Human Research Protection Program
Policies & Procedures

International Research

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Research Integrity Office
Mail code L106-RI
Portland, Oregon 97239-3098
Phone: 503-494-7887
Fax: 503-494-5081

Background:
IRB review of international research raises additional considerations related to obtaining local knowledge of applicable laws, institutional commitments and regulations, standards of professional conduct and practice, cultural norms, and local community attitudes. Physical, social and psychological risks may vary from those the OHSU IRB is accustomed to reviewing. Assessing the risks and benefits of research conducted internationally may raise challenges if there is not adequate knowledge of the local setting. Care must be taken to ensure that the cultural norms of the host country are respected and that the participants will not suffer adverse consequences from participation, such as being subjected to retaliation from local authorities or the local community.

Scope:
This policy covers research that is conducted by an OHSU investigator or student outside of the United States.

I. Policy:

A. When an OHSU investigator conducts human subject research at a non-US site, the OHSU IRB has oversight authority for that research.

B. The OHSU IRB and the PI will ensure that research under its jurisdiction conducted at international sites complies with the Common Rule or an equivalent system of human subjects projections. Special focus will be on the following:

1. Whether necessary information has been provided about the local research context,

2. If the consent process is appropriate to the population and procedures, and

3. If adequate provisions are outlined for data and safety monitoring.

C. The IRB and investigators have an obligation to be knowledgeable about the setting where the research is to be performed. IRB review of research studies that involve human subjects in other countries must include appropriate expertise for evaluation of the study in the context of the specific international setting(s) and study population(s).

D. OHRP requires knowledge of local research context and the IRB may secure knowledge of the local context in a variety of ways.

1. It should be determined whether a local IRB or other analogous review body exists to provide local context and guidance. Evaluation of the protocol by a review board local to the study site, consultation with an expert in the respective

country, and/or other means to obtain knowledge of the local context is required.

2. The level of risk, amount of community involvement, logistical complexity, and potential for interaction with local laws will dictate the type of local level review that is required.

E. The informed consent process and documents must be in a method and language that is understandable and culturally appropriate to the proposed participants.

II. Procedure:

A. Investigator's Responsibilities

1. The investigator is responsible for identifying and ensuring compliance with all applicable laws, regulations, and guidelines for human subjects research in the country(ies) where the research will be conducted. This may include visa requirements for OHSU/American researchers in foreign countries, governmental approval for non-citizens to conduct research, etc.
2. The investigator is responsible for providing the IRB with the necessary information to enable the IRB to evaluate the research in light of the local research context.
3. Allow at least 6 extra weeks for an international review.

B. Submitting an International Study for Review

1. When submitting an international study for review, a submission memo should be prepared that addresses the following:
   - **a.** Documentation of knowledge of local context, e.g., details of the local context to provide a basis for the IRB review. This can include information regarding local customs, laws, standard of care, privacy concerns, and logistics;
   - **b.** local IRB/ethics committee approval, evaluation by consultant, or input from an individual or entity with adequate knowledge of the study site;
   - **c.** agreement that consent documents will be translated after the English version is approved, if the study population is expected to include non-English speaking individuals;
   - **d.** identification of local individuals, if any, who will participate in conducting the research, and a description of their roles;
   - **e.** Identify each collaborating site/agency/institution and describe their role (e.g., performance site, data coordinating center, agency whose employees are conducting research procedures, etc.). The investigator should identify the appropriate local permissions required for the conduct of the research. If the OHSU investigator will collaborate with persons who are affiliated with a local institution (university, etc.) or the local government, the application should identify each collaborator, his/her institutional affiliation, specify their role in the research, and outline their scientific qualifications. The application should identify the institution(s)/government(s) who will have access to the data, and specify the level of data which they will access (anonymous, coded, individual-level identified, etc.).
   - **f.** Identify city(ies), country(ies) where research will be conducted.
   - **g.** Provide a scientific and ethical justification for conducting the research in an international setting.

h. Outline the investigator's knowledge of the local community. The IRB application should: (1) include discussion of planned or completed community consultation activities regarding the consent process, consent documentation, study instruments, (2) identify the participants in the planned or completed community consultation, and (3) describe the methods, discussions, and meetings.

i. Describe the literacy level of the population, discuss how subjects' comprehension of the consent process will be maximized, and explain how the cultural appropriateness of the consent process and consent document (if applicable), study instruments, etc. has been determined.

j. Discuss the status of women in the local community/country. If the status of women in the international location(s) is different than in the United States, the Investigator's application should address the following issues:

- How will you ensure women's voluntary participation in the research?
- If women's consent will be supplemented by a male (spouse, brother, father, etc.), explain why it is impossible to conduct the research without obtaining supplemental male permission for female subjects.
- Explain why failure to conduct the research could deny its potential benefits to women in the host country.
- Outline the measures to be incorporated in the research protocol to respect women's autonomy to consent.
- Provide written assurance that in no case will a competent adult woman be enrolled in research solely upon the permission of another person.

k. Discuss the status of children in the local community/country. If the status or definition of children in the international location(s) is different than in the United States, the application should explain how.

l. Describe how the research may address an important scientific question regarding the host community/country. If applicable, describe how the proposal is responsive to local health needs of the host community/country. Describe both the standard of care in the USA and the available standard of care/alternatives in the host community/country.

m. Research may provide subjects with beneficial care. In some developing countries, the type and level of clinical care provided to subjects may not be available to those subjects outside of the research context. Though it is not a misconception to believe that subjects will probably receive good clinical care it is a misconception to believe the purpose of clinical trials is to administer treatment rather than to conduct research. The investigator should:

- Explain how the investigator will minimize the likelihood subjects will believe mistakenly that the purpose of the research is solely to provide treatment rather than to contribute to scientific knowledge.
- Clarify whether there has been an effort to secure continued access for all subjects to needed experimental interventions that have been proven effective at the conclusion of the project.
- Explain how the investigator will secure continued access (for subjects) to needed experimental interventions that have been proven effective at the conclusion of the project. Alternately, explain why the investigator has not secured continued access (for subjects) to needed experimental

interventions that have been proven effective at the conclusion of the project.

- Explain whether, if proven effective, the procedures will be available to some or all of the host country population. Also explain either (1) why the research procedures (if effective) will NOT be made available to the host country's population, OR, (2) how the research procedures (if effective) will be made available to the host country's population. Please include a description of any pre-negotiations among sponsors, host country officials, and other appropriate parties aimed at making interventions available after the research.

n. If sufficient information about the proposed research site is not provided in the submission, such will be requested as a result of the administrative pre-review.

C. Inducements in Low Resource Settings

1. Inducements are permissible provided the IRB is satisfied that the amount or nature of the inducement is not unduly influential or coercive.

a. For monetary incentives, find out the local relative value.

b. For non-monetary, consider whether it would impair one's ability to make a rational decision (note that some study related benefits, such as more frequent check check-ups, may not be avoidable)

c. Seek advice from local IRB/ethics committee or persons knowledgeable about local context.

2. Recognize the tensions that are unavoidable in some circumstances.

D. Consent

1. The consent process must incorporate a delicate balance of the typical IRB requirements (procedural and ethical) and local cultural norms.

a. Respect for persons includes respect for local culture.

- Autonomy may include desire to confer with family, community, clergy and others.
- Respect for community hierarchies may require a series of permissions to be obtained before individual consent is obtained.
- Refer to the 2001 report by National Bioethics Advisory Commission for an excellent discussion of this issue.

b. Consultation with local IRB may also be helpful in ascertaining local norms for informed consent, documentation, and parental permission requirements.

c. IRBs must be satisfied that translations are accurate. This can be accomplished through various methods.

E. Responsibility of the IRB

1. The IRB will review the study in accordance with 45 CFR 46 and secure adequate information regarding local context.

2. The IRB will take into consideration input from local experts.

3. If necessary, the IRB Chair will communicate with local IRB's and experts to facilitate review.

4. Risk of Harm

a. The IRB should determine whether the study design anticipates and minimizes the political, social, economic and legal risks that are particular to prospective human subjects or their communities in the particular country and subculture.

b. The IRB should determine whether the risks of adverse events are likely to be different in this population than in the same research performed elsewhere.

c. The IRB should determine whether adequate care is readily available for injuries sustained in the course of research.

5. Justice/Benefit

a. The IRB should determine whether the study is responsive to the needs of the subject population and whether the benefits of the study will be available to this human subject population. In other words, researchers may not utilize a human subject population merely for their own convenience and without the prospect of benefit to that population. Consideration should be given to producing benefits for the population that will continue after the termination of the study.

b. If the study includes an experimental health treatment intervention, the IRB should determine whether an established effective treatment exists and whether it is available to this subject population. Incorporation of a placebo arm for a study when an effective treatment exists is always a serious ethical issue, but scrutiny must be particularly intense when there are additional issues of potential vulnerability in the subject population. If it is determined that the research intervention is an effective treatment, the IRB must determine whether it will be available to the human subjects and the subject population following completion of the research study.

c. Regulations discourage consideration of long term impact of applying the results, but social justice considerations compel the IRB to ask about how the results will be used, assuming that the research addresses a local need.

III. Definitions

Ethics Review board (ERB)/Independent Ethics Committee (IEC): A specially constituted review body whose responsibility is to ensure the protection of the rights, welfare and safety of research participants. An IEC shares the same composition and operations as an Institutional Review Board.

Local Research Context: Knowledge of the institution and community environment in which human research will be conducted.

IV. References:

World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, April 18, 1979.

U.S. Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP), *Report of the HHS Equivalent Protections Working Group*, 2003.

National Bioethics Advisory Commission, Rockville MD, *Ethical and Policy Issues in International Research,* 2001.

The Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for biomedical research involving human subjects*. Geneva, Switzerland: The Council for International Organizations of Medical Sciences (CIOMS), 2002.

U.S. Office for Human Research Protections' (OHRP, formerly OPRR) *Protecting Human Research Subjects Guidebook* (1993), Chapter VI, "Special Classes of Subjects."

OHRP Website:
- International Issues Page
- International Compilation of Human Subject Research Protections
- Terms of the Federalwide Assurance (FWA)

Harvard School of Public Health: *Global Research Ethics Map*

V. Additional Resources:

UCLA International Research Checklist for Researchers

OHSU HRPP Policies & Procedures
- Knowledge of Local Context
- Consultants