

TCPS Interpretation: Changes to and Considerations of Research-Attributable Risk in Human Research due to COVID

On September 4th, 2020, the Secretariat on the Responsible Conduct of Research released an interpretation addressing research related considerations when conducting research with human participants during a declared emergency.

Changes to definitions of research-attributable risk

There are three different categories of additional research-attributable risk that can arise in the COVID-19 environment:

- ***New risks arising from changes to researcher's plan for interacting with participants:***

For example, a researcher may decide to communicate with participants remotely instead of in-person to respect physical distancing and mitigate the transmission/spread of the virus through human contact. While this may address risks related to physical contact, researchers and research ethics boards (REBs) should be mindful that this change introduces new risks and ethics issues related to privacy and confidentiality of information when using digital platforms and home offices, and the need for new security and safety measures to protect participants' information. Where, for example, researchers attempt to reduce the risk of infection by mailing experimental drugs to participants rather than continuing in-person participation, this will likely require a change to the researcher's plan for monitoring any side effects.

Depending on the participant pool, the change from in-person to remote participation may also introduce new ethics issues related to fairness and equity, where only those with access and ability to participate remotely (e.g. due to internet connectivity, computer/ smart phone availability and capacity) can continue to participate in the research. "...[P]ractices of researchers or REBs, whether intentional or inadvertent, can exclude some members of society from participating in research" ([Chapter 4, Introduction](#)).

- ***New risks that emerge, even if the research plan remains unchanged:***

For example, the continued participation of participants who provide weekly blood samples at a hospital may subject them to new risks of exposure to the coronavirus during their commute, or as a result of their proximity to other participants or to members of the research team. Also, new public health requirements for reporting can introduce new risks related to privacy and confidentiality in ongoing research. For example, if new security standards require researchers to retain the participants' personal information for contact tracing purposes, researchers can no longer guarantee participants' anonymity (see [Application of Article 5.2](#)).

In addition to risks of increased participant exposure to the virus, there are possible societal risks of further transmitting the virus beyond the individual participants to other third parties, including family members.

- ***Changes in risk levels arising from changes to the participants' personal circumstances:***

During the extraordinary circumstances of the pandemic, “participants … may be rendered more vulnerable by the nature of the emergency” ([Application of Article 6.21](#)). Vulnerabilities can be psychological due to isolation, stress, anxiety, or for economic reasons due to financial burdens of the pandemic or unemployment. Vulnerabilities can also be social in nature due to limited access to critical services, or physical vulnerability due to pre-existing medical conditions or age. For example, when research on self-harm or suicide involving participants began in non-pandemic times and continues in a COVID-19 environment, researchers need to re-assess the vulnerability of their participants in the context of research. Researchers should consider the additional stress that participants may be experiencing in their personal life. Participants who take part in ongoing research at a research site may be anxious or fearful about exposure in a potential COVID-19 environment, and may no longer wish to continue participating in research. Similarly, a high-risk research study conducted in-person to test a new drug on immunocompromised patients may be deemed acceptable for those participants in non-pandemic times. However, the risk to participants may rise to unacceptable levels in a pandemic context. Participants may no longer accept risks they would have otherwise accepted in non-pandemic contexts. Others may be willing to accept risks they would not have otherwise accepted, in the absence of a known cure for COVID-19 or COVID related complications; for example, participation in treatment trials for those infected with the virus or participation in prevention trials, including participation in vaccine studies.

Changes required to approved or proposed protocols and consent forms due to additional research-attributable risks

Changes or unanticipated issues that may increase the level of risk for participants or that have other ethical implications affecting participants’ welfare must be submitted for research ethics board (REB) review (see Articles [6.15](#) and [6.16](#)). As with other changes to the research, the level of additional risks and their impact on the welfare of participants determine when researchers should report the changes to the REB - whether immediately, or if the researcher can document and summarize the changes in annual status reports. Where applicable, researchers must also provide to the REB their plan to manage additional risks through safety plans or technical safeguards, and their efforts to reach a favorable balance of risks and benefits for participants.

As with the assessment of the ethical acceptability of research, the REB review of the changes “involves consideration of the foreseeable risks, the potential benefits and the ethical implications of the research” ([Article 2.9](#)). REBs assess those risks that are attributable to the research. The TCPS states that “[w]hen describing the foreseeable

risks and potential benefits of research involving participants who are also exposed to other risks, researchers should clearly distinguish between the risks that are attributable to the research, and the risks to which participants would normally be exposed" ([Article 2.10](#)).

Researchers must inform participants of the changes or unanticipated additional research-attributable risks as part of their "ongoing duty to provide participants with all information relevant to their ongoing consent to participate in research" ([Article 3.3](#)). In deciding when, how, and how frequently to advise participants of additional risks, researchers and REBs should be guided by the level of those risks and their impact on the potential welfare of participants. They must also consider whether any other policies or requirements apply to the changed circumstances that create the additional risks. These policies and requirements might be sufficient measures to address the identified risk, and therefore changes to the research are not required.

Considerations in research plans for research conducted during the pandemic:

The onus is on the researcher to satisfy the research ethics board (REB) that the research can proceed during the pandemic. The following are some questions that REBs should consider in reviewing the ethical acceptability of initial submissions of research or ongoing research in a pandemic environment. Each research is different, and the nature of participant pools varies, so the issues to consider should be tailored on a case-by-case basis.

Impact on Study Conduct and its Scientific Validity

- Can the research involve participants remotely rather than in person?
- Is the research question still relevant within the context of the pandemic environment?
- Will the pandemic environment impact or alter the representativeness of the participant sample, or the sample plan, and thus its scientific validity?
- Has interruption of the research (i.e., the stopping and resumption due to the pandemic), or the availability of research funds, impacted its scientific validity or feasibility?

Impact on Risks and Benefits of Research

- Has the researcher considered new risks attributed to the research as a result of COVID-19 environment?
- Has the level of risk of previously approved research changed?
- Can the researcher maintain a favorable balance of risks and benefits?
- What measures has the researcher taken to mitigate any increased levels of risk?
- Does resuming the research impose additional burdens on participants (e.g. telecommunications cost) to continue to participate in the research?

- Does the researcher expect the vulnerability of the participants to change within the context of the research?
- Are the initial anticipated benefits of research still possible?

Impact on the Consent Process

- Do alternate consent strategies need to be considered, for example seeking consent over the internet rather than in person?
- Is the information provided to participants as part of the consent process still accurate, or does it need to be updated?
- Does resumption or continuation of approved research introduce unanticipated changes that may increase the level of risk to require informing the participants as part of the ongoing consent process, for example, informing participants about new information, changed procedures, or changed protections that might affect the participants' choice to continue to participate in the research?

Other Ethics Issues

- If there is a change to previously approved research, does it raise other ethics issues e.g. inclusion and exclusion issues or new risks related to privacy and confidentiality?
- In the case of multi-jurisdictional and international research, is the researcher sufficiently aware of the local COVID-19 circumstances in the other sites to be able to assess any changed level of risk to participants, and how this may affect any proposed changes to the study and its procedures?
- Where research is based on community engagement or research agreements, has the researcher considered how to negotiate or implement any proposed changes (e.g. additional consultation, engagement or permission needed to begin recruitment or resume the research)?
- Are there other community constraints or institutional permissions required to begin recruitment or resume the research?
- While not a formal part of REBs' responsibilities, do REBs have concerns about the safety of researchers and the research team members (e.g. the availability of personal protective equipment) that REBs should share with researchers or refer to other appropriate bodies within the institution?

TCPS