



March 1, 2010

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Dear Ms. Zimmerman,

**Re: Canadian Association of Research Ethics Boards (CAREB) Response to the Release for Final Public Comment of the Revised Draft 2<sup>nd</sup> Edition of the Tri-Council Policy Statement**

CAREB is submitting a response to the call for final public comment on the revised Draft 2<sup>nd</sup> Edition of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS). CAREB, as a national organization representing Research Ethics Boards, has a significant interest in the content and application of the TCPS and appreciates the consultation period organized by the Interagency Advisory Panel on Research Ethics (PRE) and the opportunity to comment on the draft document.

As the interests of CAREB are mainly focused on research ethics administration we have provided comments on the chapters most relevant to these. The process that we used to craft our response involved inviting CAREB members to participate in one (or more) of six working groups, to review and provide comments regarding relevant chapters as listed here:

- Chapter 2: Scope and Approach
- Chapter 5: Privacy and Confidentiality
- Chapter 6: Governance of Research Ethics Review
- Chapter 7: Conflict of Interests
- Chapter 8: Multi-Jurisdictional Research
- Chapter 11: Clinical Trials

We are grateful to the CAREB members who participated in each of the working groups and these individuals are listed in Appendix B.

CAREB believes that the revised Draft 2<sup>nd</sup> Edition of the TCPS is a substantial improvement over the initial draft circulated in 2008-2009 and we acknowledge and appreciate that a majority of the concerns outlined in our June 29, 2009 response to the initial draft have been addressed. However, we have significant concerns with the changes made to Chapters 6 and 11. We believe that the recent changes to Chapter 6 (Governance of Research Ethics Review) adversely affect the role of Research Ethics Administrators (REAs) and, in fact, gives the appearance of trivializing the important and essential functions that we deliver. We have suggested possible wording changes to relevant Articles and to their corresponding Application sections. CAREB also has concerns about the recent changes to Chapter 11 (Clinical Trials) and a section on this chapter has been added.

CAREB recommends that PRE work closely with Health Canada and the Canadian General Standards Board (CGSB) Standards Committee to ensure that any guidelines with respect to Research Ethics Board governance and composition remain consistent between the TCPS and the proposed CGSB Standard.

Once again, we have organized our comments by referring to the relevant Chapters of the revised Draft 2<sup>nd</sup> Edition of the TCPS.

### **Chapter 5: Privacy and Confidentiality**

In general, the revisions to this Chapter are improvements upon the first draft. We appreciate the efforts of PRE to provide added examples for greater clarity and to define terms related to types of information. It is also significant that there is recognition that increasingly, information is capable of being re-identified and that REBs and researchers must take this into consideration.

While we note that PRE has not included our suggestions related to the Wigmore criteria, we do understand that there are contrasting opinions on this issue. We continue to believe however, that there is a contradiction between advice at lines 1775 – 1779 and the suggestion to incorporate all applicable statute-based or other legal principles for protection of privacy contained in lines 1805 – 1807.

In Article 5.5 and the references to waiver of consent for secondary use, we are pleased to see that the requirements to consider whether or not the waiver is unlikely to adversely affect the welfare of individuals and that it be “impossible or impracticable” to seek consent have been added to the criteria. We also appreciate PRE’s attempt to provide some guidance around the interpretation of the term impracticable. In this context, we suggest that PRE consider emphasizing that the primary considerations of the REB need to be in relation to the principles of justice and beneficence, in relation to the merit and the value of the study, rather than degrees of difficulty in seeking consent.

We also think that dropping the phraseology in 5.5. (c) previously (b) which referenced minimizing harm to participants was mistaken and reconsideration should be given to re-inserting it.

While we agree with the approach of PRE not delving into the specifics of variable privacy legislation, a more specific reference to the 10 principles of privacy could be considered.

We believe that there is still a large amount of room for variation in interpretation and the potential to clarify terms and definitions remains. We understand, however, that there are limits to the consultation and re-drafting stages associated with the Draft 2<sup>nd</sup> Edition of the TCPS, and that a final document needs to be issued. We trust that PRE will be able to address some of these remaining areas in subsequent interpretation documents and perhaps in some forms of frequently asked questions.

## **Chapter 6: Governance of Research Ethics Review**

Chapter 6 is of great importance to CAREB, as it sets out the process of Research Ethics Review (RER), including operations. As indicated above, we have significant concerns with respect to some of the changes made in this chapter as they have the potential to negatively impact the role of Research Ethics Administrators (REAs). We have included specific references and suggestions in Appendix A.

Article 6.1, Application, line 2040: in accordance with the review options offered in Chapter 8, an institution has more options than to appoint an REB at another institution.

Recommendation: expand the sentence to: “In fulfilling its responsibility, institutions may opt to appoint an REB at another institution, *or an external (or independent) REB.*”

### Article 6.2

CAREB believes that because of the critical role played by Research Ethics Administration in the operation of REBs, it is essential that the Policy address the role and reporting relationship of Research Ethics Administration staff, also known as REB staff or Research Ethics Administrators (REAs), who depending on their institution, may or may not be located within a more formal structure e.g. Research Ethics Office (REO). In order to maintain the independence of the REB process, it is also essential to recognize and ensure that REAs and the REO, as applicable, also report to the appropriate highest level of the organization. For example, if the REB reports to the Senate, Board of Governors (or similar body) through a Vice-President, the REAs or the REO should report directly to that Vice-President. If the REAs or the REO do not report to the equivalent level in the institution as the Research Ethics Board, ensuring independence of the process may not always be possible as the REAs or the REO provide the vast majority of the operational and administrative duties for effective and efficient REB processes.

This could be added directly in the Article or in the Application section. This will also set the stage for further recommendations in Article 6.11 (see below).

Recommendation: Include the following wording in the Article or Application section: “To maintain the independence of the REB process, it is also essential to recognize the role of Research Ethics Administrators (REAs) and the Research Ethics Office (REO), as applicable, and to ensure that they report to the appropriate highest body of the institution.”

Article 6.11 – Research Ethics Administration (Recommendation is to include a new Article and Application section with the suggestion to renumber all subsequent existing Articles incrementally)

Institutions acknowledge the broad role of the Research Ethics Administration function as critical to the effective and efficient running of the REB and integral to the delegated ethics review process operating in many institutions. As such, the institution shall provide sufficient resources and independence to its REAs in support of REB work and maintain compliance with all aspects of this document and other regulatory requirements.

#### Application

In the majority of Canadian research institutions, REBs are administered by the Research Ethics Administration staff: REB staff, REAs or the REO, if applicable. The structure and staffing of these entities differs across institutions, as does the relationship and work distribution between the REB and REAs.

Functions of the Research Ethics Administration staff and/or the REO may include REB coordination and administration, policy development and interpretation, provision of research ethics education to researchers, students and REB members, membership and/or participation in REB meetings and delegated ethics review of protocols. It is also recognized that Research Ethics Administration staff and/or the REO may provide important ethics expertise in support of the REB’s ethical analysis, reflection, and decision-making.

As REAs are essential to the ethics review process, their decisions must be free from influence and/or conflicts of interests. Therefore, the REA or the REO reporting line should be to the same body as the REB (see suggestion for Article 6.2 above). It is also essential that each institution provide sufficient resources for the REB staff or the REO to properly administer their REB duties and maintain compliance with all aspects of this document and other regulatory requirements. All REAs should have the necessary training and qualifications, and continuing education to perform their roles appropriately.

Current Article 6.4 (to be changed to Article 6.5 as noted above)

CAREB suggests that the following sentence be added for clarification at the end of this Article (at the end of line 2132) to recognize that Research Ethics Administration staff may be REB members:

Research Ethics Administrators (REAs) can serve as REB members when they have the requisite specific expertise, relevant competence and knowledge necessary to provide an adequate ethics review of the proposals (see current lines 2275-2277).

Article 6.9 (to be changed to Article 6.10 as noted above)

The language in the Application section (lines 2278-2281) needs to be changed as follows to recognize that REAs can be REB members:

Ad hoc advisors, observers, and others attending REB meetings should not be counted in the quorum for the REB. Nor should they be allowed to vote on REB decisions (see Article 6.5). Decisions without a quorum are not valid or binding. REAs can be counted in quorum and in voting on REB decisions when they are members of the REB.

Current Article 6.12 (to be changed to Article 6.13 as noted above)

Application, lines 2365-2367: CAREB suggests that the following replace the existing wording to recognize that Research Ethics Administration staff may be involved in the delegated REB review of minimal risk research:

The REB delegates ethics review to an individual or individuals. Delegates may be selected from among REB membership, REAs or at the faculty or departmental level.

Current Article 6.16 (to be changed to Article 6.17 as noted above)

Application, line 2559: it is unlikely that an REB would ‘approve’ changes from the approved research. Perhaps the intent of this sentence is to ensure that the REB documents its handling of deviations/changes to the approved research.

Recommendation: revise the sentence to reflect that the REB also shall have written procedures on record keeping for its management of other submitted reports such as deviations/changes to the approved research (e.g., REB review of such deviations/changes, communication with the investigator regarding any corrective action).

Current Article 6.17 (to be changed to Article 6.18 as noted above)

Application, lines 2576-2581- Because this section focuses on ‘Reconsideration of REB Decisions’, there should be an emphasis in the Application section on dialogue and communication between the REB (or delegated ethics reviewer) and researchers. Language like ‘deliberation’ should be reserved for the next section on ‘Appeal of REB Decisions’.

Recommendation: Consider wording similar to the following:

“...Researchers and REBs should work together to try to resolve any disagreements that may arise during ethics review and feedback stages through a process of dialogue and discussion. If a disagreement cannot be resolved through dialogue and discussion, the

researcher shall have the option of appealing the REB's decision through the institution's established appeal mechanism..."

"In the case of protocols reviewed by delegated ethics review, when a disagreement arises during the ethics review and feedback stages that cannot be resolved through dialogue and discussion between the researcher and the delegated ethics reviewer, the researcher may forward a request for reconsideration to the full REB. The onus...Policy"

Other Comments on Chapter 6:

#### Use of the term "approval"

Several REBs have stopped using the term "approval" on letters to researchers and in our internal documents. Phrases that indicate an REB "has approved" a project may suggest to participants that the REB is giving its stamp of approval to the research as a whole, when it is more accurate to say that the REB has deemed the research plan to be in compliance with ethical standards. This is a semantic issue similar to the one that caused the move from using the term "expedited review" to the term "delegated review." One suggestion for a replacement for "approval" is "clearance." For example, "This project has received ethics clearance from the REB."

#### Tri-Council's expectation for ethics approval and release of funding: TCPS guidance

Two situations exist where the TCPS and PRE could provide guidance and interpretation. One situation is the conditional ethics approval of research in advance of data collection to enable access to research funding. For example, many researchers face a dilemma in which they need funds to buy and/or test equipment; or need to get materials translated; or need to travel to set up testing sites and/or consult with communities before they engage in data collection. However, researchers cannot get access to their funds from major granting agencies (under the federal Memorandum of Understanding on the Roles and Responsibilities in the Management of Federal Grants and Awards - MOU) until they obtain ethics approval. If their research is not at the stage where human participants are involved, they cannot submit a research ethics application. This is an increasingly common issue and the TCPS could provide guidance for such cases.

Related to this is a situation involving Tri-Council financial monitoring teams who periodically visit research institutions that are signatories to the MOU. The interpretation of the TCPS by this team seems to be applied inconsistently and the resulting recommendations are therefore questionable. Whether under the MOU there is a requirement to have ethics review and approval for the full grant period or only for the period when research involving humans is being undertaken should be clarified to reduce stress on already scarce institutional resources. Many projects in the social sciences and humanities need a period of preparatory work to define the approach and methodology that will best be suited to the funded project in question. The entire concept of "in-principle" approval is not an effective mechanism to handle the release of research funds to such researchers even though the actual research involving humans will take place at a later year of the grant. It implies that REBs should review protocols when the researcher does not yet have a fully developed plan for their research to access research funds and

that likely the REB will need review the proposal once again when the preparatory work to develop the research proposal is complete.

It has also been observed that financial monitoring teams seem to equate one grant with one research ethics application and this has been reinforced in recent communication (email from by Isabelle Beauvais, Manager, Policy, Training and Monitoring, Financial Operations and Monitoring, CIHR, and Rita Carriere, Manager, Awards Administration and Financial Monitoring, NSERC/SSHRC) to the CAURA listserv regarding "Ethics Certificates and Sub-grants, next Step" which was sent on December 23, 2009). This is not in line with the spirit of the TCPS.

Although this may require amending the MOU, CAREB feels strongly that if the spirit of the TCPS does not imply that certification must be in place for the life of a grant but only during the period of time where research involving humans is being conducted, then the MOU must be changed to reflect this fact. It appears that there is only one reference in the MOU that needs to be changed: The specific reference in the MOU is at the end of item (f) in section 2.1, which states that "in any case, the research must maintain REB approval for the duration of the project".

## **Chapter 7: Conflict of Interests**

The Conflict of Interests (COI) chapter is generally well done. At this time, we have included specific references and suggestions in Appendix A.

## **Chapter 8: Multi-Jurisdictional Research**

The chapter on Multi-Jurisdictional Research is well thought out and well written. Most of CAREB's comments on Section A and B of this chapter were incorporated and the revisions correspond with the comments. The few comments in Section A that were not addressed relate again to the use of REB when "institution" or "REB and/or institution" should be used.

### **Comments:**

Preamble, Line 3099: institutions may adopt policies that permit arrangements for REB review off-site *at other institutions*. As per the alternative review models listed in Article 8.1, *off-site* will not always mean the REB review will occur "at other institutions". *Off-site* is also not defined.

Recommendation: revise the sentence to: "*Collaborative research may require institutions to adopt policies and procedures that permit arrangements for REB review by an REB at another institution or by an external or independent REB.*"

Article 8.1, Application, lines 3145 to 3158: This section of the Application applies only to Review Model #3. In Review Model #2, in delegating to another REB completely, the

communication would be between that REB and the institution and not necessarily the local REB. In this latter instance, the local REB is not always involved in "*accepting a review of another REB*"; rather, the institution is fully delegating to another REB.

Recommendation: move lines 3145 to 3158 to under Review Model #3: "Reciprocal REB Review".

Article 8.2 (lines 3227, 3235, 3240 and 3242): the use of "REB" here instead of or in addition to "institution" conflicts with the other sections confirming that "*the adoption of alternative review models is an institutional responsibility*". This inconsistency results from confusing the term "REB" with "institution" and does not reflect the ultimate accountability of the institution for determining which review models are appropriate.

Recommendation:

Line 3227: change "REBs" to "*institutions*"

Line 3235: change "REBs" to "*institutions and REBs (when appropriate to the chosen review model)*"

Line 3240: change "REBs" to "*institutions*"

Line 3242: Change "REB: to "*institutions*".

Lines 3192 to 3194: this section should be clarified. With the current wording, the section can be interpreted as overly restrictive. The terms "*specialized REBs*" and "*multi-institutional REBs*" are used as if they are well-established and understood types of REBs. The current wording also could be interpreted to exclude the use of independent REBs, unless it is to be understood that they fall under "specialized" or "multi-institutional". Further clarity is needed.

Recommendation: the title and wording should refer to the use of an external REB, perhaps with examples such as specialized REBs (e.g., therapeutic area specific) or independent REBs.

Line 3206: in this REB review model, the agreement is not necessarily with the "institution of the REB that will review the research" unless it is intended in a broad sense (i.e., the legal authority that has established the REB). Regardless, it should be clarified. Institution in this context implies the use of a local/institutional REB.

Recommendation: clarify that it is an agreement with the organization or legal entity that has established the external REB.

The removal of Section C of this chapter and the incorporation of this section into other areas of the document seems reasonable and appropriate and is the most significant change to the Chapter. The section that was removed focused on the risks and protections for both subjects and researchers, and these elements have been moved to other sections of the document.

Recommendation: reference this information, for clarity and completeness.

The remaining Section B of this chapter now is limited to a description of the requirements for setting up the review process within this specific context, (outside the jurisdiction of the REB), which corresponds to the format and content of the rest of the chapter.

### **Chapter 11: Clinical Trials**

A major shortcoming of the revised Draft 2<sup>nd</sup> Edition of the TCPS is the chapter on clinical trials. Overall it is unclear as to which audience is being addressed. It is neither for the novice, stressing only the ethical concerns with clinical trials, leaving out the complex regulations and guidelines related to the review and oversight of clinical trials, nor a detailed consideration of such details for the REB professional or REB member that must review such trials. Instead it is a mix of both that is ultimately confusing. Moreover, many details, e.g., reporting new information adverse events to the REB and the participants, are incorrect with respect to expectations of ICH-GCP and must be corrected or removed, otherwise the TCPS risks losing its credibility in the biomedical research community.

## Appendix A

### Editorial Changes / Additional Details Recommended

#### Chapter 6 – Governance of Research Ethics Review

- Line 2045- To ensure there is no confusion with respect to ‘its administration’ (i.e. is it referring to the institution in line 2044) this should indicate clearly ‘research ethics administration group or office and research ethics education’.
- Lines 2053-2055- This sentence could be clearer if reorganized to ‘if, in the course of their other organizational activities or their supplemental professional activities, they engage in research involving human participants’.
- It should also clarify that these activities would be ones conducted under the auspices of the institution.
- Lines 2066- 2074- This section seems potentially problematic as it does not give the necessary guidance around responsibility for ethics review. Nor does it seem to recognize the complexity of the ethics review process and data collection for students in the context of a 13 week term. Often students decide to collect a modest amount of data from humans as a way to supplement their work term report. Alternatively, the idea for a work term research project may originate with the co-op supervisor. These are typically minimal risk projects. Work term placement sites generally do not have their own REBs. Further the research idea may not be identified until well into the 13 week co-op placement. This would then mean that the student would need to apply for ethics approval at his/her home institutions. Timelines make this very difficult for the student and the REB. In the event the placement site does have its own REB, then it is conceivable that a student’s modest project might be subject to two REB reviews - in a 13 week term. More guidance should be provided on approaches that can be taken to deal with these types of challenges. Further, at certain points there seems to be a distinction between host organization and institution. It appears that the host organization is the co-op placement organization while the institution refers to say the university or institution where the student is obtaining his/her degree. However, line 2070 has “institutions and organizations hosting” so it gets a bit confusing as to what is what.
- Line 2085- What is meant by ‘removal’? Does this mean ‘for cause’?
- Line 2089- The wording ‘disagreement over a decision...through discussion and reconsideration...’ would be clearer written as ‘Disagreement between a researcher and an REB over the REB’s decision...through the normal discussion and reconsideration process...’
- Line 2094- It would be helpful to provide an example of what is meant by ‘inappropriate influence’ e.g. a situation.
- Line 2098- Rather than ‘...research on behalf of the institution’ consider moving part of line 2102, to become ‘...research with which the institution is affiliated’ or ‘...research conducted under the auspices of the institution’. The lines 2101-2103 (‘This applies to ...Policy’) can be deleted.

- Line 2100- There is a distinction that should be made between ‘ethics approval’ and ‘approval’. The latter is too general whereas the former is (correctly) more focused. Adoption of this term should be considered in this paragraph and perhaps throughout the document. As an aside, and an alternative, the term ‘ethics clearance’ is one that has been used at Waterloo for more than a decade and a-half, and was selected to avoid the implications associated with the word ‘approval’.
- Lines 2114-2116- Mention should be made of ‘real, potential and perceived exertion of power over REBs... or ‘exerting of undue influence on REBs...’
- Line 2122- The absence of ‘including both men and women’ in the preamble is concerning and leaves the wording in contrast to that in other regulatory documents. This wording should be reinserted as ‘of at least 5 members including both men and women, of whom...’
- Line 2126- The expectation for a person ‘knowledgeable in the law’ regardless of the disciplinary focus of the REB is a positive change.
- Lines 2131- 2132- Because the presence of a senior administrator can influence the REB discussion and decision-making process- particularly if some REB members are junior in rank- it would be helpful if this section could be expanded. For example ‘...shall not serve on the REB, attend REB meetings or otherwise directly or indirectly influence REB decision-making process’. This wording would be more consistent with wording in Chapter 7.
- Line 2143- What is intended by ‘appropriate diversity’? How w/should this be interpreted?
- Line 2149- Persons serving on an REB who are not affiliated with the institution are more appropriately referred to as ‘community members’ than representatives’. They may indeed not be regarded as representative of any particular community. Wording should be ‘community membership’.
- Line 2190- Is ‘research ethics process’ supposed to be ‘ethics review process’?
- Line 2192- Could this wording suggest that only the community members reflect the research participant’s perspective? Shouldn’t all REB members take the perspective of the research participant to some degree during the ethics review process?
- Line 2240- The phrase ‘and should provide...REB’ is an important point and should stand alone. For example, consider use of ‘research ethics education’ rather than ‘training’ and expanding to wording such as: ‘Moreover, REB members should be provided with the necessary initial and continuing research ethics education to effectively review...REB’
- Line 2253, 2255- Change to ‘Education...’
- Line 2257- Change to ‘contributions’
- Line 2264- Since many organizations have research ethics administration (e.g. a separate office or comparable entities) and they provide continuity to and for the REB, consider wording such as ‘The Chair or designate...’
- Lines 2266- 2268- Care should be taken not to confuse the role of the REB Chair and that of the research ethics administration as it is the latter that is typically responsible for ongoing communication and interaction with researchers.

- Lines 2284- The word ‘assigned’ suggests that the REB is assigning delegated ethics review. This is not necessarily or normally the case. This is typically done via ‘careful decision-making of research ethics administration informed by detailed written SOPs’.
- Line 2293- REBs should be encouraged to identify for themselves and their organization in an a priori fashion, how they would operationalize ‘frequent absences’.
- Line 2309- What is meant by ‘formal ethics review process’? Should this be ‘initial ethics review process’?
- Lines 2319-2322- Could this section be misconstrued to refer to research ethics administration? If so, this will be problematic. The distinction between senior institutional officials and research ethics administration should be clarified.
- Lines 2323-2326- This section could be stronger if linked to other like sections that refer to the expectation that an institution will allocate the necessary and ongoing resources for initial and continuing research ethics education of REB members and research ethics administration. In fact, a separate section with specific heading would help to emphasize and focus the institution’s responsibility around this.
- Line 2333- Consider adding to the end of the line ‘or to determine the feasibility of a proposed study’.
- Line 2340- After ‘obtain REB approval’ add ‘or in the case of minimal risk research, delegated ethics review approval’...
- Line 2346- Also add ‘and/or to determine the feasibility of a proposed study’.
- Line 2354- Add ‘process’ to the end of the sentence.
- Line 2358- The wording of this sentence needs to be clarified as it may suggest that the level of review is to be decided by each Chair for each study. In fact, SOPs are generally developed and they then become the reference document for decision making by research ethics administration since this is the entry point for research ethics applications. Further, the statement “It is the REB, through its chair, that decides on the level of review to be utilized” seems to be impractical and not implementable. The Chair position is usually a small percentage of a faculty member’s time, which would not include determining the level of review for a high volume of proposal submissions.
- Lines 2365-2367: If “with the support of their institutions, REBs may develop their own mechanisms under which delegation of the conduct of review, decision making, and the associated reporting process will occur” then in lines 2366 to 2367 wording should be revised as “Delegates may, for example, be selected from among the REB membership, or at the faculty or department level.” Further, the wording in line 2366-2367 may imply that research ethics administration (REA) cannot serve as delegated ethics reviewers. This is inconsistent with the effective system that occurs in many institutions now where the delegated ethics review process relies on the skill of well educated members of REA. Moreover, if not expanded from current wording (i.e. ‘from among REB membership or at the faculty or departmental level’) to acknowledge and include current accepted and effective practices that involve REA, it will create considerable difficulty at the

- institutional level. Recall that in section 6.9, there seems to be no provision for REA to have membership on the REB.
- Lines 2381-2390 do not include greater-than-minimal risk annual renewal; however the list is examples and not an inclusive list. It appears that an REB/institution could choose delegated review for greater-than-minimal risk annual renewals.
  - Line 2386- Wording change recommended from ‘will no longer involve’ to ‘will not involve’.
  - Line 2392- This should be expanded to ‘undergraduate and graduate students...’
  - Line 2399- This should be expanded to include the following at the end of the sentence ‘unless the research poses minimal risk which would then be eligible for delegated ethics review’.
  - Line 2402- The phrase ‘through its chair’ should be qualified since some delegated ethics reviewers are REB members. These individuals should be able to make their own reports to the REB.
  - Line 2406- Change ‘ethics of all’ to ‘ethics review of all’
  - Lines 2411, 2412- This sentence does not seem to recognize that the ethics review process is a feedback process along a continuum with often many (to and fro) communications between the researcher and REB (or delegated ethics reviewer) between initial review and full ethics approval. For this reason, the sentence should be expanded.
  - Line 2416- This wording seems odd and doesn’t seem to reflect a step that many REBs typically use. When an REB or delegated ethics reviewer does not give ethics approval following first review, detailed ethics review feedback is provided to the researcher. However, this is not termed a ‘negative decision’. Some institutions refer to it as ‘provisional ethics approval’ while others refer to it as level 1 ethics review feedback. The term ‘negative decision’ in this line could be interpreted as ‘disapproval’.
  - Line 2435- Why is an end of study report required for all studies? Applying a proportionate approach to continuing ethics review, should this be necessary for minimal risk research? This expectation could more efficiently be applied if incorporated as a section in the continuing ethics review form.
  - Line 2443- Add ‘continued’ in front of ‘ethical acceptability’.
  - Line 2451- Risk level could also decrease. For example, with removal of greater than minimal risk procedures, the overall risk level of a study might decrease. An REB might then decide to adjust the continuing ethics review interval from for example, every 6 months to once per year.
  - Line 2453- This seems to be the only place where ‘no risk’ is mentioned. Is this term intended?
  - Lines 2474-to end- This section seems to rely on biomedical terminology and experiences. It does not seem to acknowledge another type of ‘departures from originally approved research’; namely, modifications or amendments that occur frequently in ongoing research and are anticipated and planned, and ones for which prior ethics approval is requested and received. For example, the addition of another researcher, more participants, a new scale. Perhaps another article should be developed to cover this with its own associated application section.

- Line 2533- This article should acknowledge that it is not REBs that keep REB documentation. It is the research ethics administration (REA) that does record-keeping for the REB. The application section needs to reflect this role.
- Line 2545- What is meant by ‘other relevant documents’ in relation to researchers’ access? Could this be problematic?
- Lines 2556- Again there is no reference to anticipated modifications.
- Lines 2560- 2562- REAs’ role in record keeping for REBs is much more comprehensive than indicated in these lines, and in the wording of the article.
- Line 2561- ‘participation in training ‘is too vague. This should stipulate research ethics education and training’.
- Line 2564- The intent of the term ‘initial review’ should be clarified in this paragraph as it can often be taken to be the first review of the application. In reality very few studies receive ethics approval following the first review.
- Line 2575- 2576- Consider wording such as ‘If a disagreement between the researcher and the REB cannot be resolved through dialogue between the two groups, the researcher....’
- Line 2577- Add ‘institution’s’ in front of ‘established appeal mechanism’
- Line 2580- There should be wording inserted similar to: ‘when a disagreement cannot be resolved between the delegated reviewer and researcher through dialogue between the two parties, requests by the...’.
- Line 2588- The wording here is ‘discussion’. However, in section 6.17 the wording is ‘deliberation, consultation and advice’. Should these be consistent?
- Line 2612- What does ‘period of reconsideration’ refer to or mean?
- Line 2621- What is a ‘representative of the REB’? Is this intended to be an REB member?
- Line 2647- Is the use of ‘should’ in this article intended as most use ‘shall’?
- Line 2713- Expand to ‘as soon as possible after the publicly declared emergency...’
- Lines 2724- 2765(Article 6.22 and application)- This section seems to deal with core principles and offers overall guidance for this section. As such it may be better positioned at the beginning of this section i.e. before section 6.20.

## **Chapter 7 – Conflict of Interest**

- Line 2768- Should the chapter title be Conflicts of Interest to indicate that conflicts can coexist?
- Should there be a statement that explains why the term is referred to as ‘conflicts of interest’ for purposes of this Policy?
- Line 2781, 2782- Would ‘position’ be a better word than ‘condition’?
- Line 2785- The wording ‘researchers and students’ might be worth reviewing because researchers can be faculty, undergraduate and graduate students and staff. Perhaps define in paragraph 1 what is meant by ‘researchers’.
- Line 2782-2784- This is a long sentence. Consider two sentences as ‘appropriate persons. This step will then...’
- Line 2808- Is the phrase ‘of individuals to participate in research’ necessary?
- Lines 2814-2818- Consider reversing the order of the last two sentences.

- Line 2817- Should be “participants”.
- Line 2824- To what does ‘all parties’ in this sentence refer?
- Line 2850- Should ‘disclose’ be added as in line 2916?
- Line 2854- In other places the wording is ‘minimize or manage’ - or all three words? Should the wording be consistent throughout?
- Lines 2862...Should the wording here be something similar to ‘to avoid interference where institutional interests may conflict with REB decisions’?
- Line 2865- Here the wording is ‘evaluate and manage’.
- Line 2881- What is meant by ‘biased judgements’?
- Line 2919- Use of ‘significant’ has not been previously mentioned.
- Line 2944- Should ‘perceived’ also be indicated in the list of COIs?
- Lines 2943 or in this paragraph- Many REBs now include graduate students as members...thus, there should be reference to students having a COI when the protocol under review is their supervisor’s.
- Line 2965- What is meant by ‘close colleague’? Is this someone with whom the member has collaborated and if so, how recently? Can the application be clearer?
- Line 2976-2981- This section is very important and should be more strongly stated. Further, there are too many points being conveyed in a single lengthy sentence. Perhaps two sentences could be created with wording similar to the following (additional wording is in italics): ‘‘The *involvement* of administrative staff dedicated to research ethics’ functions (e.g. the research ethics office administrator or director) *is* relevant and appropriate to support REB procedures *and its effective operation*. However, an institutional senior administrator (e.g. a vice president research or business development) should not serve on an REB, attend meetings, *or directly or indirectly* influence the REB decision making process...’ The mere presence of...*or his/her designate* may undermine...’
- Line 2985- If senior administrators are not to sit/serve on REBs, then ‘non-voting’ should not be needed.
- Line 2991- To avoid confusion over to whom ‘they serve’ refers, consider ‘relevant senior officers of their institutions’.
- Line 2996- It is unclear if this would also include the community member? If so, could this be perceived as a COI by the public? If not included, should another equivalent expression of gratitude for that person’s commitment be available?
- Line 3007- Change to ‘Researchers’ conflicts of interest...’
- Lines 3008-3012- There is no specific reference to family members’ COI due to financial or other involvement. Should this be included? If so, wording might be: ‘Researchers’ conflicts of interests or those of their family members may arise from...’
- Line 3015- Should ‘recognize’ be ‘identify’ for consistency with other sections?
- Line 3042- Can examples of ‘others’ be provided?
- Lines 3048, 3049- Why is ‘shall’ used here versus ‘should’?
- Lines 3054, 3055- This example seems to stop short of identifying the precise COI; that the cost of attending the seminar in an interesting location is covered by the sponsor? Also did the physician know about the seminar prior to the clinical trial?
- Line 3058- What is meant by ‘authorities’?

- Line 3063- Please expand to 'financial payments or in kind...'
- Line 3070- Can the reference to 'other delegated body in the institution' be explained i.e., under what circumstances such a body would be asked to make an assessment of COI?

## **Appendix B**

### **CAREB Working Group Members**

#### **Chapter 2: Scope and Approach**

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## **Chapter 8: Multi-Jurisdictional Review**

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## **Chapter 11: Clinical Trials**

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