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HRPP Policy 1401: International Research

14.1 General Researcher Considerations

It is a relatively common occurrence that University researchers will perform human subjects research outside the borders of the United States. When performing human subjects research in foreign countries, expectations of the University are that the research activities are consistent with the ethical principles set forth in the University Human Research Protection Plan (HRPP) and provide levels of subject protections equivalent to those provided when performing human subjects research at the University. It is also expected that researchers will comply with applicable national and local laws and take into account the cultural context of the country in which the research is taking place.

When performing human subjects research in other countries, University researchers are expected to comply with U.S. regulations and guidelines and any applicable regulations of the country in which the research is performed. In addition, for biomedical research there are international guidelines that may be applicable and with the University researchers should be familiar; e.g., The Declaration of Helsinki, the International Conference of Harmonization – Good Clinical Practice (E6) Guidelines and the International Ethical Guidelines for Biomedical Research Involving Human Subjects published by the **Council for International Organizations for Medical Sciences**.

Research in international settings may pose special or unusual risks to participants, and

PIs should articulate the cultural, political, economic and /or legal context of the research and how this may create or affect ethical considerations of a research project or research design.

14.2 Specific Principal Investigator Considerations

Federal regulations for oversight of international research require that when conducting international research the researcher:

1. Will provide the same or equivalent protections to human subjects in research conducted in other countries.
    a. The protections need not be the same as provided in the U.S., but should be equal in function or effect.
    b. Subject autonomy and dignity should be respected.
    c. Protections should encompass the ethical principles of respect for persons, beneficence, and justice.
2. Is aware of local laws, regulations, political and socio-economic factors, and cultural context in all locations where the research is conducted.
    a. Researchers must have sufficient knowledge of the local context to enable carrying out the research in ways that protect the rights and welfare of subjects.
    b. Knowledge of the local context may influence all aspects of the research design.
3. Will comply with local laws and adhere to cultural norms.
4. Will demonstrate whether the university or researcher has permission to conduct research in the country by local ethics committee review and approval or by certification (approval) by the local government when there is no local ethics committee.

Post-approval monitoring of international research will follow the same procedures used for monitoring of locally conducted research, as described in **HRPP Policy 301**.

Investigators should review the **U.S. Department of Health & Human Services International Compilation of Human Subjects Protections** for more information on evaluating whether additional safeguards or accommodations are required.

14.3 General Reviewer Considerations

There are also requirements and expectations for reviewing proposed international research. Generally:

1. IRBs or Ethics Committees (ECs) must ensure that equivalent protections are provided to research subjects enrolled in research in another country, and;
2. IRBs and ECs will make determinations and decisions based on laws and knowledge of the country in which the research will be conducted, such as:
    a. If there are laws or guidance related to human research subject protections.
    b. If there are other laws that will need to be factored into the research.
    c. If the local government has their own required approvals.

Reviewers should review the **U.S. Department of Health & Human Services International Compilation of Human Subjects Protections** for more information on making these determinations.

14.4 Specific Principal Investigator and Reviewer Considerations

More specifically, IRB reviewers and the IRB will require certain information in order to fulfill the requirements, and this information should be addressed in the submitted protocol. For example, the information provided should include, but not be limited to:

1. Whether the researcher speaks the language of the country in which participants will be enrolled and the research will be conducted. If the researcher does not speak the local language, describe how communication with the research subjects will be accomplished.
2. Whether the researcher is familiar with the local customs and culture, or whether a local collaborator will be used, and the involvement of the local collaborator will have in the conduct of the research.
3. Whether the subjects will be paid and, if paid, the amount and how it relates to the local economy and subject income.
4. If consent will be obtained, how or from whom will consent be obtained, along with the following information, if applicable:
    a. Describe local customs/culture in which the subject might not have the autonomy to provide consent, and a family member or other person will be providing consent to participate.
    b. How the researcher will assure that there is no coercion for participation if a person other than the subject will be providing consent.
5. If written documentation of consent will be obtained, and:
    a. If so, a description of how or from whom the consent will be translated.
    b. If not, a description of how consent will be documented or if there are cultural/other prohibitions regarding the use of consent forms.
6. Describe how the privacy for the subjects and confidentiality of their research data will be assured, and if there is a local custom that research data be revealed to someone other than the subject.
7. Describe how the communications with the University IRB/local EC will be achieved for requesting amendments or reporting unanticipated problems.
8. For student researchers, a description of how the academic advisor/faculty sponsor will oversee the conduct of the research.

14.5 Exemptions

1. A great deal of research in the social and behavioral sciences may pose no more than minimal risk to subjects and may qualify for exemption. However, conducting research in another country does not necessarily exclude the research from IRB review.
2. There may be other factors, specific to the locale, that would disqualify the research from exemption, such as recruiting vulnerable populations (i.e. undocumented individuals or marginalized identity groups (refugees)).
3. Even in exempt research, informed consent, parental permission, and child assent may or may not be ethically appropriate and/or required under local law.
4. Evaluating whether an international project would qualify under exempt status will be dependent on whether the research qualifies under one of the federal exemption categories.

14.6 Risk Assessment

The IRB must assure, perhaps through consultation with experts, that the risk assessment is accurate for the foreign site. Research methods that have minimal risk in the U.S. might have greater than minimal risk when conducted at certain foreign sites.

The following must be given consideration:

1. Questions that might be innocuous in the U.S. could be offensive at certain foreign sites.
2. Assuring and maintaining confidentiality may be difficult in other countries.
3. Breach of confidentiality in the research locale could have dangerous consequences.
4. Depending on political and other factors, there may be dangers to the researcher.

14.7 Translators and Translating Documents into the Language of the Targeted Study Population

During the conduct of research, an investigator may encounter potential participants who do not speak English or who have limited English proficiency ("persons with LEP"). These individuals should be allowed to participate in research studies, absent compelling reasons to exclude them, in accordance with the Belmont Report principle of Justice.

OHRP provides guidance that clarifies how to determine when an interpreter who is interacting with participants is a member of the research team. According to the guidance, interpreters are not members of the research team if:

They perform commercial or other services for researchers, provided that all of the following conditions are also met:

a. The services performed do not merit professional recognition or publication privileges;
b. The services are typically performed by the interpreters for non-research purposes; and
c. The interpreters do not administer any study intervention being tested or evaluated under the protocol.

If an interpreter who will be interacting with participants for research purposes does not meet any one of the conditions listed above, and the research requires expedited or full board review, that person:

- Is a member of the research team;
- Must be identified and their role described in the IRB application; and
- Must complete an IRB approved human subjects protection training.

14.7.1 Use of research staff as interpreters

Using study team members as interpreters may pose a conflict of interest when presenting information to the person participating in a research study. In some situations, staff members may not possess competence in the skill of interpreting, especially in non-verbal skills, nor have knowledge of generally accepted principles of interpreter ethics.

For studies that do not involve a medical treatment as part of the research, the IRB may allow for study team members who are proficient in the language of the subject to be used as interpreters, if there is documentation that they are truly capable of interpreting for subjects and are culturally aware of verbal expression and verbal comprehension. The IRB requires that **Appendix K: Translation and Interpreter From** be completed on any study member who will serve as the translator documenting their qualifications for the research record and have it included in the

IRB application.

14.7.2 Issues with using family members as interpreters

Family members are seen by some as able to address cultural and language barriers; however, having a family member does not guarantee that the translation will be done correctly. Certain cultural and family relationships may cause withholding of information that may be important to make a decision about participation. Additionally, family members may not have adequate English language knowledge to understand or translate technical or difficult medical or research information. Family members, who are minor children, are not allowed to serve as interpreters, other than in emergency, life-threatening situations. As a general rule, family members should not be used when the study involves medical treatment as part of a research study. Using a friend or family member as an interpreter introduces a potential conflict of interest that may adversely impact the rights and welfare of potential study participants, and their views may be substituted for those of the potential subject.

14.8 Informed Consent

1. The informed consent process must honor local custom.
    a. Some cultures may have a different authority structure for consent.
    b. The local consent structure may seem coercive and clash with the researcher's, reviewer's, or IRB/EC's views on autonomy.
2. Surrogate consent/permission should not substitute for a subject's informed consent unless the IRB/EC has approved an alteration or waiver to the consent process. A standard practice is to provide a research information sheet with all the related consent information if a waiver of documentation is approved by the IRB.
3. The consent process/form should, unless waived by the IRB/EC, contain all required elements of informed consent. The consent process should also make clear the conditions under which research may have direct benefits to a participant, or to be clear that there are no real or implied benefits as a result of participation in the research.
4. Consent is best obtained using the language that is most familiar to the subjects, taking into account:
    a. Some languages/dialects are not written.
    b. Subjects may be unable to read.
    c. There may be words in the foreign language that do not translate to/from English.
    d. If researchers are not fluent in the local language, interpreters/translators who are fluent should be used.
5. Documentation of consent may be difficult because:
    a. Subjects may be illiterate.
    b. In some cultures, it may be inappropriate to ask for a signature.
    c. There may be legal implications when signing documents.
    d. Subjects may be suspicious, distrustful, or fearful that they are giving up their rights when asked to sign documents.
6. Alternate consent procedures may have to be considered, such as:
    a. Use of pictures, video, or computers.
    b. Alternate forms of documentation, such as thumbprints.

14.9 International Research Involving Children

The following should be considered when the research involves children:

1. In the locale of the research, when a child is considered an adult.
2. The relationship between parents and their children in the specific country.
3. Acceptable and effective parental permission processes.
4. If child assent is acceptable/permissible by local custom.
5. If there are laws pertaining to orphans.

14.10 Communication with IRB

With the research occurring outside of the country, there should be consideration on how the communication between the researcher and the IRB will take place. The protocol should describe the following:

1. How communication will occur with the University IRB and the local EC, if applicable.
2. How ongoing review, amendments, or reporting of unanticipated problems or complaints will be handled and by whom.
3. If it is a student researcher abroad, the student's knowledge of the country and how the student will communicate regularly with their faculty advisor.
4. List local contact in case the Principal Investigator or faculty sponsor cannot be reached.

14.11 The European Union (EU) General Data Protection Regulation (GDPR)

The General Data Protection Regulation (GDPR) standardizes a data protection law across all 28 European Union (EU) countries and imposes strict new rules on the control and processing of personal information.

The following countries are part of the EU and have adopted the GDPR law:

Austria	Germany	Malta
Belgium	Greece	Netherlands
Bulgaria	Hungary	Norway*
Croatia	Iceland*	Poland
Cyprus	Ireland	Portugal
Czech Republic	Italy	Romania
Denmark	Latvia	Slovakia
Estonia	Lichtenstein*	Spain
Finland	Lithuania	Sweden
France	Luxembourg	United Kingdom

*Although not part of the EU, these countries have adopted the GDPR under the European Economic Area (EEU) Agreement.

14.11.1 Activities Requiring GDPR

The GDPR applies to the “processing” of personal information by an individual or legal entity. The term “process” is extremely broad and generally covers anything that is done to or with personal data, whether by automated or manual means. This may include collecting, recoding, organizing, structuring, storing, adapting, altering, retrieving, consulting, using, disclosing by transmission, disseminating or making available, aligning or combining, restricting, erasing, or destroying data.

14.11.2 Consent Requirements under GDPR

GDPR permits researchers to rely upon consent from research subjects as a

lawful basis for processing Personal Data for research purposes, typically under 'public interest' as the most appropriate legal basis. To obtain a valid consent to process an individual's Personal Data for research purposes under GDPR, the individual's consent must be:

- **Freely given**: The individual must have a realistic choice, or the realistic ability to refuse or withdraw consent without detriment. Similar to U.S. law, coerced consents are not compliant with GDPR.

- **Specific**: The consent must include a specific, transparent statement of each purpose of the study and including the rights articulated above. This includes specific reference for "future use" of the data.

- **Informed**: An individual must be informed of the nature and extent to which the individual is consenting to what data collection activities and to what use of data.

- **Unambiguous**: GDPR requires a statement or "clear affirmative act" that indicates the individual has agreed to the proposed processing of data activities. Silence, pre-checked boxes, and inactivity (passive consent) are not allowed for the purposes of consent.

14.11.3 Letter of Information and GDPR Compliance Consent Document
The consent process needs to be a distinct two-step process that includes a Letter of Information as one document and a GDPR Compliance Consent Document as a separate document.

- **Letter of Information**
  A Letter of Information is essentially the same as the consent document that the IRB requires, but with the optional elements and the signatures are removed to a separate sheet. The investigator should use the appropriate IRB-approved consent template for their study and complete the information as normally required, except add information in specific detail to the data management and data protection sections of the study. This part of the consent process is a separate step in support of "freely given." All of the same elements that are in the DU current consent templates are required, and at the end of the document, contact information must be provided to the potential participant.

- **GDPR Compliance Consent Document**
  This consent document is specific to studies that must comply with the GDPR and should include all of the specific elements of the study that the potential participant has read through in the Letter of Information.

  For Greater than Minimal Risk studies, the GDPR Compliance Consent must be a separate document from the Letter of Information, and the signature block on the Letter of Information should remain at the end of the document.

  For Minimal Risk studies, the Letter of Information can have the GDPR

Compliance Consent Document language embedded into the document, but it must be separated by a page break and titled as the "GDPR Compliance Consent Document."

For additional information on the consent process, please refer to **GDPR Consent Process guidance**.

14.11.4 Withdrawing Consent

Under the GDPR, individuals have the "right to be forgotten" or "right of erasure." This means that upon the withdrawal of consent of any item, the "controller" of the data should delete or anonymize the personal data immediately and its use of the data for the research study should stop. However, if the data needs to be retained after consent is withdrawn, the informed consent form must specify as such and indicate at the outset that, even if consent is withdrawn, the entity will retain the data for another identified lawful basis.

14.11.5 Instances when No Consent is Required

- **Scientific Research Purpose – No Consent Required**
  GDPR permits processing of special categories of personal information for scientific or historical research purposes. Under this mechanism, use must be limited so that it is proportionate to the aim pursued, respects the essence of the fundamental right to data protection, and provides for suitable and specific measures to safeguard the fundamental rights and the interests of the data subjects. This implies that where the research purpose can be fulfilled by further processing and does not require the identification of data subjects, then the research shall be fulfilled in a manner that does not permit such identification.

- **Public Health Purpose – No Consent Required**
  GDPR further permits the use of special categories of personal information on the basis of necessity of public interest in the area of public health, such as protecting against serious cross-border threats to health or ensuring high standards of quality and safety of health care and of medicinal products or medical devices. This basis for processing most directly authorizes health professionals to use special categories of personal data to protect public health in epidemics, pandemics, or other imminent safety threats in connection with drugs or devices. DU should only rely on this basis to process personal data if the applicable research effort has a direct, immediate, non-attenuated public health application, but this basis may permit the processing of data concerning adverse events that arise in connection with the use of a drug or medical device.

14.11.6 GDPR and Health Records

Although there are similarities between HIPAA and the GDPR, the GDPR is broader and includes information not covered by HIPAA. The GDPR applies to any information relating to an identified or identifiable natural person's "personal information". Additional protections are given to "special categories" of or "sensitive" personal information. This includes information related to an individuals' racial or ethnic origin, political opinions, religious or philosophical

beliefs, trade-union membership, processing of genetic data (including from an analysis of a biological sample), biometric data for the purpose of uniquely identifying a natural person (e.g., facial images or fingerprints), data concerning health (physical or mental), and data concerning a natural person's sex life or sexual orientation.

In general, processing health, genetic, and biometric data is prohibited unless the data subject has provided explicit consent or made the information publicly available or the processing is otherwise permitted by law.

14.11.7 Required Information - Controller's Privacy Practices
If the University of Denver or a DU investigator serves as a 'controller', DU must provide the data subject with a notice of the controller's privacy practices. This notice must be: (i) concise, transparent, intelligible, and easily accessible; (ii) written in clear and plain language, particularly if addressed to a child; and (iii) free of charge. Generally, the notice must answer the following questions related to data collection and use:

- What information is being collected/processed?
- Who is collecting/processing it (including contact information)?
- How is it collected/processed, including the lawful basis?
- How will it be used?
- How will it be stored and for how long?
- Who will it be shared with (including third parties)?
- What will be the effect of this on the individuals concerned?
- Is the intended use likely to cause individuals to object or complain?
- Will it be transferred to a third country and, if so, what is the lawful basis for such transfer?
- The data subjects must also be informed of their rights to request access, rectification, erasure or restriction of processing, to object ot processing, and the right to data portability.

In the context of consented research, such notice can be built into the informed consent form.

14.11.8 De-Identified Data and GDPR
Unlike HIPAA, the GDPR does not provide specific methods to "de-identify" data. Rather, the regulation provides that data may be "anonymized" or "pseudonymized."

- **Anonymization** of personal data refers to a subcategory of de-identification whereby direct and indirect personal identifiers have been removed and technical safeguards have been implemented such that data can never be re-identified. The GDPR does not apply to data that does not relate to an identified or identifiable natural person or to data rendered anonymous in such in a way that the data subject is not or no longer identifiable. A data set that is "de-identified" under HIPAA is not necessarily anonymized under the GDPR.

- The GDPR defines **pseudonymization** as "the processing of personal data in such a way that the data can no longer be attributed to a specific

data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organizational measures to ensure that the personal data are not attributed to an identified or identifiable natural person." Pseudonymous data refers to data from which identifiers in a set of information are replaced with artificial identifiers, or pseudonyms, that are held separately and subject to technical safeguards. Unlike HIPAA, coded data must be treated as identifiable personal data, and the GDPR does apply. Although pseudonymous data is not exempt from the GDPR altogether, the GDPR relaxes several requirements on controllers that use the technique, such as allowing for additional use beyond the original collection purpose.

14.11.9 Personal Data Breach

The GDPR has very strict rules and timelines regarding the report of data breaches. Any data breach occurring on a project involving GDPR-covered research must be reported within 24 hours upon identification of the breach to the Office of Research Integrity and to the Office of General Counsel.

The following information should be communicated:

- Type of breach
- Nature, sensitivity, and volume of personal data
- Severity of consequences for individuals
- Number and characteristics of affected individuals
- Ease of identification of individuals
- Protocol number