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From: Amy Geertsma
Sent: Mon, 4 Oct 2021 21:47:56
To: secretariat (SRCR/SCRR)
Cc: Francine Sarazin; Raphael Saginur Md; Nancy Camack
Subject: Comments to PRE on the proposed guidance for public consultation
Sensitivity: Normal
Attachments:
TCPS2 Proposed Guidelines Regarding Broad Consent for the Storage and Use of Data and Human Biological Materials.docx
TCPS2 Ethics Review of Multijurisdictional Research - Proposed Revised Guidance.docx

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Hi there,

Please accept the comments on behalf of The Ottawa Hospital (TOH) / Ottawa Hospital Research Institute (OHRI), Ottawa Health Science Network Research Ethics Board (OHSN-REB), Ontario.

Please see the comments in the attached Broad Consent and Multijurisdictional Research documents.

Thank you,

Amy

Amy Geertsma

Manager, Research Ethics

Ottawa Health Science Network Research Ethics Board | Conseil d'éthique de la recherche du Réseau de science de la santé d'Ottawa

Ottawa Hospital Research Institute | Institute de recherche de l'Hôpital d'Ottawa

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725 Parkdale Avenue, Ottawa, ON, K1Y 4E9

T: 613-798-5555, 15072 | F: 613-761-4311

Working remotely until further notice. To reach me by telephone, please call through MS Teams, or send a meeting request.

\cbpat10General inquiries | Renseignements généraux: T: 613-798-5555-16719 | rebadministration@ohri.ca

http://www.ohri.ca/ohsn-reb/default.asp

https://www.ottawahospital.on.ca/

Comments from The Ottawa Hospital / Ottawa Hospital Research Institute

Proposed Guidance Regarding Broad Consent for the Storage And Use of Data and Human Biological Materials

- Purpose
- Introduction
- The shared responsibility to protect participants
- Voluntary broad consent
- Informed broad consent
- Ongoing broad consent
- Summary
- Glossary

Purpose

The purpose of the following guidance is to introduce broad consent and describe how it can comply with the principles of the TCPS.

Introduction

Broad consent is a term used around the world to mean consent for unspecified research. It is widely used in the context of data repositories and biobanks. At one time, international ethics norms recommended seeking consent from participants only for a specific, clearly defined research project, referred to in this guidance as 'specific consent.' Now, however, there is general approval for seeking broad consent for the use of stored data and human biological materials for less or un- specified research that may be conducted in different and unspecified contexts, now or in the future.

Although this may seem to be a departure from the principles of specific consent, in fact the principles underlying broad consent are the same. "An important mechanism for respecting

participants' autonomy in research is the requirement to seek their free, informed and ongoing consent. This requirement reflects the commitment that participation in research, including participation through the use of one's data or biological materials, should be a matter of choice and that, to be meaningful, the choice must be informed" (Article 1.1). This is as true for broad consent as it is for specific consent. The difference is the nature and scope of what is being discussed by the researcher and participant during the consent process.

The informed aspect of broad consent focuses on the discussion with participants of the risks and potential benefits associated with unspecified research that is in a much broader context than specific consent. Broad consent recognizes that the details (e.g., research objectives, methods) of future research projects may be of less interest to participants who are volunteering their contributions over the long term, than other aspects of the research, such as who will have access to their contributions and in what jurisdictions. This means information about the nature and governance of the repository may take on a greater significance for some participants.

Commented [AG1]: Does this also encompass the duration of the stored samples?

The following discussion explores how to apply the TCPS guidance that consent be voluntary (Article 3.1), informed (Article 3.2) and ongoing (Article 3.3) in the context of seeking consent for the storage of data or human biological materials for unspecified research.

The shared responsibility to protect participants

Researchers, data custodians, and biobanks have a shared responsibility to protect participants. In specific research, the researcher has a responsibility to ensure that the terms of participant consent are respected (Respect for Persons) and that participant welfare is protected (Concern for Welfare) throughout the life of the research project. Where data or human biological materials are being stored for use in research, the repository assumes those responsibilities. When the stored data and human biological materials are used for new research, the researcher associated with the new project takes on the same responsibilities, i.e., that the terms of participant consent continue to be respected and that participant welfare continues to be protected throughout the new research life cycle.

In general, the TCPS requires research involving stored data or human biological materials to undergo REB review (Articles 5.5A, 5.5B, 12.3A, 12.3B). However, such research may not receive REB review if conducted in jurisdictions that are not subject to the TCPS, i.e., research in other countries or research conducted under the auspices of institutions that are not eligible to manage Agency funds. Researchers who intend to make their collections of data or human biological materials available to other researchers not subject to the TCPS must consider the repercussions of this decision for participants. The consent process must reflect the intention of the researcher collecting the data or human biological materials. For example, if a researcher assures participants that all subsequent research will undergo REB review, then that researcher must make sure procedures are in place to realise that assurance (e.g., through governance policies, or contractually). Alternatively, if the researcher is unable to make such an assurance, they must make that clear to participants during ~~in~~ the consent process.

Commented [AG2]: Is there a backup plan to support the researcher's responsibility in the event that the researcher is unavailable at the future time of sample usage?

Where the data or human biological materials are from a specific or unique community or group, researchers and repositories may be required to further consult with or seek permissions from such groups, or respect existing agreements. See Articles 9.1 and 9.11 on research involving First Nations, Inuit and Métis Peoples of Canada. This guidance can be applied to other communities when appropriate (Article 2.11).

Voluntary broad consent

Withdrawal

In general, participants must be able to withdraw from research at will and without reprisal (Article 3.1). In practical terms, this means they must be able to request withdrawal of their stored data or human biological materials from the repository. The withdrawal of their data or human biological materials may not be possible after a certain point in time. For example, their data may have been anonymized prior to storage and cannot be separated from the pool of participant data. Or, their contributions may have been widely disseminated. Researchers must justify any limitations to the withdrawal of data or human biological materials to their REB. These limitations must be explained to participants during the consent process.

Free of coercion and undue influence

Consent must be free of coercion and undue influence (Article 3.1). Sometimes researchers collect data or human biological materials for a specific research project, and with the intention of subsequently storing those data or materials (or excess materials not used for the specific purpose) in a repository for subsequent unspecified research. In this situation, both specific and broad consent must be sought. Participating in a specific and known research project must not be contingent on the participant consenting to unspecified research.

Informed broad consent

The notion of broad consent raises the question of what information is meaningful to participants in deciding whether they wish to have their contributions stored for unspecified research. Like specific consent, the broad consent process must focus on what is relevant to participants' decision-making. In general, this would include informing them of potential benefits of the research, risks to participants, how their interests will be protected and any limitations to those protections. They should also be informed about potential uses, and any limitations to the range of uses, if known at the time of seeking broad consent.

However, sometimes not all of this information is known at the time of seeking consent. An important part of the consent process, therefore, is informing participants of areas of uncertainty that may be relevant to their decision to participate. For example, when little is known about the nature of the future research, there is a risk that the participant's contributions could be used for a purpose that the participant might not agree with or support. However, participants who care only that their contributions are to be used for research in the broadest sense, may wish to consent despite this risk. In determining what might be relevant to participants' decisions to participate, researchers must be mindful of the perspective of the participant and their willingness to accept uncertainty. This may involve considering the various contexts (e.g., social, economic, cultural) that shape the participant's life (Chapter 1, Section C).

The repository is an important part of the shared responsibility to protect participants. However, it must be acknowledged that not all participants are interested in the details of a repository's governance and their inclusion in the consent form may distract from information that is more relevant to the participant at the time of initial consent. The researcher should consider what information is meaningful to the participant's decision to participate at the time of consent, and what information might be more appropriate as an addendum, which may be of more interest to them later. Researchers should provide a means for participants to obtain ongoing repository information as the repository's governance may change. This could be accomplished by providing participants with a repository contact and information about how to find repository information, should they wish it, in the future, e.g., a website.

The elements of informed broad consent listed below are the same elements associated with specific consent listed in Article 3.2, only they are broader in scope.

For broad consent to be informed, it must include information about:

- What is being collected and stored for reuse, and why;
- Voluntariness and the ongoing nature of the participant's consent, including options for withdrawal (if any);
- Risks and potential benefits of storage of data and human biological materials and of their use in unspecified research, including areas of uncertainty where risks cannot be estimated;
- Information about the repository and its governance (if known).

The following is a more detailed description of these requirements that can be used to make sure that key issues associated with broad consent are considered.

What is being collected and stored for unspecified research and why

- Description of what data and human biological materials will be stored for research, for what purpose, if known, and whether they can be identified as being from a specific or unique community or group.

- Description of potential uses. Consideration should be given to whether the research could involve technologies that would compromise participant privacy/confidentiality, such as whole genome sequencing or other emerging technologies, as these may increase participant risk.
- Description of any potentially identifying information that will be stored.
- Length of time the data and human biological materials will be stored, location of storage, process for disposal, how any human biological materials will be preserved, and whether the human biological materials will be converted to information, e.g., DNA sequencing.

Voluntariness and the ongoing nature of consent

- Assurance that prospective participants are under no obligation to agree to the storage of their data or human biological materials for research.
- Assurance that not agreeing to storage will not jeopardize participants' chances to receive any current or future services.
- Explanation of how participants may withdraw their consent for research, including any limitations to the withdrawal of their data and human biological materials from storage.
- Explanation of what and how to obtain information that will be provided as part of ongoing consent (e.g., details of research) or that participants will not have access to this information.
- Description of how the terms of consent will be respected in research (e.g., contractually, through governance mechanisms).
- Assurance that participants have not waived any rights to legal recourse in the event of harms associated with the storage and research use of their data or human biological materials.

Risks and potential benefits of storage and participation in unspecified research, including areas of uncertainty where risks cannot be estimated;

- Description of the reasonably foreseeable risks that may arise from the storage and

research use of the data and human biological materials, for example:

- o Risks of re-identification;
- o Possibility that participant data or human biological materials will be used for research of which the participant is unaware and to which the participant might object.

- Description of the potential benefits of the research, to the degree possible.
- Discussion of areas of uncertainty, where the risks are unknown, that may be relevant to participants' decision to participate.

Information about the repository and its governance

- Purpose of the repository.
- Information about the type of research supported by the repository.
- Identification of sponsors or funders associated with the repository and any conflicts of interest between the sponsor and the repository.
- Description of how privacy and confidentiality will be protected during storage and research, and any limitations to that protection.
- Description of whether results will be disseminated and if so, how.
- Description of how or if material incidental findings will be handled.
- Description of how stored data and/or human biological materials will be shared with other researchers and under what conditions.
- Information about whether the data or human biological materials will be shared with researchers in other jurisdictions who are not subject to the TCPS. A description of how or whether participant autonomy will be respected and how or whether participant privacy will be protected in the new jurisdiction, e.g., by contractual arrangement.
- Information concerning whether the repository financially benefits from the commercialization of findings, the data or human biological materials or products derived from them and whether participants will financially benefit.
- Any requirements the repository may have to provide data or human biological materials to third parties for non-research purposes (e.g., as required by law) and its process for

informing participants when this is required.

- Information about what would happen to the data or human biological materials if the repository were to be closed, if known.

- Who to contact at the repository for information.

Ongoing broad consent

As the elements of informed consent may change over time, repositories and researchers have a duty to provide participants who wish it, with information relevant to their consent throughout the storage and use of their data or human biological materials for research (Article 3.3). Participants should have the option of indicating (and periodically confirming or withdrawing) their consent to being re-contacted over the years and their consent for the continued use of their materials for research. Researchers must respect the wishes of participants who do not want to be re-contacted. For practical reasons, the onus may be on the participant to provide the repository with any updates to their contact information, and to confirm their ongoing consent. In some cases, repositories may not be able to keep in contact with participants, making ongoing consent impracticable. In this case, consent is, in effect, limited to a one-time event that takes place when the data or human biological materials are collected.

Change in participant capacity is an important element of ongoing consent. For example, longitudinal studies may involve children who have assented to research and whose decision-making capacity is maturing to a point where they can consent for themselves whether to continue to participate in research, without an authorized third party (Article 3.9). Mechanisms should be in place to accommodate such changes.

Any deviations from, or limitations to, the notion of ongoing consent must be justified to an REB and must be explained to participants as part of the consent process.

Summary

Broad consent is used when data or human biological materials are collected for storage for unspecified research. In this situation, the responsibility to protect participants is shared between the researcher who is collecting the data or human biological materials, the repository, and future researchers. The principles underlying broad consent and specific consent are the same. In both cases, consent should be free, informed and ongoing. The difference is the nature and scope of what is being discussed by the researcher and participant during the consent process.

Glossary

Consistent with the TCPS:

- Biobank means a collection of human biological materials. A biobank may also include "associated information about individuals from whom biological materials were collected" (Glossary). The term biobank as defined in the TCPS applies regardless of the size or location of the collection. It includes small collections held by an individual as well as large collections held by commercial institutions. It includes collections intended for research as well as collections not intended for research.
- Consent means free, informed and ongoing consent (Articles 3.1-3.3).
- Human biological materials are tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, and other body fluids. The term also includes materials related to human reproduction, including embryos, fetuses, fetal tissues and human reproductive materials (Article 2.1.b).

For the purposes of this guidance:

- Broad consent means consent for unspecified research;
- Specific consent means consent for a specific research project, the details of which are known at the time of consent;
- A repository is a data repository or biobank;
- A data repository is a collection of research data.

Comments from The Ottawa Hospital / Ottawa Hospital Research

ETHICS REVIEW OF MULTIJURISDICTIONAL RESEARCH –

PROPOSED REVISED GUIDANCE

PURPOSE

The Tri-Agency Panel on Research Ethics proposes policy guidance to require harmonized ethics review of multijurisdictional minimal risk research. The goal of this proposed guidance is to promote the expeditious review of research while maintaining appropriate protections for research participants. This guidance may also apply to research of more than minimal risk.

BACKGROUND

The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS) requires researchers and REBs "to navigate a sometimes difficult course between the two main goals of providing the necessary protection of participants and serving the legitimate requirements of research." (Chapter 1, Section B, Conclusion). Striking that balance presents a particular challenge where more than one eligible institution[1] or REB has a connection to the research.

The 1998 TCPS did not have detailed guidance on the review of multi-jurisdictional research. The 2010 version added a chapter explicitly permitting multiple models for the ethics review of research involving multiple sites/multiple REBs. Canada now has a number of successful initiatives at the disciplinary, provincial, or regional level that provide harmonized ethics review for multi-site research. Some established examples include models organized by jurisdiction (health research in Quebec, health research in Newfoundland and Labrador), by discipline (the Ontario Cancer Research Ethics Board, Clinical Trials Ontario, pediatric oncology clinical trials between the IWK Health Centre, and the Nova Scotia Health Authority, the Prince Edward Island health authority and parts of New Brunswick) or by region (a harmonization agreement among three western universities: University of British Columbia, University of Alberta, and University of Saskatchewan). Others are in the planning stages (for example, the CHEER project for pediatric research across the country.)[2]

Nevertheless, many institutions have not established, or do not participate in mechanisms for multi-jurisdictional ethics review. Instead, they review all research conducted under their

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Commented [AG2]: The proposed guidance as written does not respect the right of institutions to determine the model of review acceptable for streamlining ethics review for multi-site studies, for example in determining the most qualified Board to conduct the review.

auspices, even when they are not the host institution or the main site for the research. One factor undoubtedly contributing to this approach is the statement in the TCPS that "Each institution is accountable for the research carried out in its own jurisdiction or under its auspices." (Art. 6.1, Application). Another factor is likely the broad interpretation from the Tri Agency Panel on Research Ethics and Secretariat on Responsible Conduct of Research of what constitutes research carried out within an institution's auspices and jurisdiction.

We are unaware of evidence that multiple ethics reviews provide commensurately greater protection for research participants. They do cause significant burdens and delays for researchers and for prospective participants. Many researchers believe that they may unnecessarily hinder the progress of research. This can certainly be true of minimal risk research, but may also be true of research involving more than minimal risk.

It has become clear that the added guidance in TCPS 2 has not been sufficient to increase the use of more harmonized approaches to ethics review. With the benefit of a decade of experience with TCPS 2, the Tri-Agency Panel on Research Ethics believes it is time to establish new guidance that mandates a departure from the model of multiple single-site reviews of multi-jurisdictional studies toward a model of single review for multiple sites, unless local circumstances merit additional scrutiny.

This guidance is proposed as mandatory only for minimal risk research at this stage, and optional for research that is greater than minimal risk. The examples of harmonized ethics review noted above are not limited to minimal risk research. We note however that these examples are the result of formal agreements which took time to negotiate. Similar effort may be required to extend harmonized ethics review to other models involving more than minimal risk.

GUIDANCE

What is the policy basis for a single review of multi-jurisdictional research?

All institutions eligible to administer Agency funds must comply with the TCPS. Consequently, all researchers based at eligible institutions must apply a common set of ethical principles to the design and conduct of their research. Similarly, all REBs must review research based on

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Commented [FS4]: Even with minimal risk studies, a frequent concern is ensuring that what is in the ethics application re data usage/transfer matches what the study team will actually be doing. Often, there are discrepancies on the use and/or type of data that will be sent off to the lead site. In the absence of formal agreements between institutions, if another institution who may or may not communicate with other REB offices is providing the ethics approvals, it is unclear when contracts office from other sites would become involved.

The proposed changes may mislead investigators to believe they can start the study at their site when in fact they should not because contracts have not been put in place between the respective institutions for data sharing. The proposed change has the potential to increase risks to the institution, and therefore potentially increase risks of privacy breaches.

those same common ethics principles and guidance. The driving force behind this guidance is the principle of a proportionate approach to research ethics review (Chap.1, Sec. C): "[T]he intention is to ensure adequate protection of participants…while reducing unnecessary impediments to, and facilitating the progress of, ethical research."

A single review of minimal risk research should not compromise participant protection. Researchers are the first to consider participant protection as they design their research. That consideration must include how the research will affect participants at all contemplated sites. Review by a single REB affords a second opportunity for consideration of the ethical impact of the research on all participants, at all sites. The proposed guidance is based on confidence that a single, comprehensive ethics review of minimal risk studies should, in the vast majority of cases, be sufficient to provide the appropriate protection to participants.

Through the Tri-Agency Framework: Responsible Conduct of Research (the RCR Framework), there is also a shared accountability mechanism for the responsible conduct of researchers, and the appropriate oversight of research by institutions. Taken together, the shared principles and shared accountability framework provide a sound basis on which institutions may accept the review of REBs at other eligible institutions.

What is the scope of this guidance?

This guidance is mandatory for all minimal risk research conducted under the auspices of multiple institutions. This includes:

- research conducted by researchers from more than one eligible institution;
- research conducted using the resources of more than one eligible institution;
- research involving researchers from one eligible institution and resources from another.

The expectation is that a single REB of record will conduct the ethics review. Its decision and reasons, along with the final study materials, would then be available to the REBs of all sites, for acknowledgment. Ideally, that consideration and acknowledgment would be done by a single individual at the local REB. This could be a member, or a research ethics administrator "with the appropriate experience, expertise and knowledge" (Art. 6.4, application)[3] . Both the researcher (research team) and the REB of record should have considered local circumstances (i.e.

circumstances unique to the particular site, such as a specific participant demographic, language, culture not necessarily present at other sites) as part of the study design and the review, respectively. If the local REB identifies a missed local circumstance, or a substantive missed issue, these should be flagged to the REB of record for consideration. The intention is to keep the REB of record as the sole REB that can make changes to the terms of the ethics approval.

This guidance may also be extended to research that is more than minimal risk, in accordance with the policies of the local institution, or where mandated through a formal agreement or by law (see discussion in the final section).

Who is responsible for ethics review of minimal risk research involving multiple institutions?

The REB of record is the research ethics board with authority to conduct the review. The REB of record has the responsibility for continuing ethics review. The REB of record must be from an eligible institution. The starting premise is that the REB of the (lead) principal investigator (PI) is usually the REB of record. However, it is possible for another REB to serve as the REB of record – for example, the one with the greatest expertise in the research topic, the one at the site closest to recruitment for the research, or with some similar important connection to the study. If the researcher(s) believe(s) that the REB of record should be from an institution other than that of the PI's institution, the onus would be on the PI to justify to their home REB why another REB would be better suited. They would also have to demonstrate that the other REB is willing to serve as the REB of record.

Normally, local REBs will acknowledge the decision of the REB of record. Exceptionally, a local REB may advise the REB of record to reconsider its decision in light of local circumstances or a substantive issue that had not been addressed. Examples of local circumstances that might warrant flagging to the REB of record for reconsideration:

- Issues that only affect a locally recruited population (e.g. language, culture);
- Issues imposed by unique characteristics of the local site (e.g. remoteness, limited access to needed resources to support local participants, issues specific to the local investigator);
- Statutory requirements (federal, provincial, or those of the country where the

research is being conducted) that would have an impact on how the study was conducted;

- Substantial differences in access to services or standards of care normally followed at the local site.

Process for researchers and local REBs to follow

Researchers should provide involved institutions with the complete study documentation, along with evidence of the ethics approval from the REB of record, and the final version of the study application, as approved by that REB. The designated individual at the local REB should consider these documents and determine whether there are local circumstances or substantive issues requiring further review by the REB of record. If there are not, the local REB should acknowledge the ethics approval by the host institution's REB.

If there are local issues, or substantive issues, the local REB must flag them for the REB of record. REBs are encouraged to communicate among themselves, as this may be a way to resolve informally some of the issues that may arise during the process of multijurisdictional assessment. If local REBs do raise substantive issues, even if only for participants at their site, the REB of record must address those in consultation with the REB that raised them.

Timelines should be established by the REB of record for researchers to provide the necessary documents, and for local REBs to provide their acknowledgement. In general, local REBs should complete their process and issue a letter or notice of acknowledgment within three weeks of receiving the complete package from the researcher, including the decision of the REB of record. [4]

Once the REB of record has completed its ethics review and made a decision, it is the researcher's responsibility to send that decision and associated final approved materials to the local REBs from all institutions involved in the research. When the local REBs have provided their acknowledgment, the researcher is responsible for sending the local acknowledgments to the REB of record. In addition, any further decisions by the REB of record during the course of the research must be communicated to the local REBs, and it is the responsibility of the researcher to do so.

No formal agreement between institutions is required to implement the process described above.

How does this guidance apply to ethics review for more than minimal risk research involving multiple institutions?

While this guidance is mandatory for minimal risk research, institutions may also apply it to more than minimal risk research. The same policy basis that applies to a single review of minimal risk multi-jurisdictional studies applies to studies of more than minimal risk. The same procedures described above could therefore also apply to more than minimal risk multi jurisdictional research. A single REB of record would carry out the main ethics review, in general intended to be the only ethics review. In the case of research involving more than minimal risk, however, there is a greater likelihood that a missed issue could have a substantive impact on participant welfare. For this reason, there should be an opportunity for local review. One way to address this is to allow a designated period for local review, following receipt of the main review – perhaps four to six weeks.

In situations where all local REBs have not completed their review, the research may begin at the other sites, if appropriate in the context of the specific study (for example, if the inclusion of the site is not essential in order to respond to the study question). Research may not begin at a local site until review is complete at that site.

Researchers and REBs should consider whether there is a preponderance of similarities among the sites, rather than features requiring local review. In this regard, it is useful to look at the examples given earlier of the factors that justify local review:

- Issues that only affect a locally recruited population (e.g. language, culture);
- Issues imposed by unique characteristics of the local site (e.g. remoteness, limited access to needed resources to support local participants, issues specific to the local investigator);
- Statutory requirements (federal, provincial, or those of the country where the research is being conducted) that would have an impact on how the study was conducted;
- Substantial differences in access to services or standards of care normally followed at the local site.

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Commented [AG5]: The timelines suggested (4-6 weeks) do not put Canada in a completive position for research.

In addition, the proposed changes do not support a harmonized single review system. This has implications for different consent forms used at different sites, or if a single consent form is approved for use, it may not align with institution policies of the different sites.
Please discuss with Clinical Trials Ontario regarding review of consents specificity for each site.