Washington University in St. Louis
Human Research Protection Office

International Human Subjects Research

Overview

Human subject research conducted outside of the United States poses complex regulatory and ethical challenges. To protect participant's rights and welfare, the research must follow the ethical standards, legal requirements, and cultural norms of the country in which the research takes place. This guidance document outlines the responsibilities of the researchers and provides information about the documentation that is necessary for WU IRB review.

Researcher Responsibilities

The researcher is responsible for completing all requirements applicable to their international research project. In addition to this guidance document, the International Research Prep Work Checklist provides valuable information on the requirements that must be completed prior to submitting the study to the WU IRB. Completing these tasks prior to WU IRB submission will avoid delays with IRB review and approval.

Preparations for WU IRB submission should start at the initial planning stages of the research to allow time to obtain the necessary approvals from the country in which the research will take place. These approvals can take several months depending on the requirements of the country. The WU IRB is not able to approve the research until the necessary approvals are obtained and any other applicable requirements are completed. The WU IRB does not have the legal authority to waive these requirements. WU IRB submissions may be withdrawn if the research is not ready for review.

When submitting the WU IRB application, the Dean, Department Head, or designated signatory signs an assurance to verify that the researcher has the necessary qualifications to conduct the project consistent with ethical, legal and cultural standards. Depending on the type of study and the country's legal requirements and cultural norms, the IRB may require additional information about the researcher's qualifications. All researchers conducting human subjects research under the oversight of the WU IRB are required to complete CITI training.

Local Context Review Process

When conducting research in another country, the WU IRB must ensure that the research is designed and conducted in manner that is compliant with all applicable laws of that country and that all aspects of the research are culturally appropriate. This requires a review from a committee or individual that has the appropriate expertise to evaluate the research, taking into consideration the country in which the research will be conducted. For additional information, refer to the "Flow chart – Do I need a Local Context Advisor or approval from a Foreign IRB/Ethics Committee?"

Ethics Committee (EC)/Institutional Review Board (IRB)

If a country has a local EC/IRB requirement, approval from this committee must be uploaded into the myIRB form at the time of submission. The approval documentation must be in English. Both the translated and original version should be submitted to the IRB. IRB applications submitted prior to the completion of local IRB or Ethical Committee review will be withdrawn. When a foreign IRB/ethics committee requires WU IRB approval first, the researcher must provide documentation of this requirement to the WU IRB.

There may be times when the laws of other countries do not require a local ethics review or there is a local EC/IRB but review is not required for the type of research that will be conducted. For example, some local EC/IRBs review clinical trials but do not review other types of research or may not require review for minimal risk research.

It is the responsibility of the researcher to review the United States Health and Human Services OHRP International Compilation of Human Research Standards to determine whether there are local/national regulatory requirements. If there are no known local/national regulations per the OHRP International Compilation document, the researcher can seek the assistance of an informed local partner. Based on the information from OHRP and informed local partner, as applicable, if the researcher determines there are no known local/national review requirements the researcher will be asked to give the name of a person to serve as the Local Context Advisor (see details below).

Local Context Review

If review by a local EC/IRB is not required, an individual (Local Context Advisor) with the appropriate expertise is required to ensure:

1. All local ethical and regulatory requirements are met; and
2. The research is designed to take into account cultural standards of the participant population.

It is the responsibility of the investigator to identify a Local Context Advisor (LCA). The LCA does not have to reside in the country where the research will take place, or be a native of that country, but s/he must have research expertise in the country or culture in which the research is occurring. The LCA cannot be involved with the research study proposed (including faculty sponsors). If the research is conducted with different populations within a single country or different countries, the WU IRB will require more than one LCA unless a single individual can be identified who has expertise in all applicable legal and ethical requirements and standards.

In assessing whether the LCA has appropriate qualifications, the WU IRB will ask the individual to describe how they have obtained knowledge about the local ethical and regulatory requirements and the applicable cultural standards of the local participant society. It is expected that they will have obtained direct experience with the participant society through having conducted similar research with the research community, the participant population, and/or the research institution (if applicable).

The LCA will review the research proposal to determine if the research intervention/interactions pose any potential physical, psychological, social or economic risk to individuals who would participate in the research. They will assess whether the recruitment and consent process is consistent with the norms

of the participant society and whether the consent and recruitment documents (as applicable) are written in a language that is understandable to the participant society. They will also inform the WU IRB whether the proposed research is regulated by any governmental agencies and whether there are any national or local approvals that must be obtained in order to conduct the research.

Other requirements from the international site

In addition to EC/IRB review, there may be additional requirements such as licenses, permits, or tribal or community permission. Some of these requirements may have an associated cost. It is the researcher's responsibility to ensure these requirements are completed.

There may be a specific order in which these approvals and/or documentation are obtained. For example, some countries require local EC/IRB approval prior to obtaining a permit.

Student Conducted International Research

Students are required to have a WU Faculty Sponsor. This includes undergraduate, graduate, and PhD students. A Faculty Sponsor is not required for postdocs. The Faculty Sponsor is considered a key member of the study team and should support the student in their responsibilities as the Principal Investigator. The student must have training necessary to conduct the research consistent with the study design and the degree of risk posed by the research. All students conducting human subjects research under the oversight of the WU IRB are required to complete human subjects training (CITI). The WU IRB may take into consideration the experience of the Faculty Sponsor if the student is lacking experience in conducting research in the participant society. Faculty Sponsors should have the time, resources and expertise to support the student in the conduct of their project.

Students must complete the International Research Prep Work Checklist prior to submitting to the WU IRB. It is the responsibility of the Faculty Sponsor to verify that the student has completed the checklist.

If the Faculty Sponsor will not be in the country with the student, there must be a plan in place to ensure the student receives the appropriate support and guidance on their research project.

Translation and Translator Requirements

All documents seen by the participant in non-exempt research must be provided in English and in the language of the participant society. The consent version in the language of the participant society will be requested after the English version is finalized. For exempt research (as defined in WU IRB policies) or research where WU is not involved in the consent process, or where WU's role is limited to data analysis, it is not necessary to provide versions of the documents in the language of the participant society.

Documents such as local EC/IRB approvals or permits must be translated into English. Both the original and translated versions must be submitted to the IRB.

The WU IRB accepts translations from the study team and/or machine translations.

Regardless of whether the research is exempt or non-exempt, the IRB must review the plan to recruit and consent participants. If the PI is not proficient in a language that is understandable to participants, the plan should explain whether collaborators in-country will be responsible for all communications with participants, or whether the PI will rely upon other study team members to serve as a translator(s). The languages to be used and the name(s) and qualifications of the translator(s) should be provided to the IRB. In rare cases, if the translator(s) has not been identified at the time of IRB submission, then the PI should describe the proposed plan to hire or use others to serve as translators once the PI is in country.

Online research

For the purposes of this guidance, online research is research that takes place fully or partially on the internet and does not involve a direct, personal interaction with the participant. Examples include completion of surveys or tasks, using online platforms such as Qualtrics, mTURK, REDCap, or commercial survey panels.

A foreign EC/IRB review or local context review is not required if the online research does not target a specific country or the online research only collects anonymous information. In the latter case, identifiers can be collected if related to payment but they cannot be linked to the participant's responses. Otherwise, online research requires review by all targeted country's foreign EC/IRB (if there is such a requirement) or by a Local Context Advisor.

If minors are targeted, there may be additional requirements or restrictions

If the online research is not anonymous, the General Data Protection Regulation (GDPR) or other privacy laws in a specific country may apply.

Virtual interviews (e.g. Zoom) are not considered online research because they involve a direct interaction between the interviewer and the participant. Research involving interviews conducted via Zoom or other virtual platforms will require review by a foreign EC/IRB (if there is such a requirement) or by a Local Context Advisor.

HRPO may require the researcher to obtain a security review of the online platform through the Office of Information Security. See discussion below regarding Data/Data Privacy and Security.

Research Collaborators

IRB oversight is required for all individuals that are engaged in the conduct of non-exempt human subject research. An individual is engaged in research if they intervene or interact with research participants, obtain identifiable private information or biological samples or they are the prime awardee of a federal grant that involves human subjects research. For information about engagement in research, refer to United States Health and Human Services OHRP's guidance on this topic: "Engagement of Institutions in Human Subjects Research (2008)." The WU IRB does not assume oversight of research collaborators on international research projects if they are not WU faculty, staff or students.

If you are conducting research in a country that does not have an Ethics Committee or IRB review requirement and you have international research collaborators, contact HRPO for further guidance. If certain criteria are met, as described in the "Oversight of International Collaborators Guidance," the WU IRB will not require that these individuals obtain a separate IRB approval for their research activities.

Data/Data Privacy and Security

Data privacy laws and regulations are quickly evolving and may vary significantly between countries. It is the responsibility of the PI to ensure that data is collected, managed, and shared in compliance with the law where the data was collected.

Whether publicly available or not, documentation of permission for the data is required. For example, for publicly available data, a link to a website or terms of service may be appropriate. For non-publicly available data, an email from the person who is responsible for the data or a copy of the signed data use agreement will be required.

While data coming from publicly available sources with no human contact and no identifiable data may not meet the US definition of human subjects research, it is important to confirm the laws of the country where the research will be conducted or the data is collected, obtained or stored. Definitions of "identifiable" vary by country. Refer to the United States Health and Human Services OHRP International Compilation of Human Research Standards for guidance on foreign laws regarding collection, use and transfer of data and specimens. If this guidance does not address the foreign site, then consult with an informed local partner.

Data Use Agreements

When collaborating with another institution or non-WU researcher, a data use agreement may be required prior to the start of the research. A data use agreement facilitates the proper sharing of research data between WU and other research sites or collaborators. It describes the data being shared, how the data may be used and the confidentiality and security expectations for the data. Contact the Joint Research Office for Contracts (JROC) to see if an agreement is needed: researchcontracts@wusm.wustl.edu.

Data Security

Many countries require the application of data security measures to protect the privacy and integrity of identifiable data. Appropriate protections may include the following:

- Ensure computing devices are encrypted and have antivirus software installed
- Ensure access to data is password protected
- Use Box, REDCap or other WU vetted secure tools to share data
- Share only the minimum amount of data necessary to achieve the goals of the research
- Use encrypted storage devices when storing data on portable storage devices, e.g., thumb drives
- Limit physical access to paper records
- Limit access to data to only those on the study team that are listed on the protocol and consistent with the individual study team member's role in the study.
- Conduct periodic reviews to ensure that access was terminated for former study team members and to validate the proper access and use of data

- Use secure email when transmitting data, similar to the encryption required when transmitting health information protected by HIPAA

For additional guidance, refer to the Office of Information Security:
Home | Office of Information Security | Washington University in St. Louis (wustl.edu)
Email: Infosec@wustl.edu.

HIPAA
HIPAA regulations do not apply when identifiable health information is collected in another country and transferred to the US; however, researchers that are part of the HIPAA Covered Entity at WU must follow HIPAA regulations once the data is transferred to WU. See "Accountability for Compliance with HIPAA Privacy Rules" Policy at https://hipaa.wustl.edu/policies-procedures/.

The General Data Protection Regulation (GDPR)
GDPR is a European law that went into effect on May 25, 2018 and establishes protections for privacy and security of "personal data" about individuals in European Economic Area ("EEA")-based operations and certain non-EEA organizations that process personal data of individuals in the EEA.

GDPR has strict requirements for transfer of data collected from citizens of the EEA (most countries in Europe including the United Kingdom) and transferred outside of Europe. HRPO has developed language to include in the informed consent form that complies with the GDPR. For more information on GDPR, see United States Health and Human Services OHRP's website: https://www.hhs.gov/ohrp/international/gdpr/index.html or https://gdpr.eu/

GDPR does not apply if the data is anonymous.

Federal Wide Assurances (FWA)
All institutions (foreign or otherwise) engaged in the conduct of the research funded by the federal government must obtain a FWA with the Office of Human Research Protections. A FWA is an assurance of compliance with the U.S. federal regulations for the protection of human subjects in research. Instructions for the application process can be found here: https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/fwas/file-a-new-fwa/index.html

Other institutions are not allowed to rely on the Washington University FWA to meet this requirement.

IRB Review
Once all pre-submission requirements are completed as outlined in the International Research Prep Work Checklist, the study may be submitted to the IRB. The IRB will review the research taking into consideration the local context review, if required, and other legal requirements.

The IRB application should carefully describe WU's role in the research. If WU will only receive de-identified data, IRB review is not required unless WU is the prime awardee of a federal grant.

HRPO uses the HIPAA definition of identifiers to determine if a dataset is de-identified.

Consent Forms

When the Washington University research team is involved in the consent process in a foreign country, the researcher is encouraged to use one of the WU HRPO consent templates because they are acting as a representative of Washington University. This consent should include the WU IRB stamp and list the WU PI and HRPO contact information as indicated in the template instructions.

If WU researchers are not involved in the consent process, the consent form approved by the local EC/IRB should be translated into English and attached as a miscellaneous document in the IRB submission. HRPO will review the consent document required by the local EC/IRB to make sure it does not include exculpatory language and that it accurately describes the study procedures, risks and benefits to ensure there are equivalent protections in place. The WU IRB may require edits to the consent even though it has been or will be approved by the foreign IRB.

The consent form must include:

- A "key information" section if the study is federally funded
- Language about a certificate of confidentiality (COC) for studies that have a COC
- HRPO's future use template language is required if you submitted a Data Management and Sharing Plan (DMSP) to NIH. If your DMSP includes sharing data open access or sharing identifiable data, contact HRPO.
- Language about the European General Data Protection Regulation (GDPR) for studies that take place in the European Union

When another template is used, in addition to the required information in the bulleted list above, the WU IRB will confirm that the consent form includes the name of the local PI(s) (in country) as well as the corresponding contact information for the local institution or local Ethics Review Committee. The WU IRB stamp should not be included on the consent form when the WU research team is not involved in the consent process, or when the local EC/IRB requires that their template be used. The WU IRB stamp includes the WU IRB approval and expiration dates (if applicable), which would not be applicable when a consent form is approved by the local EC/IRB. When a study is approved by the local EC/IRB, the approval and expiration dates (if applicable) would be determined by the local EC/IRB.

Unless the research is exempt or the WU research team is not involved in the consent process, translated versions of the consent form should be included in the IRB submission after the English version is finalized by the WU IRB.

Most minimal risk research qualifies for a waiver of documentation (no signature is required) when the research meets the criteria described in 45 CFR 46.117. When in doubt as to the appropriateness of requiring a signature, the IRB will rely upon the Local Context Advisor's recommendations or the requirements of the local EC/IRB committee as long as the recommendations are equivalent to the US protections.

Modifications

The WU IRB must approve all modifications to the research prior to implementation. If an EC/IRB is also overseeing the research, their approval should be included when submitting the modification to the WU IRB.

WU IRB Review and Local EC/IRB Review

One rare occasions there may be conflicting requirements between the local EC/IRB and WU IRB review. This most commonly relates to consent language. To avoid delays, it is very important to include the consent language, as described in the Consent Form section above, prior to submitting to the local EC/IRB. Otherwise, contact HRPO for assistance.