BC Ethics Harmonization Initiative

Determining if a study is minimal risk – Common criteria guideline

Resource Document

BC Ethics Harmonization Initiative: Minimal Risk Working Group

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This resource document outlines common criteria generally used by research ethics boards (REBs) to determine what constitutes a minimal risk study when reviewing multi-jurisdictional health research involving multiple REBs. It also flags criteria that are specific to some REBs to distinguish between an assignment of minimal risk and above minimal risk.

Adapted from the UBC Office of Research Ethics, Clinical Research Ethics Board, Guidance Notes for Minimal Risk Studies.

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BCEHI – Guideline:
Common Criteria in Determining if a Study is Minimal Risk

Introduction

This guideline has been created by the British Columbia Ethics Harmonization Initiative (BCEHI) to assist BCEHI Research Ethics Boards (REBs) in their determination of what constitutes a minimal risk study and the scope of review required when involved in multi-jurisdictional health research requiring multiple REB approvals. The foundation for this document is the definition of 'minimal risk' as put forth by the Tri-Council Policy Statement (TCPS2) on Ethical Conduct for Research Involving Humans (Chapter 2B). Primarily, the objective is to help REBs apply the definition to various types of research and come to a consensus on the scope of the review required.

The document is intended as a guideline rather than a procedural directive as each project will need to be judged based on the unique context, and the probability and magnitude of risk exposed to the participants. An independent assessment will be required for each study based on the specifics of the study methods and sample populations because risks and benefits of research can be perceived differently in different contexts.

Article 1: Definitions

Minimal Risk Research – 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 the aspects of their everyday life that relate to the research (TCPS Chapter 2B). Minimal risk research is generally reviewed by a delegated review.

Above Minimal Risk Research **–** Research in which the probability and magnitude of possible harms implied by participation in the research is greater than those encountered by participants in the aspects of their everyday life that relate to the research. If the research does not meet the requirements for minimal risk, the reviews are conducted by the full membership of the REB (full board review), as it is the default requirement for the ethics review of research involving humans.

Delegated Review: - Any review of a study deemed minimal risk that applies a proportionate approach to the level of risk (i.e. not full board). The review may be conducted in a variety of ways according to the REB institutional policies and procedures including delegating to an individual e.g. office REB administrator; Chair; REB member or to a combination of individuals selected from the REB membership.

Article 2: Delegated Review Approach for Minimal Risk Studies

In accordance with the TCPS2, full review by an REB is the default requirement, unless the REB decides to authorize delegated review based primarily on the assessment of vulnerability of the participants and the possible harms that are expected to arise from the research. Research that may be reviewed by the REB through delegated review include new research activities that present no more than minimal risk to human participants, and minor changes to and renewals of approved research.

NOTE: An REB retains the right to decide to put any application submitted for minimal risk review forward for full board review. The following detail some of the reasons why this may occur:

1. The REB deems the study to involve more than minimal risk;
2. The study might establish a precedent;
3. The study uses a novel approach the REB has not previously seen; and
4. The REB only conducts full board review

Article 3: Overarching Minimal Risk Criteria Consideration

BCEHI REBs concur that minimal risk is a broad category and that each REB independently determines its minimal risk criteria and when a study is considered minimal risk. However, when looking at the specific study types/designs outlined in Article 4 below, there are key criteria that most of the REBs flagged as being "threshold" criteria or considerations when assessing minimal risk. For example, if a study includes one of these threshold criteria or considerations, there may be a requirement to raise the study to the full board review level regardless of the other characteristics inherent in that study.

3.1. Risk

The assessment of risk is ultimately made by the REB, which considers the character (type) of the risk, the probability (likelihood) of its occurrence, the magnitude (size/amount) of the risk, and the vulnerability of the intended participant(s).

Types of risk include (not an inclusive list):

Physical risk: Risk of harm through bodily contact or administration of any substance, device or other intervention

Psychological or emotional harm: Risks of harm due to feeling embarrassed, uncomfortable, anxious or upset

Social Risk: Risk of harm due to loss of status, privacy, or reputation, and includes legal, financial or employment risk.

Vulnerability exists along a continuum and is influenced by many factors. The presence of these factors (including but not limited to those listed below) in combination with the research design can influence the level of risk and ultimately the designation of risk for the research study:

- Participant capacity (mental, emotional, cognitive)
- Wellness or health status
- Power relationships
- Setting and recruitment
- Socio-economic status
- Age
- Institutionalization
- Gender and gender identity
- Dependency

Example 1: Professionals and experts who are being interviewed for their expertise in relation to their field would generally be considered a "very low" vulnerability group. However, this same group, if being interviewed regarding personal/sensitive topics, may no longer be considered 'very low' in terms of vulnerability.

Example 2: Power relationships may include doctor-patient relationships, employer-employee relationships, and so forth. The presence of power relationships in the conduct of a study (e.g. recruitment, procedures etc.), may increase the level of risk of a study depending on nature of the study and the level of influence the power figure may have over the participant.

The following matrix provides a high level assessment of risk, which a REB administrator or REB may use to initially determine if the research to be reviewed is minimal or above minimal risk. It should be noted that this Matrix uses generalized terms such as "vulnerability" and "high, medium and low". A more detailed analysis of the specifics of the study should be conducted to ensure that the appropriate level of scrutiny is applied. Specific examples are included in the sections that follow.

		Research Risk		
		Low	**Medium**	**High**
Group Vulnerability	**High**	Full Board	Full Board	Full Board
	Medium	Minimal Risk (Delegated Review)	Full Board	Full Board
	Low	Minimal Risk (Delegated Review)	Minimal Risk (Delegated Review)	Full Board

3.2. Participation of Individuals under the BC Age of Majority

1. Age

The age of majority in BC is 19 and some REBs consider all individuals under this age as 'vulnerable' and therefore full board review is applied to any studies involving these individuals.

Conversely, other REBs do not consider that age alone is a sufficient deciding factor. These REBs consider that the topic of study, the approach of the research, and the risks are all factors that together influence the level of risk to a participant and the resulting level of REB review that is necessary when involving this age group. In this case, vulnerability of individuals under the BC age of majority is influenced by the research context and the "life" context of these individuals, rather than age alone.

2. Exceptions

An exception to #1 above may be made for minors who no longer live in the home of a parent of legal guardian when the research is otherwise deemed to be minimal risk. This group includes (but is not limited to): 17 to 18 year olds attending University and homeless youth[1].

3. Capacity for consent or assent

The TCPS2 states: "The determination of capacity to participate in research, then, is not a static determination. It is a process that may change over time, depending on the nature of the decision the prospective participant needs to make, and on any changes in the participant's condition. Assessing capacity is a question of determining, at a particular point in time, whether a participant (or prospective participant) sufficiently understands the nature of a particular research project, and the risks, consequences and potential benefits associated with it" (TCPS 2, Chapter 3C).

The general rule of thumb adopted by most REBs at this time, is that parental consent is required for research involving individuals under the BC age of majority. Often REBs will also have guidelines/policies regarding the requirement for "assent" from the individual as well. Some REBs, though, who are generally supportive of the requirement of parental consent in many circumstances, believe that there are research contexts in which parental consent is not necessary or beneficial. In some cases the REB may approve alterations or removal of

[1] Tri-Council Policy Statement 2 Interpretations: "How do researchers manage the consent process for post-secondary student participants who have not reached the age of majority?" (August 2011). http://www.pre.ethics.gc.ca/eng/policy-politique/interpretations/consent-consentement/

parental consent if the researcher has clearly stated the reasons and justification for this alteration or removal.

Some individuals under the BC age of majority may have the capacity to provide consent for their involvement, especially in health research that poses no or little risk (e.g. commenting about their physical activity, nutrition etc.)[2]. Some believe that requiring parental consent in these scenarios might be disrespectful to this individual. In other studies parental consent and participant assent may be the norm depending on the school district or health organization and its practices and policies. In some instances it may be appropriate that the individuals under the BC age of majority consent and parents are informed of their child's participation in the research.

3.3. Funding Source

1. Studies funded or supported by the US Federal government or subject to the US Food and Drug Administration regulations:

   ONLY studies that meet the US Office of Human Research Protection definition of minimal risk[3] ***<u>may</u>*** be considered as qualifying for delegated review. US funded and FDA regulated studies will generally not qualify for delegated review.

2. Study funding by for-profit sponsor/organization

   Pharmaceutical, biotech and medical device companies are common examples of for-profit funders of health research. For most of the REBs involved, the funding source as a stand-alone criterion does not determine the level of risk for a study. However, studies funded by these companies could require a full board review if issues such as privacy, confidentiality and consent, or intellectual property are involved, and the REB's policies require it.

[2] Tri-Council Policy Statement 2 Interpretations: "Does TCPS 2 specify an age of consent for children?" (August 2011). http://www.pre.ethics.gc.ca/eng/policy-politique/interpretations/consent-consentement/

[3] Office for Human Research Protections (OHRP) - Categories of Research – Expedited Review http://www.hhs.gov/ohrp/policy/expedited98.html

Article 4: Types of research studies that *may* qualify as Minimal Risk

4.1. Studies using previously collected/existing clinical data or health/medical records (secondary use)

1. Studies using existing database/registries or linking information between databases
2. Studies using previously collected data from existing documents or records or charts (generally "retrospective chart reviews")
3. Studies using *previously* collected clinical specimens where there is no further clinical need for the specimens

4.2. Studies intending to collect and analyse specific types of data

1. Studies that will involve only the collection of hair, nail clippings, deciduous teeth, excreta, salivary secretions, additional swabs or other external secretions that have been collected in a non-invasive manner and that may also be collected as part of routine clinical care
2. Studies that involve only the collection of placenta or amniotic fluid as a consequence of childbirth, or fetal tissue collected as a consequence of therapeutic abortion or miscarriage
3. Studies that involve only the collection of blood samples obtained either by venipuncture or a central line already put in place as part of clinical care

Note**:** The collection of blood may meet the criteria for minimal risk depending on the context of the collection, the participant population, the amount of blood to be collected, the number of times blood is to be collected, and whether the blood will be stored for further use or destroyed soon after testing is completed.

4. Studies that involve clinical data collected prospectively as part of clinical care.

4.3. Exercise Studies

1. Studies that will involve the collection of output data obtained as a result of moderate exercise undertaken by healthy volunteers
2. Studies that will involve the collection of output data obtained as a result of maximal exercise by healthy volunteers who are less than 40 years old. In these cases, the REB must receive and approve a safety protocol

Note: Exercise in a patient population will generally be referred to the full board.

4.4. Scans

Studies using data recorded using non-invasive procedures such as EEG, EKG, MRI, ultrasound or x-rays ***may*** meet the criteria for minimal risk depending on the context of the scanning, the participant population, the number of times the subject will be exposed to the radiation, and if the radiation exposure is in excess of 0.1 mSv (the approximately equivalent of one return transcontinental airline flight or 1/100 of the Canadian recommended dose limit per year).

4.5. Stem Cell Research

1. Stem cell research may qualify for delegated review with the exception of any research that concerns the derivation of stem cell lines from human somatic tissue, umbilical cord or placenta OR research involving the grafting of stem cell lines into humans.
2. Research that uses permanent stable cell lines[4] in laboratory research (i.e. in vitro) does not require ethical review.

4.6. Observational research on Standard Treatment(s)

Observational research on standard treatment(s) where the treatment(s) is (are) determined clinically and not assigned by research methodology (e.g. randomization)

4.7. Studies that involve only questionnaires or surveys

Questionnaire(s) that do not involve the collection of highly personal, sensitive or incriminating information; vulnerable populations; and/or impose a substantial burden on participants

4.8. Studies that involve only interviews and/or focus groups

Interviews/focus groups that do not involve collecting highly personal, sensitive or incriminating information; vulnerable populations; and/or impose a substantial burden on participants

[4] Permanent Stable Cell Lines Definition: Secondary Tissue Cultures which are derived from cells in Primary Tissue Culture by serial passages and dilution, often leading to clonally derived lines of cells having relatively uniform properties that have adapted to growth in tissue culture. Once characterized and described in the public domain, these cultures may be considered Established Cell Lines or Permanent Stable Cell Lines that can be maintained or stored indefinitely. Established Cell Lines can normally be obtained commercially or as a gift, but identifying information about the donor is not provided with the cells.

4.9. Other research studies that ***may*** qualify as Minimal Risk

1. Research with no direct interaction with participants (e.g. secondary use of data)
2. Usability studies in health information

   Participants are asked to use a special computer program to find or enter information, navigate mock or real websites while the program records their navigational patterns and/or verbal descriptions on why they navigate or use a program in a certain manner. If existing hospital or health authority programs are being used as the "platform," participants are typically the staff and frequent users of the programs (e.g. patients who attended a health workshop) and the patient information is anonymized or the researcher has obtained a data access agreement with the health authority or hospital.

Article 5: Types of "Minimal Risk" studies that may require Full Board Review

Minimal risk studies where a waiver of consent or alteration of the required elements of informed consent is being requested ***may*** or ***may not*** require Full Board review; this is determined on a case-by- case basis. (Waiver of consent does not apply to UNBC because informed consent is always required)

Note: The following types of studies often ***do not*** require full board review when a waiver of consent or an alteration of the required elements of informed consent is being requested.

a. Retrospective chart reviews;
b. Studies using data obtained from previously banked anonymized tissue that is not linked to other sources of data;
c. Studies using data from provincially regulated databases/registries (e.g Medical Services Plan, BC Centre for Disease Control) or from disease specific registries with data collected from subjects who have already consented to its use for the sort of research being done;
d. Prospective chart or medical record reviews where the data is anonymous, has been anonymized, or is de-identified and the code is being held by an approved privacy guardian (data steward) and there is no potential harm to the subject; or
e. Prospective chart or medical record reviews where members of the research team are not in contact with subjects during the data collection and where the researcher has provided an appropriate justification for why contacting the participants to obtain consent would be impracticable (e.g. a prospective chart review that was conducted remotely and the researchers were never in contact with the patients).