Research Ethics Board

REB Guidance and Information Document

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Title	**Application of US Regulations**
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1) Purpose

This document is to be used in conjunction with REB.SOP.109 - Addendum for US Regulated Research to help Researchers, REBs and REB administrators determine when and how US regulations must be used in the ethics review of research. This includes describing the differences between TCPS and the US Common Rule (USCR) in definitions and process. Federal-wide assurance (FWA) and Institutional Review Board (IRB) registration will also be discussed.

2) Definitions

See the MSVU **REB Glossary of Terms (REB.INFO.001)**

3) Notice to Researchers

The information in this document is for information and guidance purposes only. Each research study poses unique properties and/or situations that may require additional or different guidance than what is presented in this document. The information in this document is meant to provide general situational advice and does not constitute research ethics compliance in absolute form. If you have any questions, please contact ethics@msvu.ca .

4) Guidance/Information/Procedures

What is the United States Common Rule?

The Federal Policy for the Protection of Human Subjects is codified in US law and is regulated by the Department of Health and Human Services (HHS). HHS regulations 45 CFR part 46 include four subparts: subpart A, also known as the "Common Rule"; subpart B, additional protections for pregnant women, human fetuses and neonates; subpart C, additional protections for prisoners; and subpart D, additional protections for children. Several US federal departments and agencies have signed on to follow the revised (2018) Common Rule, while others have stayed with the pre-2018 rule. However, for the purposes of Canadian research institutions, it is understood that the Revised Common Rule should be applied for compliance with ethics review requirements.

When must Canadian institution apply the US Common Rule?

When a Canadian institution receives funds through a grant or subgrant from a US department or agency that is a signatory to the USCR or is a sponsor or charity that has self-determined to subscribe to the USCR, ethics review must comply with both Tri-Council Policy Statement (TCPS) and 45 CFR part 46. This is sometimes complicated, as definitions, procedures and requirements often differ.

Differences between TCPS and US Common Rule

Definition of human participants/subjects

- TCPS: an individual whose data, biological materials, or responses to interventions, stimuli, or questions by a researcher are relevant to answering the research question(s). Also referred to as a "human participant," and in other policies/guidance as "subject" or "research subject."
- USCR: a living individual about whom an investigator (whether professional or student) is conducting research:
  (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
  (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

The differences of importance between the definitions used by the USCR versus the TCPS involve are two parts. The first is the status of the individual – living versus dead. The US does not consider biospecimens or data from a person no longer alive to be human research. The second is the identifiability of the biospecimens or data; once irrevocably stripped of identifiers, they are no longer considered to be human research under the USCR. Research involving information or biospecimens from deceased individuals and anonymized data or biospecimens are human research requiring REB review under TCPS.

Name and composition of review body

The Institutional Review Board (IRB) has a somewhat different composition to the REB, as prescribed by TCPS. Like the REB, an IRB must consist of at least five members of varying backgrounds to provide appropriate scientific and ethical review. One member must be unaffiliated with the institution, i.e., a community representative. The IRB must also have at least one scientist member (which would be covered in TCPS requirement for having at least two members with expertise in relevant research disciplines, fields and methodologies covered by the REB) and at least one member whose primary concerns are non-scientific. USCR does not indicate whether this individual should be affiliated or unaffiliated with the institution. There is no specific requirement for individuals with ethics or legal knowledge. Finally, the IRB requests "appropriate representation with respect to gender, race and cultural heritage". This last point is broader than the current requirement stated in TCPS for "men and women".

Differences in processes

For the most part, TCPS and USCR are quite similar in review requirements. Both are based on Belmont principles. The major difference is how the concept of minimal risk is applied. While TCPS considers proportionate risk based on the area and discipline of research, the USCR determines minimal risk primarily on the method employed. Moreover, because the 2018 revision was done for the purpose of "modernizing the regulations by enhancing protections for human research participants and reducing unnecessary burden and ambiguity for researchers"[1] changes have been made to how minimal risk research is handled.

Exempt

The TCPS and USCR conflict with respect to what activities may be deemed exempt. Categories of exemption under the USCR which would require review under TCPS include education research, surveys, interviews, behavioural interventions, and secondary analysis of de-identified data and biospecimens. However, also unlike TCPS, exempt research still requires review by the IRB/REB office, to ensure that in fact it is exempt, and that the activity is minimal risk.

[1] Menikoff J, Kaneshiro J and Pritchard I. The Common Rule, updated. N Eng J Med 2017;376:7.

Expedited review

The USCR defines research that may be reviewed through an expedited process as being no greater than minimal risk and falling into one of 7 categories. These are:

- Some types of clinical trials
- Studies involving collection of blood within a certain volume and frequency
- Studies involving collection of other biospecimens not involving invasive procedures
- Research involving data collected through non-invasive procedures routinely used in clinical practice
- Secondary use of data or biospecimens that were collected for non-research purposes
- Research with data from voice, video, digital or image recordings made for research purposes, so long as they would not put participants in social or legal risk
- Research on individual or group characteristics or behaviour using surveys, interviews, oral history, focus groups, program evaluation, human factors evaluation or quality assurance methodologies

Expedited review may be conducted by one member of the IRB/REB, like delegated review under TCPS. However, the seventh category includes program evaluation and quality assurance, which are exempt under TCPS, needing no review process.

Full Board review

Must be done for all human research greater than minimal risk, the same as required under TCPS. Decisions must be made through voting, with tallies of the votes and any dissenting opinions maintained in the minutes.

Continuing Review

Under USCR, studies approved under expedited review do not require continuing review, only a final report once complete.

Complement of US-compliance with TCPS

When reviewing US-funded research that requires both TCPS and USCR compliance, the REB should ensure to follow the more stringent of the two systems. In most instances, under the revised Common Rule, this will be TCPS, particularly for research that would be exempt under USCR. REB offices should be aware that because activities that fall under program evaluation or quality assurance may require review under the USCR, these should be reviewed through the delegated review process and not exempted.

REB administrators and chairs should ensure that some US-funded research will need ad hoc members not specified under TCPS for quorum. For example, research involving prisoners as participants must be reviewed by a prisoner advocate or representative.

Need for Registration

Institutions that conduct human research that is funded by US federal agencies and other signatories to the USCR must register themselves for a Federal-Wide Assurance (FWA) and their IRBs/REBs through the Office of Human Research Protections (OHRP). These mechanisms are used to enforce compliance with the USCR.

FWA registration involves providing information on the institution and oversight of human research ethics and compliance, including naming which policies the institution adheres to. Registration must be updated and renewed every five years.

IRB registration is also required, and involves naming the respective boards, its chairs and members, and characteristics and roles of members on the IRB/REB. These include gender, earned degrees, whether

the member is a scientist or non-scientist, primary scientific or non-scientific specialty, whether the member is affiliated with the institution, and any comments such as whether the person is a prisoner representative or advocate, or whether there are alternative members for that role.

OHRP expects that the IRB registration be updated within 90 days of change of the contact person (usually the REB administrator) or REB chair. Renewal of IRB registration must be done every 3 years.

Institutional Authorization Agreements / Reliance Agreements

As part of the USCR's focus on reducing administrative burden, domestic multi-site research must follow a single IRB (sIRB) policy, whereby one or more institutions formally rely on one IRB to conduct the review and provide oversight. While this is not required for projects that involve US and international sites (i.e., US and Canada), there are situations where REBs may be asked, or want to consider an sIRB model. Deciding to enter into an SIRB agreement whereby the REB is board of record or relies on IRB review involves consideration of compliance to both Canadian and American requirements and should not be done lightly.

National Institutes of Health (NIH) requirements

Ethics Training

Some US sponsors, such as NIH require that all research team members who receive grant funds have taken ethics training. They do recognize the TCPS Course on Research Ethics (CORE) tutorial as sufficient to meet this requirement. CITI Canada training, through N2 membership similarly is recognized as sufficient.

Certificates of confidentiality

NIH provides Certificates of Confidentiality (CoCs) to "protect the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations."[2] Certificates of confidentiality are currently not officially recognized in Canada. However, to date, precedence exists under privacy legislation and in case law to protect confidentiality through Wigmore Criteria[3].

5) Acknowledgements

The development of this document has benefited directly a document shared by the University of Toronto. The MSVU REB has chosen to adopt this guideline in its entirety.

- *Guidance Document #6*, University of Toronto - Ethics in Human Research | VPRI (utoronto.ca) (retrieved July 2021)

6) Modification History

INFO Number & Version	Key Changes	Effective Date
REB.INFO.101	Original version, adopted from University of Toronto	September 23, 2021

[2] https://grants.nih.gov/policy/humansubjects/coc/what-is.htm
[3] http://www.sfu.ca/~palys/Wigmore.html