reasonable expectation of access will make the first contact with potential Research Participants.

Informed Consent

4.5.9.4 Procedural documents shall describe the circumstances when a research protocol would be exempted from requiring prospective informed consent for *de novo* data collection.

Primary Data Collection

4.5.9.5 Wherever practicable, research data will be collected directly from the Research Participant. Procedural documents shall describe the circumstances wherein data will not be collected directly from the Research Participant (eg, from their legally authorized representative).

Data Management and Analysis

Procedural documents shall:

4.5.9.6 describe the acceptable options for how the collected research data will be kept secure at time of collection, in transmission, and in storage.

4.5.9.7 identify the limits on protecting research data due to professional or regulatory requirements, if applicable (eg, when there is the duty to warn of imminent harm, when required to be released under court order, when research data will be stored in, or accessible from, another jurisdiction).

4.5.9.8 describe the procedures for managing a privacy breach, including reporting to the individual(s) whose data were breached, senior management, the original data custodian, and the REB, as applicable.

4.5.9.9 where applicable, describe the additional procedures for managing human biological materials and associated data including, but not limited to:

(a) the roles and responsibilities regarding custodianship;

(b) any future uses, including material transfer agreements to third parties, and any subsequent requirements for Community engagement;

(c) where and for how long biological materials and associated data will be stored and secured;

(d) whether biological materials may be used for secondary purposes or by individuals other than those of the approved investigation for secondary use;

(e) what measures are in place to ensure that secondary uses of biological materials respect the privacy and other interests, including consent provisions, of the Research Participants; and

(f) the process for Research Participants to withdraw their biological materials and associated data.

Reporting

Procedural documents shall:

4.5.9.10 describe the circumstances where it would be permitted for a Research Participant to be identified in publications.

4.5.9.11 outline the provisions for ownership of and access to creative works (eg, digital stories, artwork) where the identity of authors may be revealed.

4.6 Human Research with Indigenous Peoples and Other Communities

The RE shall develop procedural documents for conducting human research with communities that foster better understanding of the unique characteristics and needs of each Community and establish collaborative partnerships. This enables the good of the Community to be considered along with the good of the individuals that comprise it.

4.6.1 Research with Indigenous Peoples

Where there is a NSC for research with Indigenous Peoples, the RE shall recognize and follow it. If a NSC does not exist, the RE shall ensure that it has procedural documents that describe how it will promote a respectful research environment when conducting research with Indigenous Peoples.

Procedural documents shall describe the process for ensuring that:

4.6.1.1 an authentic partnership with the Indigenous Community is established, including, but not limited to, how the Investigators/Researchers will:

(a) demonstrate that they entered into a voluntary and mutually beneficial relationship with the Indigenous Community prior to designing the research;

(b) continue to develop the relationship; and

(c) sustain the relationship throughout the research process and thereafter.

4.6.1.2 Indigenous research governance processes are adhered to, including, but not limited to, describing how:

(a) Indigenous governance structures and REBs will intersect (eg, ensuring that the Indigenous Community's process is followed in terms of the order of REB review and approval in relation to Indigenous Community review and collective consent);

(b) collective consent is to be obtained from the Indigenous Community; and

(c) ongoing collective acceptability of the research to the Indigenous Community is to be monitored.

4.6.1.3 the RE promotes Indigenous sovereignty over research data, including a process for ensuring:

(a) Indigenous ownership of research data;

(b) Indigenous control of research data; and

(c) that organizational structures within the RE (eg, legal requirements, financial policies) do not unduly burden or restrict Indigenous sovereignty over research data.

4.6.1.4 research funding respects the infrastructural needs of Indigenous Communities, including, but not limited to, the following:

(a) how the RE will ensure that Investigators/Researchers do not unduly burden Indigenous Communities; and

(b) how Research Participants and Indigenous Community leaders are appropriately compensated for engagement in research.

4.6.1.5 Individuals who Play a Role in the RE and plan to conduct research with Indigenous Peoples have been appropriately trained on research with Indigenous Peoples before any elements of research are undertaken.

Procedural documents should describe the process for ensuring that:

4.6.1.6 Indigenous research governance processes are adhered to, including describing how the research partnership would be dissolved and the Investigators/ Researchers' involvement in the research terminated, should collective consent no longer apply.

4.6.1.7 research funding respects the infrastructural needs of Indigenous Communities, including how the RE will support a goal of having research funds managed by the Indigenous Community rather than the research institution, whenever possible.

4.6.2 Research with Other Communities

The RE shall ensure that it has procedural documents that describe how it will promote a respectful research environment when conducting research with humans based on their membership in specific communities. Examples of communities include, but are not limited to, individuals who have the shared experience of a common impairment (eg, hearing, vision), disease (eg, HIV AIDS, breast cancer, Alzheimer's Disease), genetic

history, cultural history, social relationship, or marginalization. In developing its procedural documents, the RE shall consider the relevant requirements described in section 4.6.1 - Research with Indigenous Peoples.

Procedural documents shall describe the process for ensuring that:

4.6.2.1 an authentic partnership with the Community is established, including, but not limited to, how Investigators/Researchers will:

(a) identify and consult with the Community leadership, or if such leadership does not exist, identify and consult with individuals who represent various groups within the Community;

(b) demonstrate that they entered into a voluntary and mutually beneficial relationship with the Community; and

(c) continue to develop the relationship, and sustain the relationship throughout the research process and thereafter.

4.6.2.2 the Community is engaged in the human research from design to completion.

4.6.2.3 research funding respects, and where possible enhances, the infrastructural needs of the Community, including, but not limited to, the following:

(a) how the RE will ensure that Investigators/Researchers do not unduly burden or over-solicit communities; and

(b) how Research Participants and Community leaders are appropriately compensated for engagement in research.

4.6.2.4 the research is likely to generate knowledge that could benefit the Community (eg, to increase the understanding of causal factors, to contribute to the health or well-being of Community members).

4.6.2.5 where appropriate, approval from the Community is granted prior to the commencement of any human research activities (see section 4.3.1 – Obtaining Approvals to Conduct Human Research).

4.6.2.6 where appropriate, Community research governance processes are adhered to, including, but not limited to, describing how:

(a) collective consent will be obtained, if required; and

(b) ongoing collective acceptability of the research to the Community will be monitored.

4.6.2.7 results and knowledge derived from the human research are transferred, translated, and exchanged (eg, Knowledge Translation and Exchange, Knowledge Mobilization) with the Community.

4.6.2.8 where applicable, any agreements with the Community include details for ownership of and access to data and include arrangements for co-authorship in situations where Community members are collaborators or partners in the research.

4.7 Research that may Place Individuals in Situations of Vulnerability

In Canada, the relevant policy regarding human research is the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2). The TCPS 2 considers that individuals should not be deemed vulnerable simply because of assumptions made about the vulnerability of the group to which they belong (eg, impoverished) (Article 4.7). However, in some circumstances, individuals or groups may be placed in situations of vulnerability in the context of a research study. Therefore, the RE shall have procedural documents to identify and consider situations where Research Participants may be vulnerable in the context of the proposed human research.

Procedural documents shall:

4.7.1 outline the process for determining which situations and criteria render a Research Participant vulnerable in the context of the proposed research. For example, there are situations in which Research Participants are confined or lack accessibility, situations that disadvantages Research Participants economically or socially, and situations that place Research Participants in a relationship of power imbalance with the Research Team.

4.7.2 ensure that individuals placed in situations of vulnerability are neither inappropriately included (eg, over-researched populations), nor excluded from research (eg, avoiding research addressing individuals in situations of vulnerability). The selection of Research Participants should be guided first and foremost by the goals of the research.

4.7.3 outline the process for ensuring ethical oversight of research involving Research Participants in situations of vulnerability, including consultation with affected Research Participants, referral to support services, or applying safety protections, where appropriate.

4.8 Monitoring and Reporting of Human Research

The RE shall have procedural documents for the monitoring and reporting of human research. Monitoring of human research includes, but is not limited to, an examination

of records and source data to ensure the safety and welfare of Research Participants, and integrity of the research data.

Procedural documents shall:

4.8.1 define monitoring within the context of the RE, including the purpose of monitoring human research, and the applicable regulatory governance framework.

4.8.2 outline the elements and criteria for determining the scope and frequency of monitoring human research (eg, regulatory status, phase of research, type of research, risks), and the process for making this determination. Annex G provides examples of elements and criteria that may impact the scope and frequency of monitoring human research.

4.8.3 describe the qualifications and selection process for the individual(s) making the determination in section 4.8.2.

4.8.4 describe the qualifications and selection process for the individuals monitoring the human research.

4.8.5 outline the process for managing conflicts of interest and conflicts of roles of individuals described in sections 4.8.3 and 4.8.4.

4.8.6 describe the roles and responsibilities of individuals involved in the monitoring process (eg, Research Monitor, Investigator/Researcher, Research Coordinator, research sponsor).

4.8.7 outline the elements and criteria for determining the scope, frequency, and format of reporting human research monitoring, and the process for making this determination.

4.8.8 outline the process for identifying the monitoring report recipients (eg, REB, regulatory authorities, individuals within the RE, research sponsors/funders), including the issue escalation pathway.

4.8.9 outline the process and timeframe for managing non-compliance and critical issues identified during the monitoring process (see section 4.1.7 Compliance and Quality Improvement, Managing Incidents of Non-Compliance).

4.8.10 outline a contingency plan for monitoring during disruptive events and publicly declared emergencies (see section 4.1.9 Operations During Disruptive Events and Publicly Declared Emergencies).

4.8.11 outline the requirement for a project-specific monitoring process (eg, Monitoring Plan), that includes, but is not limited to:

(a) the monitoring methodology;

(b) the types of monitoring (eg, on-site, remote);

(c) the monitoring tools (eg, checklists, data metric reports, safety listings);

(d) the level of monitoring (eg, all records, targeted records, critical variables);

(e) the elements and criteria for determining the scope and frequency of reporting, and the process for making this determination (see Annex G);

(f) research site and Research Participant non-compliance reporting (see section 4.1.7 Compliance and Quality Improvement, Managing Incidents of Non-Compliance);

(g) the identification of the report recipients including the issue escalation pathway;

(h) monitoring report writing, review, and follow-up process; and

(i) reference to other ancillary documentation required (eg Communication Plan, Safety Management Plan, DSMB Charter, Data Cleaning and Data Management Plans).

4.9 Data Governance in Human Research

Data governance in human research serves several purposes. It optimizes research data use to meet the needs of the RE, it ensures that the use of research data meets ethics and legal obligations, and it applies safeguards to ensure appropriate access and protection against data corruption or other misadventure. When good data governance is demonstrated, it also generates trust among parties – most notably Research Participants – that research data are being used responsibly and in the public interest.

Increasingly, research sponsors are required to make research data more broadly available at the conclusion of the research. The RE needs to consider the implications of this throughout the lifecycle of the research data, for example, at the point of data collection (informed consent considerations), data processing (meta-data records), and data storage and archiving (managing external data requests).

The exercise of data governance will vary greatly across REs, depending on the degree of centralization of decision-making and accountability. For example, accountability for research data will be much more decentralized in an academic setting than in a corporate setting. Also, increasingly, research datasets are being created by consortia of research organizations, requiring a collaborative governance structure across

organizations. These contextual factors will promote innovative accountability structures, and harmonization across REs of policies and processes that govern the research data, the elements of which are described below.

Where there is a NSC for data governance in human research, the RE shall recognize and follow it. If a NSC does not exist, the RE shall ensure that it has procedural documents for data governance that address authority and accountability over the definition, production, and use of research data, to ensure the integrity, quality, and responsible use of research data.

4.9.1 Authority, Accountability, and Responsibility

4.9.1.1 Authority

The RE shall identify the relevant laws, normative texts, and NSCs governing their collection and processing of data concerning human Research Participants.

4.9.1.2 Accountability and Responsibility

The RE shall identify to whom accountability and responsibility are delegated for the management of research data in its custody over the lifespan of the data. Domains to be addressed include, but are not limited to:

(a) tracking of data holdings related to current and past research projects;

(b) development and adherence to project-specific Data Management Plans;

(c) data quality (eg, accuracy, completeness, consistency, reliability, timeliness);

(d) where applicable, locking of the dataset with no further changes to the raw data;

(e) compliance with relevant laws, normative texts, and NSCs;

(f) secure data infrastructure and access to data, with particular emphasis on who has access, for what purpose(s), and for which specific points in the lifecycle of the research project. (This includes archiving for purposes of open access to other researchers and plans for secure data destruction, as appropriate.); and

(g) the oversight process to ensure compliance with the Data Management Plan, including the pathway for escalating issues.

In addition, the RE shall have policies and procedures that specify:

(h) who retains custody over any research data collected should the Investigator/Researcher cease to participate in the RE; and

(i) the disposition and governance of the research data (eg, destroyed, transferred) should the RE fold or change ownership.

4.9.2 Tracking of Data Holdings

The RE shall have procedural documents that outline the process for tracking:

(a) active and past research projects for which research data have been collected;

(b) the individual(s) or group(s) accountable and responsible for each project-specific Data Management Plan;

(c) who has been granted access to a research project's dataset; and

(d) to whom and under what conditions datasets have been disclosed for specific purposes (eg, multi-centred studies, secondary analyses, as a part of open-access publishing).

4.9.3 Data Access

The RE shall have procedural documents that outline the processes for ensuring that:

(a) Investigators/Researchers have timely and unrestricted access to their original research data for the duration of the research to ensure that they can report findings accurately and make informed decisions regarding the involvement of Research Participants;

(b) external Investigators/Researchers have ready access to information (including meta-data) about research datasets that are available for secondary analysis and the process for accessing them (eg, through a public registry); and

(c) only those authorized are granted access to the data, and that access is monitored, and time limited.

4.9.4 Data Systems Validation

The RE shall have procedural documents that outline the process for validating data systems used to collect and process research data

(eg, systems for informed consent, electronic data capture, electronic participant reported outcomes, wearables).

4.9.5 Data Management Plans

The RE shall have procedural documents to describe how Data Management Plans are developed and maintained for each research project, including, but not limited to:

(a) what types of research data will be, or have been collected or created (eg, interview data, samples);

(b) any and all relevant laws, normative texts, NSCs, and contractual requirements that apply to the research data and to the uses and users of the research data;

(c) who is accountable for, and who will be responsible for managing the research data;

(d) the relevant meta-data, including but not limited to:

- data definition(s)
- data source(s)
- data lineage
- data limitations (eg, accuracy, completeness, consistency, reliability, timeliness) that may impact analyses or generalizability
- any procedures used for cleaning of the dataset to ensure accuracy in preparation for analyses
- time stamps (for reproducibility of results);

(e) what validated electronic data capture system and methods will be used to collect, validate, process, and document the research data;

(f) how the research data will be organized and documented;

(g) any restrictions on data use, linkage or retention as indicated through either consent of the individual who is the subject of the data or user agreement with the original data custodian. This includes use of de-identified data;

(h) who may have access to the data for primary or secondary purposes, the level of access (eg, read-only, read, write, delete), and how access for each role or group is justified and managed;

(i) where the research data will be stored and how they will be accessed during and after the research, including measures (eg, physical, technical, procedural) to secure the research data;

(j) whether and, if so, how individuals who are identified in the data (often referred to as data subjects) may request access to their data, corrections to their data, or transfer or removal of the data from the dataset; and

(k) when and how research data will be either securely destroyed or archived.

4.9.6 Data Quality

The RE shall have procedural documents that outline the process for ensuring that research data are accurately collected, recorded, and validated, that they are complete, unique (non-redundant), and that inconsistencies are managed.

4.9.7 Compliance with Relevant Laws, Normative Texts, and NSCs

The RE shall have procedural documents that outline the process for ensuring that the collection of research data, including both primary data collection and secondary uses of previously collected data, are consistent with relevant laws, normative texts, and NSCs. This includes, but is not limited to, considerations of:

(a) individual consent (including Community authorization, as appropriate);

(b) REB-approved exemption from requiring consent; and

(c) current best practices for collecting data from public sources.

4.9.8 Data Security

4.9.8.1 The RE shall have procedural documents that outline the process for ensuring that the necessary resources and infrastructure are present to enable the secure management of the research data throughout its lifecycle.

4.9.8.2 The RE shall have procedural documents that describe the process for ensuring that members of the RE, and sub-contractors, service providers and collaborators engaged in the collection, processing, and analysis of research data are:

(a) adequately credentialed and trained in accordance with section 4.1.2 Qualifications and Training of Individuals who Play a Role in the RE (both technically and regarding their duties, responsibilities, and obligations); and

(b) provided with supervision, and their access to research data is controlled and monitored.

4.9.8.3 The RE shall have procedural documents that describe the strategy and outline the processes for applying physical, technical, and procedural controls to address risks to the security (including cybersecurity) of the research data at each stage in its lifecycle, including, but not limited to:

(a) data loss or corruption (eg, ransomware, industrial espionage, theft, logical or physical segregation);

(b) social engineering or similar attacks (eg, phishing); and

(c) unsecure communication or data transfer (eg, VPN, two-factor authentication).

4.9.8.4 The RE shall have procedural documents that describe how identifiable research data may be de-identified and how those de-identified data may be used.

4.9.8.5 The RE shall have procedural documents that describe the long-term disposition of research data (eg, secure destruction, irreversible anonymization, archiving).

4.9.9 Audit

The RE shall have procedural documents that outline the process for monitoring compliance with:

(a) relevant laws, normative texts, and NSCs; and

(b) relevant project-specific data management documents.

(For further information, see sections 4.1.7 Compliance and Quality Improvement, and 4.9.1.2 Accountability and Responsibility.)

4.10 Dissemination of Research Results

The RE shall have procedural documents to ensure and monitor that the results of human research are responsibly disseminated in a timely manner, without undue restrictions, and, where applicable, in compliance with funding and public registry requirements.

Procedural documents shall ensure that:

4.10.1 all results (data analyses, interpretation of data, findings) of research are responsibly disseminated to Investigators/Researchers, Research Participants, and the public in a timely manner.

4.10.2 no prohibition or undue restrictions will be placed on Investigators/Researchers regarding the research results they can publish or responsibly disseminate.

Annex A: Examples of Elements Associated with the Proper Functioning of a RE (Informative)

Proper functioning of a RE includes elements that support the type, volume, and complexity of the human research that it conducts, including, but not limited to, the following:

Human Resources

- qualified Investigators/Researchers
- qualified research support personnel (eg, Research Coordinators, Research Associates, Research Monitors, laboratory, pharmacy)
- qualified administrative support (eg, individuals responsible for finance, human resources, security)

Other Resources

- ongoing training and continuing education
- access to appropriate equipment properly calibrated and maintained
- access to appropriate human research supplies
- adequate space, including spaces designed:
  - to protect the privacy of Research Participants
  - to maintain the integrity of biological materials
  - for secure and accessible storage and archiving of human research data
  - for specialized human research purposes (eg, laboratory, pharmacy)
- access to current and validated technological systems
- sufficient and uninterrupted funding of the human research

Oversight

- capacity for ongoing monitoring of study conduct
- access to specialists in relevant privacy laws, conflicts of interest, conflicts of roles, and responsible conduct of research
- access to relevant regulatory specialists, such as occupational health, biosafety, and others
- access to a properly constituted REB
- access to a properly constituted DSMB, if applicable
- regular, internal compliance auditing, including a process for managing incidents of non-compliance
- continuous quality improvement

Insurance and Legal Counsel

- adequate professional liability and property insurance
- adequate professional liability and property insurance of sub-contractors
- access to independent legal counsel
- appropriate and current licenses for validated screening or data-collection instruments (eg, questionnaires, quality of life measurements)

Annex B: Examples of Acceptable Training, Credentials, Certification, Education, and Experience for Individuals who Play a Role in the RE (Informative)

Individuals who Play a Role in the RE include members of a team who contribute to the research and share the responsibility for the protection of Research Participants, such as Investigators/Researchers, Administrative Personnel, Student Researchers, Research Coordinators, Research Monitors, Research Associates, and Community or Patient Partners involved in the conduct of the research.

Examples of acceptable training, credentials, certification, education, and experience of research team members include, but are not limited to, the following:

	Investigators/ Researchers	Administrative Personnel	Student Researchers	Research Coordinators Research Monitors Research Associates	Community or Patient Partners
Training					
Human Research Protection	X	X	X	X	X
Research Methods	X	X	X	X	X
Research Protocol	X	X	X	X	X
Equity, Diversity, and Inclusion (EDI) Training	X	X	X	X	X
Credentials					
Current *Curriculum Vitae**	X	X	X	X	
Professional licences**	X			X	
Certification***					
CRCC, CCRA (ACRP)				X	
CPI (ACRP)	X				
CCRP (SoCRA)	X			X	
ICH-GCP, if applicable	X	X	X	X	
TCPS CORE	X		X	X	
CITI – Division 5	X			X	
CRPC (CRAC)	X			X	
PHRP	X			X	
PHRP-SBER	X			X	
IATA (transportation of dangerous goods)	X			X	
RACS (RAPS)				X	
Education					
High school		X	X	X	
College/CEGEP		X	X	X	
Bachelor's Degree		X	X	X	
Graduate School Degree(s)	X		X	X	
Professional Degrees	X		X		
Other Degrees	X		X		
Experience					
Human research	X			X	
Research discipline	X				

*Current *curriculum vitae* demonstrating education, training, and experience to assume responsibility for the intellectual direction of the research or research-related activity, and to assume administrative responsibility for the grant, award or contract, if applicable.

**If the research involves restricted activities regulated by a professional licensing and regulating body, a valid professional license issued by the professional licensing and regulating body from the province where the research will be conducted.

***Depending on the nature or type of research, additional certification may be required (eg, communicating with people with disabilities, First Nations sensitivity training)

Certification Acronyms

CCRC:	Certified Clinical Research Coordinator (Certification from the Association of Clinical Research Professionals)
CCRA:	Certified Clinical Research Associate (Certification from the Association of Clinical Research Professionals)
CITI–Division 5:	Health Canada Division 5 – Drugs for Clinical Trials Involving Human Subjects (Certification from the Collaborative Institutional Training Initiative)
CPI:	Certified Principal Investigator (Certification from the Association of Clinical Research Professionals)
CCRP:	Certified Clinical Research Professional (Certification from the Society of Clinical Research Associates)
ICH-GCP:	International Conference on Harmonization, Certificate on Good Clinical Practices (Certification from by several organizations)
TCPS2 Core:	Certificate on the Tri Council Policy Statement (Certification from the Panel on Research Ethics)
CRPC:	Clinical Research Professional of Canada (Certification from the Clinical Research Association of Canada)
PHRP:	Protecting Human Research Participants (Certification from PHRP Online Training Inc. - fulfills NIH human subjects research training requirements)
PHRP-SBER:	Protecting Human Research Participants – Social, Behavioral and Educational Research (Certification from PHRP Online Training Inc. - fulfills NIH human subjects research training requirements)
IATA:	Certification on transportation of dangerous goods recognized by the International Air Transport Association
RACS:	Regulatory Affairs Certification (Certification from the Regulatory Affairs Professional Society)

Annex C: Examples of the Types of Information Contained in a Human Research Protocol (Informative)

Below are some examples of the types of information that may be contained or referred to in a Research Protocol, for various types of human research.

Background and Rationale

- General introduction
- Suitability of the researchers for the proposed research, including familiarity with the methodology, experience, and ability to work with the proposed Research Participant population
- Clearly defined research question
- Rationale or justification to conduct the research on humans, including why research in humans is necessary, appropriate, and why other alternatives to humans, such as animal or computer models, are not appropriate
- Stakeholder involvement

Study Objectives

- Primary, secondary, exploratory objectives or goals
- Clearly defined hypothesis(es)
- Key questions and research goals (Qualitative Research)
- Clearly defined, specific, measurable goals (Quantitative Research)

Research Population

- Inclusion and exclusion criteria
- Sample size or number of Research Participants, including the justifications or assumptions used during calculation or estimation
- Justification for inclusion and exclusion of Research Participants based on geography, language, race, gender, age, legal status, socio-demographic characteristics, lived experiences, pre-existing medical conditions or co-morbidities, overstudied or understudied populations
- Process for determining data saturation

Research Methods

- Study Design
  - description of the study design, such as:
    - qualitative/quantitative
    - interventional/observational
    - data collection methods (eg, semi-structured interview, focus group, questionnaires, secondary use of data)

- Engagement with Community or Patient Partners, as appropriate;
  - identification of Community leadership
  - qualification of Patient Partners (eg, lived experiences, responsibilities)

- Chronology and timelines of what is to be accomplished;
  - time period for:
    - Research Participant recruitment
    - conduct of the study
    - reporting, including dates

- Workflow and/or schedule of assessments;
  - number of study visits
  - details of study visits (eg, procedures, assessments)
  - study visit windows and/or follow-up time and/or member checking
  - prospective or retrospective research data collection procedures

- Intervention, if applicable, including allocation;
  - description of the intervention:
    - randomization procedures
    - group allocation
    - adaptive design
    - blinding and unblinding procedures

- Human research population sampling techniques;
  - description of the population sampling techniques:
    - convenience
    - quota
    - self-selection
    - snowball
    - cluster
    - simple random
    - systematic
    - stratified

- Process for recruiting Research Participants;
  - types of recruitment techniques employed:
    - circle of care

        - participant-facing advertisement
        - registry
        - Community outreach
        - student recruitment
        - self-referral
        - word of mouth
        - prior participation in related research
    - the use of incentives, where applicable
    - secondary use of previously collected data or biological materials that exist in databases or repositories

- Process of soliciting consent from Research Participants;
    - types of consent employed:
        - written
        - verbal
        - remote (electronic, paper)
        - assent
        - implied
    - other details:
        - timing and place of consent
        - who solicits consent, and method of contact
        - who provides consent eg, authorized third parties
        - capacity to consent
        - consent witnessed or unwitnessed
        - documentation of consent
        - waiver of consent
        - language concordance
        - comprehension

- Elements of masking and unmasking (also known as blinding and unblinding), if any, and plan to debrief;
    - justification for not debriefing
    - eligibility for alternative care, if any
    - timeframe for debriefing
    - format for debriefing
    - personnel responsible for debriefing, and their qualifications
    - level of disclosure
    - relevant materials, if applicable

- Elements of partial or full deception, if any, and plan to debrief;
    - rationale for partial or full deception
    - justification for not debriefing (eg, when debriefing could cause significant harm to the Research Participant)
    - resources for coping with deception
    - timeframe for debriefing
    - format for debriefing

  - personnel responsible for debriefing, and their qualifications
  - level of disclosure
  - relevant materials, if applicable

- Research data collection process, including the types of research data that will be collected;
  - retrospective and/or prospective research data collection
  - place of research data collection
  - personnel responsible for research data collection, and their qualifications
  - mode of collection (eg, audio or video recordings, paper, electronic)
  - types of research data collected:
    - biological materials
    - observations of behaviour
    - responses to questionnaires, interviews, focus groups, participant reported outcomes
    - images, pictures
    - prospective evaluations (eg, laboratory medical exams, medical assessments, psychological assessments)
  - secondary use of research data (eg, records, data linkages, data mining, recorded interviews, previously collected research data)
  - secondary use of public data (eg, public archives, social media posts, websites)
  - secondary use of private data collected by corporations
  - safety database review

- Plan for data governance and management;
  - Data Management Plan prepared according to specific guidance documents, if applicable (eg, Tri-Agency Research Data Management Policy, Good Clinical Data Management Practices, OCAP®, CARE Principles for Indigenous Data Governance)
  - personnel with access to the research data, their qualifications and responsibilities
  - case report or data collection forms development
  - database development (eg, edit check/validation specifications, data dictionary, program of reports, dashboards)
  - case report completion guidelines, data entry guidelines
  - data validation and quality control/data correction guidelines
  - data exports/transfer specifications
  - database lock
  - final database export
  - data archival storage
  - data sharing
  - management of licensed data, sensitive data, and secondary use of data
  - user management
  - withdrawal of data plan
  - administrative or technical safeguards to protect privacy and data integrity

- Data and safety monitoring plan, if required;
  - outline of criteria to determine the need for, and extent of monitoring
  - procedures for monitoring and reporting negative impacts of research
  - circumstances that would lead to the premature termination of the research
  - premature stopping rules are clearly defined
  - identification of parties involved (eg, DSMB, medical monitors)
  - appointment of personnel involved and their qualifications
  - identification of report recipients (eg, research sponsors, REB)
  - timelines for reporting

- Data analysis plan;
  - description of plan and type of analysis(es)
  - population(s) to be analyzed (eg, Intent to Treat, per protocol)
  - endpoints or questions to be analyzed
  - analysis methods, software, and programs employed
  - approach for missing research data
  - approach for multiplicity
  - approach for addressing inter-coder or inter-rater reliability

- Plan in the event that a Research Participant withdraws or is withdrawn from research;
  - plan for follow-up and care of Research Participant
  - rationale for Investigator/Researcher withdrawal of Research Participants
  - implications of withdrawal and plan to maintain research validity (eg, replacement strategy)

- Management of Research Participants' requests for withdrawal of research data and biological materials;
  - timing, process, and feasibility of accommodating requests
  - time for follow-up with Research Participants
  - personnel responsible for managing requests

- Dissemination plan for research results;
  - provision for timely and unrestricted access to original research data for the duration of the research from all Investigators/Researchers involved in multi-site research
  - plan for responsible and timely dissemination of the research results (eg, data analyses, interpretation of data, findings) to Investigators/Researchers, Research Participants, communities, registries, and the public
  - plan for presentations and publications
  - a statement that no undue restrictions will be placed on Investigators/ Researchers regarding what research data they can publish or responsibly disseminate

- Plan for early termination of the research
  - Outline of criteria for research termination

- plan for follow-up and care of Research Participants
- a plan for communicating with Research Participants, REB, sponsor, regulatory authorities

Management of Risks

- all benefits and potential physical and non-physical harms to Research Participants and non-participants (eg, families and communities) are clearly described
- harms to Research Participants are minimized and managed by using procedures and protocols that demonstrate concern for the welfare of the Research Participants
- harms to Research Participants are minimized by using procedures already being performed for other purposes (eg, diagnostic or treatment)
- harms to Research Participants are minimized by using procedures consistent with sound research design
- an assessment demonstrating that the benefits of the research outweigh the risks
- potential harms to Research Participants are reasonable in relation to anticipated benefits and importance of the knowledge that may be gleaned from the research
- a process is described to provide Research Participants with post-research information (eg, debriefing, provision of generalized research results in lay language)
- Research Participants' perceptions of benefits and harms has been assessed and there is evidence supporting the described benefits and harms

Ethical Considerations

- plans for REB review and approval
- plans for communicating modifications to approved research to relevant parties (eg, Investigators/Researchers, REBs, Research Participants, public registries, regulators)
- how personal information about potential and enrolled Research Participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the research
- plans for disclosing incidental findings to Research Participants
- provisions, if any, for restitution to Research Participants who suffer harm or loss due to research participation
- management of conflicts of interest and conflicts of roles of Investigators/ Researchers
- plans for collection and use of Research Participant data and biological materials in ancillary studies, if applicable
- authorship eligibility guidelines and any intended use of professional writers
- statement of who will have access to the final dataset, and disclosure of contractual agreements that limit such access for Investigators/Researchers

Research Team

- description of the Research Team:
  - identification
  - qualifications
  - affiliations
  - locations
  - roles
  - contact information
- experience of Research Team with similar research populations

Quality Control and Quality Assurance

- responsibilities of Research Team including availability for quality assurance audits
- process for reporting deviations
- process for data quality monitoring

Documentation and Record Keeping

- paper or electronic data collection
- data retention plan:
  - period of retention
  - retention location
  - responsibilities of personnel
  - funding
- access management plan

For more information:

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2018) Chapter 10 https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2018.html

Tri-Agency Research Data Management Policy (2021)
https://www.ic.gc.ca/eic/site/063.nsf/eng/h_97610.html

International Council for Harmonization (ICH) of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice Guideline https://www.ich.org/page/efficacy-guidelines

SPIRIT 2013 Statement: Standard Protocol: Recommendations for Interventional Trials
https://www.spirit-statement.org

Good Clinical Data Management Practices (GCDMP) https://scdm.org/gcdmp/

The First Nations Principles of Ownership, Control, Access, and Possession OCAP®
https://fnigc.ca/ocap-training/

CARE Principles for Indigenous Data Governance https://www.gida-global.org/care

Annex D: Examples of Research Activities Requiring Approval Prior to their Commencement (Informative)

Examples of research activities requiring approval prior to their commencement include, but are not limited to, the following:

- Research Participant recruitment activities
- review of a potential Research Participant's clinical chart, or other relevant records (eg, school records, performance evaluations)
- collection of any research data
- access to and analysis of research data
- secondary use of research data or biological materials
- collection of biological materials

Annex E: Examples of the Main Elements of an Informed Consent Document (Informative)

The Informed Consent Document reflects the research proposed and includes, but is not limited to, the following elements (based on CAN/HRSO-200.01-2021, Annex C). The extent to which these elements apply depends on the type of research undertaken.

- an introduction to the research
- the objective(s) of the research
- the research procedures and methods including all tests and procedures to be performed
- the details of Research Participant responsibilities including expected duration and schedule of participation
- the details of research participation, withdrawal, and early termination
- the risks and benefits associated with research participation
- any reasonably anticipated benefits
- details of compensation or incentives with respect to amount, conditions, and distribution schedule
- any financial impact that compensation or incentives may impose on Research Participants (eg, if some research related expenses will not be compensated, if compensation is subject to taxation)
- any anticipated expenses associated with participation
- the details of provisions for restitution for research related injury or loss
- the resources available to Research Participants should they experience research related injury or loss, such as medical care referrals, counsellors, legal services, support services (eg, emotional, psychological, trauma)
- any alternatives to participation
- who will be granted direct access to Research Participants' information and for what purpose
- how new information that may impact a Research Participant's willingness to continue participation in the research will be made available
- the methods used to safeguard Research Participant privacy and confidentiality
- the contact details for information regarding the research, Research Participants rights, and whom to contact in the event of research-related injury
- appropriate allowance for signatures and signature dates

Annex F: Considerations for Research Participant Compensation, Restitution, and Incentives (Informative)

Compensation and Incentives

The following are various elements to consider when compensating Research Participants or offering incentives to encourage their participation in human research:

- neither compensation nor incentives should create a situation of undue influence or exploitation of Research Participants
- Research Participants are informed of the:
    - details of compensation or incentives with respect to amount, conditions, and distribution schedule
    - any financial impact that compensation or incentives may impose on Research Participants (eg, if some research related expenses will not be compensated, if compensation is subject to taxation)
- where appropriate and feasible, capacity building is offered for individuals, groups or communities in situations of vulnerability
- the process of compensation or incentivization does not cause harm to Research Participants (eg, by breaching the privacy of Research Participants)
- compensation for time and effort:
    - is commensurate with participation in the research
    - is proportionate to the duration of participation for a Research Participant who withdraws or is withdrawn from the research for any reason
    - accrues as the research progresses
    - is provided at regular intervals throughout the research, and is not contingent upon the Research Participant completing the research

Restitution for Research Related Injury or Loss

The following are various elements to consider when providing restitution to Research Participants for research related injury or loss:

- Research Participants are informed of:
    - the details of such provisions
    - the resources available to them should they experience research related injury or loss, such as medical care referrals, counsellors, legal services, support services (eg, emotional, psychological, trauma)
- the RE has adequate liability insurance for restitution to Research Participants who suffer research related injury or loss

Annex G: Examples of Elements and Criteria that May Impact the Scope and Frequency of Monitoring Human Research (Informative)

The following are examples of elements and criteria that may impact the monitoring of human research. The RE should consider the following elements and criteria when making a determination of the scope and frequency of human research monitoring paying particular attention to the risk of harm to Research Participants.

Human Research Project

- design complexity
- duration of the research
- research population's characteristics
- complexities related to the informed consent or process of obtaining informed consent
- type of research
- type(s) and methods of research data collected (eg, participant reported outcomes, questionnaires, imaging, wearable devices)
- therapeutic or care area, if applicable
- type of intervention, if applicable
- current regulatory status of intervention, if applicable, and potential for changes to this status during the research
- development phase, if applicable (eg, clinical research phases I, II, III, IV)
- regulatory governance framework
- complexity of laboratory analyses including collection, storage, and processing of biological materials, if applicable

Investigators/Researchers and the Research Site

- qualifications and training
- experience with the type of research
- experience with the type of intervention, if applicable
- experience with the varied characteristics of the research population under investigation
- suitability of the research site for the research project
- presence of or potential for other competing research projects that affect the time commitment for the research project or the ability to recruit Research Participants
- ability to meet Research Participant recruitment targets
- RE's compliance concerns with the Investigators/Researchers and the research site, if any

Annex H: Informative References

The following Informative documents are meant to help with the conceptual understanding of this NSC. The user of this NSC should refer to the latest edition or revision of these informative documents.

CARE Principles for Indigenous Data Governance https://www.gida-global.org/care

Institute of Medicine - Preserving Public Trust: Accreditation and Human Research Participant Protection Programs
https://www.nap.edu/catalog/10085/preserving-public-trust-accreditation-and-human-research-participant-protection-programs

Report on the Evaluation of Control Mechanisms in Clinical Research in Quebec (The Deschamps Report), authored by Pierre Deschamps, BCL, CM
https://www.hracanada.org/hra/wp-content/uploads/2021/12/Deschamps-Report.pdf

The Governance of Health Research Involving Human Subjects (HRIHS), Report to the Law Commission of Canada, authored by Michael McDonald, BA, MA, PhD
http://publications.gc.ca/site/eng/9.690651/publication.html

Council for International Organizations of Medical Sciences (CIOMS): International Ethical Guidelines for Biomedical Research Involving Human Subjects
https://cioms.ch/wp-content/uploads/2016/08/International_Ethical_Guidelines_for_Biomedical_Research_Involving_Human_Subjects.pdf

World Medical Association - Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects
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