

**Guidance and Procedures Number: 46**  
**Title: Research Conducted in International Settings**  
**Date of Last Revision: July 5, 2007**

**I. Introduction**

It is the policy of the University of California, Los Angeles (UCLA) Institutional Review Board (IRB) to assure that adequate provisions are in place for research under its jurisdiction conducted at international sites.

**II. Definitions**

- A. **Assurance:** A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).
- B. **"Engagement"** in human subjects research is defined in the U.S. Office for Human Research Protections' the U.S. Office for Human Research Protections' (OHRP) October 2008 [Guidance on Engagement of Institutions in Human Subjects Research](#).
- C. **Institutional Review Board (IRB):** A specially constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.
- D. **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.
- E. **Local Research Context:** Knowledge of the institution and community environment in which human research will be conducted.
- F. **Office for Human Research Protections (OHRP):** The office under the U.S. Department of Health and Human Services (DHHS) responsible for implementing the DHHS regulations governing human subjects research (45 CFR 46).

### **III. IRB Considerations for Approval**

The IRB will consider local research context when reviewing international studies to assure protections are in place that are appropriate to the setting in which the research will be conducted. The IRB may require an expert consultant to address issues of local research context if the IRB does not have a Committee Member with the expertise or knowledge required to adequately evaluate the research in light of local context.

The informed consent documents must be in a language understandable to the proposed participants. The IRB encourages investigators to obtain back translations of the foreign language informed consent document(s) to verify translation accuracy. The translator's credentials should be detailed in the application or written response to the IRB.

#### **A. UCLA OPRS/IRB's Responsibilities**

OPRS staff will provide the IRB Chair or the convened IRB Committee with the "International Research Checklist" for use as a guide for determining whether (1) necessary information has been provided about the local research context, (2) the consent process is appropriate to the population and procedures, and (3) adequate provisions are outlined for data and safety monitoring.

The level of local knowledge required of the IRB Chair or convened IRB is dependent on the degree of risk presented by the research.

#### **B. 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 UCLA/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. The Investigator should include the following information in his/her application to the UCLA IRB for all human subjects research in international settings:
  - a. Identify city(ies), country(ies) where research will be conducted.
  - b. Provide a scientific and ethical justification for conducting the research in an international setting.
  - c. 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 UCLA 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.).
- d. 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.
  - e. 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.
  - f. 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:
    - (1) How will you ensure women's voluntary participation in the research?
    - (2) 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.
    - (3) Explain why failure to conduct the research could deny its potential benefits to women in the host country.
    - (4) Outline the measures to be incorporated in the research protocol to respect women's autonomy to consent.
    - (5) Provide written assurance that in no case will a competent adult woman be enrolled in research solely upon the permission of another person.
  - g. 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.
  - h. 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.
  - i. 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:

- (1) 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.
- (2) 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.
- (3) 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.
- (4) Explain whether, if proven effective, the procedures will be available to some or all of the host country population. Also explain either:
  - why the research procedures (if effective) will NOT be made available to the *host country's population*, OR,
  - how the research procedures (if effective) will be made available to the *host country's population*. Please include a description of any pre-re negotiations among sponsors, host country officials, and other appropriate parties aimed at making interventions available after the research.

#### **IV. When Foreign Institution or Site IS “Engaged” in Research**

Based on UCLA’s assurance with OHRP, approval of *Federally funded* research where a foreign institution/site is “*engaged*” in research is contingent upon the following:

- (1) the foreign institution/site must hold an Assurance of compliance (FWA) with OHRP, and
- (2) local IRB/IEC review and approval must be obtained.

Approval of research is permitted if the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46.<sup>1</sup>

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<sup>1</sup> 45 CFR 46.101(h) states: When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

## A. UCLA OPRS/IRB's Responsibilities

If non-UCLA sites are involved in the research, the UCLA IRB must determine<sup>2</sup> whether or not each non-UCLA site is *engaged*<sup>3</sup> in the research. The UCLA IRB's correspondence to the investigator will identify those sites which the IRB has determined are "engaged" in the research; the correspondence may request additional information which may be required in order for the IRB to determine whether a site is "engaged."

## B. Investigator's Responsibilities

The UCLA Investigator is responsible for notifying the UCLA IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site previously "not engaged" begins consenting research participants) in order to obtain the UCLA IRB's updated determination regarding engagement.

### 1. When research is federally funded and sites are "engaged"

Performance sites which are *engaged* in federally-funded human subjects research must obtain a Federalwide Assurance (FWA) and IRB/IEC approval for their participation in the research. Information about how to obtain an FWA, and when an FWA is required is available on the OHRP website at:  
[http://www.hhs.gov/ohrp/assurances/assurances\\_index.html](http://www.hhs.gov/ohrp/assurances/assurances_index.html)

The UCLA Investigator is responsible for: (1) identifying each engaged site's FWA# to the UCLA IRB, and (2) providing written assurance to the UCLA IRB that he/she will retain copies of IRB/IEC Approval and that he/she will not initiate research at a site until he/she has obtained the site's IRB/IEC Approval.

### 2. When research is NOT federally funded and sites are "engaged"

Performance sites which are *engaged* in human subjects research which is **not** federally funded must obtain **either IRB/IEC approval or a letter of compliance**. Investigators should contact the appropriate authority at the participating site to determine whether the site has its own IRB/IEC. If the site has its own IRB/IEC, the investigator should obtain written approval for the research from the site's IRB/IEC.

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<sup>2</sup> In accordance with Section B8 of the "Terms of the Federalwide Assurance (FWA) for International (non-U.S.) Institutions" (accessed May 18, 2006 at: <http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm#sectionb>),

"When the Institution holding the FWA is either a) the primary awardee under a U.S. federal grant, contract, or cooperative agreement supporting research to which the FWA applies, or b) the coordinating center for U.S. federally-conducted or –supported research to which the FWA applies, the Institution is responsible for ensuring that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved or other U.S. federally-approved assurance for the protection of human subjects.

... For U.S. federally-conducted or –supported research covered by the FWA, the U.S. federal department or agency that conducts or supports the research retains final authority for determining which institutions are engaged in the research and need to hold an assurance for the protection of human subjects."

<sup>3</sup> See "Definitions" for additional guidance regarding "engagement".

If the site does not have its own IRB/IEC, the investigators should obtain a letter of compliance. The letter of compliance must be on letterhead from each respective agency/institution, and be signed by the institutional official who can speak on behalf of the agency/institution and provide permission for the conduct of the research at their site. A letter of compliance should indicate that the agency agrees to the performance of the research and "will abide and comply with the UCLA IRB requirements for the protection of human research subjects."

The UCLA IRB's requirements for the protection of human research subjects include compliance with the federal regulations for human subjects research (45 CFR 46), federal and state law, and university policies, as well as adherence to the details of the research protocol approved by the UCLA IRB.

### **3. Recordkeeping requirement**

The investigator is responsible for maintaining in his/her research files copies of all performance site(s)' current IRB/IEC approval notice(s), IRB-approved consent document(s), letter(s) of compliance, and/or letter(s) of permission, including approval for all protocol modifications. These materials must be received by the investigator prior to the initiation of research activities at a given site, and must be available at any time for audit by the UCLA IRB.

## **V. When Foreign Institution or Site is NOT "Engaged" in Research**

### **A. UCLA OPRS/IRB's Responsibilities**

UCLA IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site's IRB/IEC determination, or letter of cooperation, as applicable.

### **B. Investigator's Responsibilities**

1. When the foreign institution or site has an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/IEC has determined that approval is not necessary for the Investigator to conduct the proposed research at the site.
2. When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
3. It is the responsibility of the UCLA Investigator and the foreign institution or site to assure that the resources and facilities are appropriate for the nature of the research.
4. It is the responsibility of the UCLA Investigator and the foreign institution or site to notify the UCLA IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.).

## **VI. Monitoring of Approved International Research**

### **A. UCLA OPRS/IRB's Responsibilities**

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction. The IRB will require documentation of regular correspondence between the Investigator and the foreign institution or site. The IRB may require verification from sources other than the Investigator that there have been no substantial changes in the research since its last review.

### **B. Investigator's Responsibilities**

1. The Investigator is responsible for providing to the UCLA IRB any reports of correspondence with the foreign institution or site and appropriate documentation of data and safety measures throughout the course of the study, including serious and unexpected adverse events and unanticipated problems to participants or others (e.g., a breach of participant confidentiality resulting in local ramifications).
2. The Investigator is responsible for notifying the UCLA IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants).

### **Regulations:**

45 CFR 46  
21 CFR 50 & 56

### **References:**

World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. <http://www.wma.net/e/policy/b3.htm>

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.

<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>

OHRP International Issues page: <http://www.hhs.gov/ohrp/international/>

OHRP, *International Compilation of Human Subject Research Protections*.

<http://www.hhs.gov/ohrp/international/HSPCompilation.pdf>

Harvard School of Public Health, *Global Research Ethics Map*.

[http:// www.hsph.harvard.edu/hsc/gremap](http://www.hsph.harvard.edu/hsc/gremap)

Terms of the Federalwide Assurance (FWA) for International (non-U.S.) Institutions

<http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm#sectionb>

U.S. Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP), *Report of the HHS Equivalent Protections Working Group*, 2003  
<http://www.hhs.gov/ohrp/international/EPWGReport2003.pdf>

National Bioethics Advisory Commission, Rockville MD, *Ethical and Policy Issues in International Research*, 2001 Available from  
<http://www.georgetown.edu/research/nrcbl/nbac/pubs.html>.

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.  
[http://www.cioms.ch/frame\\_guidelines\\_nov\\_2002.htm](http://www.cioms.ch/frame_guidelines_nov_2002.htm)

U.S. Office for Human Research Protections' (OHRP, formerly OPRR) *Protecting Human Research Subjects Guidebook* (1993), Chapter VI, "Special Classes of Subjects".  
( [http://www.hhs.gov/ohrp/irb/irb\\_chapter6ii.htm#g12](http://www.hhs.gov/ohrp/irb/irb_chapter6ii.htm#g12)