OFFICE OF
RESEARCH PROTECTIONS

Office of Research Protections

Villanova University Guidance International

Research with Human Subjects

July 1, 2019

Villanova University researchers sometimes conduct research outside of the United States. When conducting international research with human subjects, Villanova and its researchers must ensure that these activities not only meet the ethical and regulatory requirements for conducting research at Villanova, but also respect the cultural norms and comply with the regulations and laws in the host country.

This shared responsibility can be achieved by evaluating the following criteria and providing appropriate information to the Villanova Institutional Review Board for the review of applications for international research.

I. Host Country Research Review & Oversight

Researchers who would like to conduct international research must plan in advance **(usually 3-6 months before the visit)** to obtain any review or oversight of the research that is required by laws, regulations or custom in the host countries, in addition to fulfilling Villanova IRB review requirements. Approval from the appropriate oversight body, if any, in the host country is required for approval by the Villanova IRB. Researchers are responsible for determining what additional requirements apply in the host country. Initial guidance and information may be found on the Office of Human Research Protection's (OHRP) website, but researchers may also need to seek additional expert advice. Given the additional complexity that often accompanies international research, Principal Investigators (PIs) should ensure adequate time for protocol creation, submission to the Villanova IRB and any external review body (if applicable), protocol review, etc.

1. Obtaining local approval

Applications for international research submitted to the Villanova IRB should indicate which local IRB, Ethics Committee, or government entity, if any, will perform review in the host country.

- Studies not yet approved in the host country:
  Clearly indicate the status of the local ethics review.
- Studies that that been approved:
  Provide a copy of the approval letter or notice from the host country's ethics review (with translation into English, as needed). Provide the name and contact information/website of the ethics review body.

2. Locations not requiring local approval:

In some international settings, national and local regulations do not require review or oversight of the research (e.g., social/behavior/educational research or use of existing data/samples) or there is no ethics committee to review the research in the host country. In these cases, researchers must provide a letter of support from an individual in the host country who has the relevant expertise or authority to review the research. Evidence of expertise should be included (e.g., curriculum vitae, bibliography, and/or other material may be needed). This person *cannot* be associated with the conduct of the proposed research. The letter must state that there is no formal review process available or needed, and that the research is acceptable according to national and local context.

- This standard may apply to research that would qualify as exempt if conducted in the U.S., depending on a variety of factors such as the country in which the research will be conducted, the PI's and IRB's familiarity with the country's research regulations and local context, the nature of the research, the experience of the investigator, etc. Please contact the Villanova IRB to discuss proposals for exempt research that will be conducted internationally.
- If the researcher is proposing to conduct a *clinical trial* in a country where there is no local ethics committee to review the research, additional local oversight may be required by Villanova's IRB, such as an ad hoc review committee. Please contact the Villanova IRB to discuss proposals for clinical research that will be conducted internationally.

3. **Federal Wide Assurance (FWA):**

When non-exempt research is sponsored by a U.S. federal agency, all domestic and international sites engaged in the conduct of federally-funded research must hold a Federal Wide Assurance (FWA) with the Department of Health and Human Services (DHHS). For U.S. federally-supported research, the international site must rely upon the approval of an IRB that is registered with DHHS and is designated on the site's FWA. This requirement applies to all Villanova's research conducted with federal funding or support. Any international research that is funded by the Food and Drug Administration (FDA) must comply with DHHS, FDA, and any applicable local regulations.

4. **Federal guidance addressing international research**

T h i s is periodically released by the OHRP. Investigators involved in international research are strongly advised to consult federal sources, including the *International Compilation of Human Subject Research Protections* guidance document.

5. **Personnel additions post study start:**

If a Villanova University faculty member, employee, student, etc., becomes involved in international research after it has been initiated, approval from the Villanova IRB is required prior to the time of the new personnel member's involvement. The PI must delineate the components of the research that the new research member will be involved in and provide documentation of prior IRB (or host country equivalent) approval of the modified study protocol

6. **Local Expertise of record:**

Provide the name and contact information of a person not affiliated with the research who has expertise on the cultural context of the country or community where the research will be conducted. A member of Villanova's IRB may contact this individual as an expert content reviewer or consultant.

II. Host Country & Local Context

Both the Principal Investigator (PI) and Villanova IRB must consider the local context of the host country(ies) or community(ies) to ensure that adequate provisions for protecting human subjects are in place during the conduct of international research. Cultural, economic, and/or political conditions of the host country/community should inform decisions about how the research is conducted, and in some circumstances may even alter the risks and/or benefits for participants.

The Villanova IRB strongly recommends that the PI develops a relationship with an in-country consultant w ho can guide him or her on local culture, customs, and laws, and provide guidance about the research context. Without such a consulting partner, the Villanova IRB approval process may take longer than it otherwise would.

The PI and research team members conducting international research must include relevant context information in their IRB applications. Such context must be evaluated for each location of the research. This includes, but is not limited to, the following:

1. Countries, cities, and regions where research will be conducted
2. Scientific/ethical justification for conducting the research in an international setting
3. Economic status of the country/community
4. Current events or socio-political environment in the country/community that may impact research conduct or alter the risks or benefits to subjects
5. Societal and cultural beliefs in the country/community that may impact research conduct or alter the risks or benefits to subjects
6. The role of potentially vulnerable study populations (e.g., women, children, and certain minority groups) in the society, including their autonomy and legal capacity to make decisions
7. Literacy rate of the potential subject population
8. Languages and dialects of the potential subject population
9. Involvement of organizations, community leaders, or experts in engaging the subject population or conducting the research

10. Description of the research team's knowledge of or experience in the host country (e.g., related to language, customs, and culture)
11. Relevance of the research to the country's/community's health, economic, educational, or other needs
12. Distribution of risks and current and future benefits

III. Ethics Approval at Host country

The investigator is responsible for obtaining ethical clearance from all national, regional, local bodies, as applicable, to complete the study. The Villanova IRB requires the following documentation to review the study:

1. Certification or approval from a local IRB (or other equivalent)
2. Or an official letter from a local IRB (or other equivalent) indicating that local approval is not required
3. If the first two options are not viable, documentation can be obtained from a research ethics expert or an organization based in the host country
4. If the first three options are not valid, investigators should obtain a letter from an experienced in-country researcher in the field of study

Details to be covered in the support letter for the research to be provided to the IRB:

1. How the writer knows the PI: for how long, collaboration, shared publications etc.
2. Assurance that they do a similar kind of work and have an active research program
3. The number of years of experience the individual has working in the field and in the country
4. Assurance that they have familiarity with the IRB (or equivalent) rules of the country, province, state or jurisdiction
5. Would the type of study being performed require IRB (or equivalent) approval in the host country?
6. Does the local law specify that the study requires informed consent procedures to be implemented for the study to occur?
7. Based on the nature of the study, what are the risks to the potential participants?
8. Description of the customary expectations around confidentiality and privacy by participants in that culture
9. Any other pertinent information that may be useful for the IRB to understand the local situation

IV. Informed Consent Process

Unless a waiver or alteration of the consent process is requested and approved by the Villanova IRB, researchers are expected to adhere to the U.S. federal requirements for obtaining informed consent, whether the research is conducted in the U.S. or internationally. Villanova's IRB acknowledges that consent procedures typically followed in the host country/community may differ from those required by U.S. federal regulations. Villanova's IRB may approve alterations to consent requirements if the proposed procedures provide equivalent protection to research subjects and are approved by the host country or local oversight body (as referenced in the *Research Approval* section above).

Please address any of the following informed consent topics that may apply to your research in your IRB application:

1. **IRB approval for information provided to subjects:**
   Any materials presented to subjects during the course of the study must be submitted to Villanova IRB for review and approval; the host country or local review body may also require review and approval of this information. This includes, but is not limited to recruitment material, consent documents, educational or instructional material, hand-outs, presentations, or scripts for oral interactions.

2. **Requesting a waiver of documentation of consent:**
   If the research team would like to request a waiver of documentation of consent for research in which written consent is typically required, please provide justification for the request and describe how consent will be documented if not in writing. Examples for justification may include low literacy levels within the population, the cultural significance of providing signatures, etc.

3. **Enrolling minors:**
   If minors will be enrolled in the research, provide the legal age of majority and describe an appropriate assent process for the host country and local community.

4. **Considerations regarding autonomy:**

   Consider the potential role of family and community within the consent process or issues related to autonomy (e.g. consent from community leaders or supplemental consent from male family members). Describe how the research team will address additional consent processes, if they need to occur.

5. **Socio-cultural context:**

   Consider whether the research intersects with any cultural sensitivities or societal norms. If so, describe how this will be addressed in the consent process, in informed consent forms (ICFs) and other study documents (e.g vaccine trials on a disease that is heavily stigmatized in the host country).

6. **Language and Informed Consent:**

   ICFs and other study documents and oral explanations, questions and instructions must be presented in language understandable to the participants.

   - All documents provided to participants should take into account the literacy and education levels of the study population. Please ensure that all study documents are written in simple, readable language, while clearly communicating the purpose of the research.
   - ICFs and study documents must be translated in local language. This process entails being translated to the host country's primary language or the language and dialect of the participating subjects and then back-translated to English for verification. Translated study documents must be submitted to the Villanova IRB, along with translator credentials or translation certifications, for review and approval prior to use with human subjects. As a best practice, IRB recommends that the local collaborator could verify and confirm that the content of the translated consent form matches the original version. This confirmation must be submitted to IRB.

7. **Contact Information for Study Participants:**

   The research team must provide subjects with locally-based and U.S.-based contact information. Researchers must provide contact information that will ensure subjects have

access to individuals who can answer research-related questions, even after the research team has left the host country.

8. Confidentiality:

When studying populations that are marginalized or at risk in some way, attention must be paid to train people providing transcription, interpretation, and translation.

V. Post-Approval Responsibilities

When developing an international research study, the PI must consider how he/she will fulfill the following responsibilities once study approval has been granted (responsibilities #1 and #2 also require documentation in the study protocol):

1. **Data and Record Retention:**

   The PI must describe and implement a data and record retention plan consistent with Villanova IRB policies. Study records such as executed consent forms, case histories, and regulatory correspondence must be accessible for inspection and copying by authorized representatives of the IRB and/or federal agencies, whether the records are maintained in the host country or in the US. Describe this plan in the study protocol.

2. **Adverse Events and Unanticipated Problems:**

   The PI must describe and implement a plan to provide Villanova IRB with reports of serious adverse events and unanticipated problems in accordance with Villanova IRB reporting timelines. Promptly notify the IRB of non-compliance, protocol deviations, and subject complaints. Promptly submit study updates, correspondence with the local oversight body, and data and safety monitoring reports to Villanova's IRB. Describe this plan in the study protocol.

3. **Communication with Local Site:**

   Make sure that there is a well-understood line of communication with the local site.

   - Ensure that members of the study team and international collaborators are up-to-date with regard to the approval status of the protocol and other study documents and any modifications or adverse events.
   - For student projects, there must be a well-defined plan or schedule to ensure communication and oversight between the advisor and student during the conduct of the research.

4. **PI Oversight and Responsibility:**

   Whether the PI operates domestically or in the host country, he/she must maintain oversight of the study and ensure proper conduct of the protocol and compliance with U.S. and international regulations. If Villanova is the primary awardee of a

grant for the overall project, the PI is responsible for overseeing the research of any international collaborators. If the Villanova's PI delegates responsibility for host country or local oversight to another person, he/she ultimately remains responsible for the proper conduct of the study.

5. Requests for Study Modifications:

Request modifications to the approved protocol from both the Villanova's IRB and any local oversight bodies before initiating any changes in the research. The only exception to the requirement of obtaining IRB approval before initiating a change in the protocol is when a change is necessary to eliminate apparent immediate hazards to a subject(s). Under such circumstances, the PI is to contact the IRB Chair or the Office of Research Protections within 5 days of the event.

VI. Other Clearances at Villanova

Approval by the Villanova IRB does not constitute institutional clearance to complete the study. Here are some other steps the researcher needs to complete.

1. **Villanova Policy on Travel**:

   Researchers must refer to the Policy on Travel and adhere to the instructions provided there. If Villanova funds are being used for travel and research, approval must be obtained per the University's Travel Policy. Faculty must have all department approvals necessary to have trip expenses covered.

2. **Villanova Insurance and Risk Management for Foreign Travel**:

   The University's Manager of Insurance and Risk Management must be notified of all foreign trips, so the trip can be covered under the University's International Insurance and Emergency Assistance Policy and legal waivers can be obtained, if appropriate. Certain types of warnings/ratings from the State Department may exclude certain destinations from coverage under insurance policies.

3. **Additional Considerations**:

   Depending on the research plan and the country(ies) in which it will be conducted, certain other legal and regulatory requirements may apply (e.g., grant or sponsorship terms, immigration laws, Foreign Corrupt Practices Act, export controls regulations, etc.). Contact the Office of Grants and Contracts, the Office of General Counsel, or University Compliance Office for further information.