OCREB Standard Operating Procedures
Glossary of Terms

Ad hoc advisor: a person with relevant and competent knowledge and expertise consulted by a research ethics board for a specific research ethics review, and for the duration of that review, in the event that the board members lack specific expertise or knowledge to review with competence the ethical acceptability of a research proposal. The ad hoc advisor is not a member of the research ethics board and is not counted in the quorum or allowed to vote on board decisions.

Administrative changes and pre-approved centre-specific consent changes: all provincially approved OCREB study documents (including participant materials such as wallet cards and consent forms) are approved for use by participating centres with the application of centre specific 'administrative changes' to the document, without further OCREB review. Administrative changes include, for example, the addition to the document of centre contact information, centre letterhead (header and footer), removal of instructional text and spelling corrections. Pre-approved centre-specific changes are changes to the consent form that have been authorized (pre-approved) by OCREB as noted in the approval letter and as documented in the centre's profile in the online system.

Adverse event (AE): any untoward medical occurrence in a research participant administered an investigational product, including an occurrence which does not have a causal relationship with this product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product.

> **Local adverse event:** those adverse events experienced by study participants enrolled by the Investigator at the centre under the jurisdiction of the REB.
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> **Non-local (external) adverse event (EAE):** those adverse events experienced by research participants enrolled by Investigators at <u>other</u> centres/institutions outside the REB's jurisdiction.

Assent: affirmative agreement to participate in research by an individual unable to provide consent.

Alternate member: a formally appointed voting member of the REB who may substitute for a regular member of the REB but who is not expected to attend every meeting. An alternate member's presence at the OCREB meeting in the place of an absent regular member is used to establish quorum.

Amendment: a written description of a modification or change(s) to the previously approved research study. Amendments include any changes to the provincial application including modifications to the protocol and/or consent forms, revisions to the Investigator brochure, updated participant material, etc.

Authorized Signatory: individual(s) authorized to sign documents on behalf of an institution or organization.

Authorized third party: any person with the necessary authority to make decisions on behalf of the prospective participant who lacks the capacity to consent to participate, or to continue to participate, in a particular research study. (Also known as a 'legally acceptable representative' or 'substitute decision-maker').

Confidentiality: refers to the agreement between the Investigator and the participant as to how personal data will be managed and used.

Conflict of Interest (COI): the incompatibility of two or more duties, responsibilities or interests (personal or professional) of an individual or an institution as they relate to the ethical conduct of research, such that one cannot be fulfilled without the other. A conflict of interest may arise when activities or situations place an individual (i.e., researcher or REB member) or institution in circumstances that create a risk that an independent observer would reasonably question whether professional judgments or actions regarding a primary interest may be unduly influenced by a secondary interest thereby creating a real, potential or perceived conflict between the duties or responsibilities related to research, and personal, institutional or other interests.

Examples of secondary interests for a researcher include the following:

- Is receiving or expecting to receive compensation from the sponsor in which the value of the compensation could be affected by the outcome of the study;
- Acts as an officer, director, or agent of the sponsor;
- His/her job status or compensation is impacted by the research (e.g., payment for speaking or leading study groups on behalf of the sponsor);
- Is receiving a finder's fee for the recruitment of research participants;
- Has a proprietary interest (e.g., patent, trademark, copyright interest, licensing agreement) in the tested product;
- Has [or family, spouse, close relationships] any equity interest in the sponsor;
- Receives payments of other sorts, which are made by the sponsor exclusive of the costs of conducting the clinical study (e.g., a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria);
- Is intending to recruit his/her own patients as research participants;
- Has identified him or herself for any other reason as having a conflicting interest. (i.e. institutional conflict that may impact the research).

Examples of secondary interests for an REB member include the following:

- Is an Investigator or sub-Investigator on the protocol
- Is directly involved in the conduct of the research;

- His/her job status or compensation is impacted by the research (e.g., study coordinator, payment for speaking/leading study groups on behalf of the sponsor);
- Is receiving or expecting to receive compensation from the sponsor in which the value of the compensation could be affected by the outcome of the study;
- Acts as an officer, director, or agent of the sponsor;
- Has a proprietary interest (e.g., patent, trademark, copyright interest, licensing agreement) in the tested product;
- Has any equity interest in the sponsor that when aggregated for the member and the member's spouse and dependent children;
- Any equity interest in the sponsor, i.e., any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices;
- Significant payments of other sorts, which are payments made by the sponsor exclusive of the costs of conducting the clinical study (e.g., a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria);
- Is in direct competition with the Investigators of the study for limited resources, funding, sponsorship, or research subjects; acts as a consultant for the sponsor; is considered a personal or professional adversary of the Investigator;
- Has identified him or herself for any other reason as having a conflicting interest.

Institutional conflicts of interest: an incompatibility between two or more substantial institutional obligations that cannot be adequately fulfilled without compromising one or another of the obligations.

Continuing research ethics review (also referred to as "continuing review"): any review of ongoing research conducted by a research ethics board (REB) occurring after the date of initial REB approval and continuing throughout the life of the project to ensure that all stages of a research project are ethically acceptable in accordance with the principles in the Policy.

Controlled forms: documents that require formal change control, and that form part of the permanent record of REB operations and processes;

Data and Safety Monitoring Board (DSMB): a multi-disciplinary, expert advisory group established by a research sponsor, that is responsible for safeguarding the interests of participants by reviewing emerging data**,** assessing the safety and efficacy of research study procedures, and monitoring the overall conduct of a research study.

Electronic signature: an electronic fingerprint associated with an activity or a document and attributed to an individual with the intent to authorize the activity or to sign the record. The OCREB Online (O2) system incorporates an electronic signature that is unique to each user. The date, time and user name is recorded in the history and tied to the activity executed or to the record signed.

Expedited review (also referred to as delegated review): the level of REB review assigned to minimal risk research studies. Expedited review procedures also may be used for the review of: centre-specific applications for which the main provincial submission already has undergone full REB review; researcher responses/affirmation that conditions of REB approval have been met; minor changes in approved research; and, continuing review applications that meet the expedited review criteria. Under an expedited review procedure, one or more qualified reviewers are selected from among the REB membership to conduct the review.

Expiry date: the first day that the REB approval of the research study is no longer valid without further review and approval by the REB. For annual reviews, the expiry date is the one-year anniversary of the date of the initial approval by either the convened REB or via expedited review, as applicable. When the REB determines that review more than annually is required, the expiration date will be determined by the REB (e.g., six months from the date of the approval).

Formal relationship (with OCREB): indicates that an institution has signed a Letter of Intent to authorize the use of OCREB and has registered OCREB under their Federal Wide Assurance. Once a formal relationship is established, the affiliated institution may delegate OCREB as the REB of Record on a study-by-study basis by executing a Board of Record Study Agreement**.**

Full research ethics board (REB) review: the level of REB review assigned to above minimal risk research studies. Conducted by the full membership of the research ethics board, it is the default requirement for the ethics review of research involving humans.

Human genetic research: the study of genetic factors responsible for human traits and the interaction of those factors with each other, and with the environment.

Identifiable information (also referred to as "personal information"): information that may reasonably be expected to identify an individual, alone or in combination with other available information.

> **Directly identifying information**: the information identifies a specific individual through direct identifiers (e.g. name, social insurance number, personal health number).
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> **Indirectly identifying information:** the information can reasonably be expected to identify an individual through a combination of indirect identifiers (e.g. date of birth, place of residence, or unique personal characteristic).
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> **Coded information:** direct identifiers are removed from the information from which direct identifiers are removed and replaced with a code. Depending on access to the code, it may be possible to re-identify specific participants (e.g. the principal Investigator retains a list that links the participants' code names with their actual name so data can be re-linked if necessary).

Anonymized information: the information is irrevocably stripped of direct identifiers, a code is not kept to allow future re-linkage, and risk of re-identification of individuals from remaining indirect identifiers is low or very low.

Anonymous information: the information never had identifiers associated with it (e.g., anonymous surveys) and risk of identification of individuals is low or very low.

Identifying information: information that identifies an individual or for which it is reasonably foreseeable in the circumstances that it could be utilized, either alone or with other information, to identify an individual.

Impartial: without prejudice or bias, fair; a principle of justice holding that decisions should be based on objective criteria, rather than on the basis of bias, prejudice, or preferring the benefit to one person over another.

Impracticable: incapable of being put into practice due to a degree of hardship or onerousness that jeopardizes the conduct of the research; it does not mean mere inconvenience.

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

Incidental findings: unanticipated discoveries made in the course of research that are outside the scope of the research.

Inspection: a systematic examination and evaluation of study-related activities and documents in comparison to specified requirements and standards.

Institutional official (IO): a senior official who signs an institution's human subjects' assurance, making a commitment on behalf of the institution to comply with 45 CFR Part 46, the US Code of Federal Regulations covering protection of human subjects, and with Health Canada regulations.

Investigational product: refers to new or new usages of drugs, biologics, medical devices or natural health products.

Mature minor: an individual who demonstrates adequate understanding and decision-making capacity.

Medical device trials: clinical trials that test the safety and/or efficacy of one or more instruments used in the prevention, diagnosis, mitigation, or treatment of a disease or abnormal physical condition or the restoration, correction or modification of body function or structure.

Minimal risk: research in which the probability and magnitude of possible harms implied by participation in the research is no greater than those encountered by

participants in those aspects of their everyday life that relate to the research. For those individuals or groups who live with relatively high risk on a daily basis, researchers and REBs have a responsibility to ensure that:

- their circumstances are not used as a rationale to expose them to unnecessary risks,
- including them as participants does not increase their vulnerability.

Minor change: any change that would not materially affect an assessment of the risks and benefits of the study or the integrity of the data, and does not substantially change the specific aims or design of the study.

Multi-centred: in the context of OCREB, multi-centre means that the research study is reasonably expected to be conducted at more than one centre in Ontario.

Natural health product (NHP) trial: a clinical trial testing the safety and/or efficacy of one or more natural health products. The term natural health product is used to describe substances such as vitamins and minerals, herbal medicines, homeopathic preparations, energy drinks, probiotics, and many alternative and traditional medicines.

Noncompliance: failure to follow applicable guidelines and regulations governing human research; failure to follow the protocol approved by the REB, or failure to follow stipulations imposed by the REB as a condition of approval.

Non-controlled forms: documents that are not part of the permanent record of REB operations and processes. Non-controlled forms also will contain version dates.

OCREB online (O2): a transparent, secure, web-based online system used for the preparation, submission, review, tracking and reporting of ethics applications to OCREB.

Ongoing research: research that has received REB approval and has not yet been completed.

Ontario Institute for Cancer Research (OICR): an independent, not-for-profit corporation funded by the Government of Ontario. OICR is a translational research institute dedicated to research on prevention, early detection, diagnosis and treatment of cancer. The Ontario Cancer Research Ethics Board (OCREB) is a program of OICR.

Participant: an individual whose data or responses to interventions, stimuli, or questions by a researcher are relevant to answering a research question; also referred to as “human participant and in other policies/guidance as “subject” or “research subject.”

Periodic safety update or summary report: a summary report, created by the sponsor, listing all of the reported unexpected serious adverse events that have occurred in a given reporting period, and which includes any significant areas of

concern and the evolving safety profile of the investigational product. *Adverse events that are considered to be unanticipated problems should be reported immediately.*

Personal health information: identifying information about an individual in either an oral or in a recorded form, if the information:

- relates to the individual's physical or mental health, including family health history;
- relates to the provision of health care, including the identification of persons providing care;
- is a plan of service for an individual requiring long-term care;
- relates to payment or eligibility for health care;
- relates to the donation of body parts or bodily substances or is derived from the testing, or examination of such parts or substances;
- is the individual's Provincial health number; or
- identifies an individual's substitute decision-maker.

Any other information about an individual that is included in a record containing personal health information is also included in this definition. This definition does not include information about an individual if the information could not reasonably be used to identify the individual.

Personal information: identifiable information about an individual. See "Identifiable information."

Principal Investigator (PI): the leader of a research team who is responsible for the conduct of the research, and for the actions of any member of the research team.

Privacy: an individual's right to be free from intrusion or interference by others. Privacy refers to persons and their interest in controlling the access of others to themselves (their personal information).

- **Privacy breach**: the unauthorized collection, use, or disclosure of personal information or personal health information (PHI) in the custody and control of an individual or a Health Information Custodian (HIC) or in the custody and control of OCREB or its affiliated partners. **External privacy breach:** an unauthorized disclosure of personal information outside the confines of OCREB's employees, contractors, and researchers.
- **Internal privacy breach:** an unauthorized collection or use of personal information by OCREB's employees, contractors, and researchers.

Proportionate approach to research ethics review: the assessment of foreseeable risk to determine the level of scrutiny a research study will receive (i.e., delegated review for minimal risk research or full REB review for research above minimal risk), as well as the consideration of foreseeable risks, potential benefits, and ethical implications of the research in the context of initial and continuing review.

Protocol deviation: the term protocol deviation is not well defined by regulations or guidelines, but deviations are identified as any unplanned or unforeseen change to a REB approved protocol or protocol procedures. Deviations are different from amendments in that they generally apply to a single occurrence or participant and are not intended at the time to modify the entire protocol.

Provincial Applicant: the individual who takes overall responsibility for submitting the initial and ongoing provincial study materials to OCREB on behalf of the participating centres using OCREB. This includes the initial provincial application, any proposed provincial amendments to approved research, all provincial reportable events and all provincial continuing review applications. The PI at any of the participating centres using OCREB may serve as the Provincial Applicant. A representative from one of the academic or cooperative group sponsors (e.g., NCIC CTG, OCOG, PMHC) also may serve as the Provincial Applicant.

Quorum: a simple majority of REB members (50% + 1), who collectively have sufficient expertise in the scientific, methodological and clinical areas of the research study under review and are knowledgeable about relevant ethical and legal matters. The quorum will include at least one community member and a member whose primary experience and expertise are in a non-scientific discipline. Quorum includes members participating by telephone or video conference. Quorum also includes alternate OCREB members substituting for regular members in the same membership category.

REB of record: the research ethics board (REB) that has been granted ultimate authority for the ethics review and oversight of a research study.

Reportable event: includes anything that could significantly impact the conduct of the study or alter the REB's approval or favourable opinion to continue the study. Reportable events are submitted at the provincial or at the centre level, as applicable. Reportable events that meet the criteria for reporting to OCREB would be reported in one of the following categories, as applicable:

- **Provincial**:
    - DSMB/C Report
    - Interim Analysis Results
    - Safety Notice/Update (e.g., Action Letter)
    - Periodic Safety Update or Summary Reports
    - External Adverse Event
    - Other
- **Centre**:
    - Local Serious Adverse Event (SAE)
    - Protocol Deviation
    - Summary report of inspection or audit
    - Privacy Breach
    - Participant Complaint
    - Other

Research: an undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation.

Research ethics board (REB): a body of researchers, community members, and others with specific expertise (e.g., in ethics, in relevant research disciplines) established by an institution to review the ethical acceptability of all research involving humans conducted within the institution's jurisdiction or under its auspices.

Risk: the possibility of the occurrence of harm. The level of foreseeable risk posed to participants by their involvement in research is assessed by considering the magnitude or seriousness of the harm and the probability that it will occur, whether to participants or to third parties.

Suspension: a temporary or permanent halt to all research activities pending future action by the REB, by the sponsor and/or by the Investigator.

Termination: a permanent halt by the REB, by the sponsor and/or by the Investigator to all or some research activities.

Unanticipated issues: issues that: occur during the conduct of research; may increase the level of risk to participants or have other ethical implications that may affect participants' welfare; and were not anticipated by the researcher in the research proposal submitted for research ethics review.

Unanticipated Problem: any incident, experience, or outcome [including an adverse event] that meets **all** of the following criteria:

- ***Unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the REB-approved research protocol and informed consent document, or the Investigator Brochure; and (b) the characteristics of the research participant population being studied; **and**
- **+Related or possibly related** to participation in the research, (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the [investigational product(s)] or procedures involved in the research); **and**
- Suggests that the research **places research participants or others at a greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

  ***Unexpected:** an event is "unexpected" when its specificity and severity are not accurately reflected in the protocol-related documents such as the REB-approved research protocol, the Investigator brochure, or the current REB-approved informed consent document, or other relevant sources of information such as product labeling and package inserts; or when the event is not associated with the expected natural progression of any underlying disease,

disorder, predisposing risk factor, or condition of the participant(s) experiencing the adverse event.

+Related to the Research Procedures: an event is “related to the research procedures” if in the opinion of the Investigator or sponsor, the event was more likely than not to be caused by the research procedures.