

Wayne State University Human Investigation Committee	
Subject	International Research
Form Date	October 3, 2006 (Rev. 6/30/10)
Approvals	Office of the General Counsel 2/13/07, Steering Committee 03/12/07, Administrative Approval 03/26/07, Administrative Approval 9/30/10

Background

The conduct of human subject research in an international setting requires not only adherence to the laws, regulations, and local customs where the research takes place, but also requires mandatory compliance to the policies set forth in the Department of Health and Human Services (DHHS) (see 45 CFR 46), and the requirements of Wayne State University's (WSU) Federal Wide Assurance (FWA). All international human research must be reviewed and approved by the WSU Institutional Review Board before the project can be initiated.

The National bioethics Advisory Commission and the Declaration of Helsinki both provide guidance to investigators and institutional review boards (IRB's). Many international institutions comply with guidelines consistent with the World Medical Assembly Declaration of Helsinki. The Office of Human Research Protections (OHRP) has provided information that can be found on the following website <http://www.hhs.gov/ohrp/international/index.html#ethicalcde>. This website includes information on international issues, ethical codes, regulatory standards, and national policies and may provide valuable assistance to researchers preparing for international research.

International research has been the focus of a great deal of scrutiny in the past several years. The conduct of research by United States institutions in international settings is on the rise. In less developed countries, DHHS protections (federal regulations 45 CFR 46) are not necessarily known or understood or may differ from this HIC policy. Some local laws and regulations may be substantially different from those in the U.S. and investigators must be aware of cultural differences that are relevant to the proposed research. Investigators conducting research in an international setting, under a grant or contract from a federal agency, should consult that agency concerning any special requirements that may apply.

In addition to individual protections, export control regulations must also be observed. Export control laws are federal regulations that govern how certain information, technologies, and commodities can be transmitted to other countries and to anyone, including U.S. citizens, or to a foreign national on U.S. soil. For further information, call the Research Compliance Office at (313) 577-9064.

When research is to be carried out in less developed countries, local investigators may have limited experience with U.S. sponsored studies. Additionally, potential research participants may be unfamiliar with concepts, such as informed consent, and local institutions may not have established formal human

participant protection programs. Therefore, additional safeguards are required. This challenge is to encourage necessary research while providing clear guidance on protecting vulnerable communities and individuals against exploitation.

Scope

This HIC Policy/Procedure applies to all WSU research that will occur in an international setting. All research should be guided by the highest ethical principles embodied in the Belmont Report which include *respect, beneficence and justice*.

Definitions

Respect – acknowledges the dignity and freedom of every person. When conducting research outside the United States, the meaning of freedom or autonomy may be different depending on the culture of the potential participants. Some customs do not allow for individual rights. Care must be taken not to impose American values of individual consent on potential research participants in other countries. If the culture in question does not recognize individual rights, approval from a local leader (i.e., tribesman or community spokesman) must be obtained prior to initiating contact with potential research participants.

Beneficence – refers to the ethical obligation to maximize benefits and to minimize harm. This principle gives rise to norms requiring that (1) the risks of research be reasonable in the light of the expected benefit(s), (2) the research design is sound, and (3) the investigators are competent both to conduct the research and to safeguard the welfare of the research participants. Special attention must be made to the local culture and acceptable norms.

Justice – refers to the ethical obligation to treat each person in accordance with what is morally right and proper; to give each person what is due to him or her. In the ethics of research involving human participants, the principle refers primarily to “distributive justice”, which requires the equitable distribution of both the burdens and the benefits of participation in research. Differences in distribution of burdens and benefits are justifiable only if they are based on morally relevant distinctions between persons; one such distinction is *vulnerability*.

Vulnerability – refers to a substantial incapacity to protect ones’ own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group. Accordingly, special provision must be made for the protection of the rights and welfare of vulnerable persons.

HIC Procedures

Review and approval of international research requires special considerations. The HIC Chair will conduct a pre-review of all international protocols in consultation with the Assistant Vice President for Research prior to the regular IRB review process.

Review of international research, regardless of whether it requires full board review, or meets the criteria for an expedited review, will evaluate the following as part of the review process:

- Confirmation of the qualifications of the investigator(s) and research staff for conducting research in the respective countries.
- Ensure that there is initial review, continuing review, and review of modifications in accordance with WSU policies and procedures.
- Ensure that post-approval monitoring is conducted in accordance with WSU policies and procedures.
- Ensure that complaints, non-compliance and unanticipated problems involving risk to participants or others are handled in accordance with WSU policies and procedures.

Required documents for International Research

The following must be included when submitting international research studies for consideration:

1. Medical/Behavioral Protocol Summary Form with Appendix A (International Research)
2. Local Review and Approval from the international site
3. Letter of Support/Permission from the international site
4. Informed consent/assent written both in English and in the native language of the proposed research site.
5. Questionnaires/surveys that will be administered to potential participants, written both in English and in the native language of the proposed research site.
6. For research being conducted by a VA investigator, a waiver must be obtained from the Chief Research and Development Officer

Local Review and Approval in the International Setting

To protect potential participants, when conducting research in an international setting, it is extremely important to ensure that the proposed research is acceptable within the ethical standards of the "local" community.

An IRB or equivalent body in the country, province, town, or village where the proposed research will take place should review the proposal. This IRB or equivalent body should be comprised of

- at least five (5) members,
- at least one of those members should be a representative from the community where the potential participants will be found.
- There should also be a non-scientist on the review committee.

If the local IRB or equivalent body has a Federal Wide Assurance (FWA) from DHHS, they are deemed to be in compliance with the Common Rule (45 CFR 46); therefore, the investigator does not need to provide information on the specific membership characteristics of the local IRB to the HIC.

If local review has been conducted, a copy of the approval letter/notice should be included with the HIC application. If the local IRB or its equivalent body does not have an FWA from DHHS, qualifications of the review committee must accompany the submission.

There are countries in which a local review board or government review is not available. In such cases, the HIC requires documentation of approval from local experts or community leaders. This individual(s) providing approval must be familiar with the cultural background, local context, and community attitudes of the country in which the research will be conducted and should not be associated with the conduct of the proposed research.

For Social Science research, [including research sponsored by the Department of Defense, (DoD)] if a local IRB does not exist or does not review such research, then review by the WSU IRB will suffice. The researcher, however, must document (1) the lack of local IRB review and (2) plans for observing local ethical standards.

For research sponsored by the DoD, WSU or the PI must have documented permission to conduct research in the country by certification or local ethics review; the investigator must follow all local laws, regulations, customs, and practices.

Letters of Support/Permission

In accordance with local laws or customs, a letter of support or permission from each site where the research is being conducted must accompany the protocol submission to the WSU IRB. Letters of support/permission may be obtained from the following:

- Local community leaders
- State officials
- Heads of households
- Clinic or other health facility officials, and/or
- Representatives from other sites where the research is to be conducted

Informed Consent/Assent

It is presumed that written informed consent is required for international research. Requests for waiver of written consent or for the use of an oral consent process may be permitted if the protocol has received local IRB approval or other approval. A local consultant (expert on culture) may be needed to determine an appropriate informed consent process. However, the HIC reserves the right to make the final decision whether to allow an informed consent process other than written informed consent.

The WSU IRB cannot impose its standards for written documentation on other cultures, but will enforce standards for ethical conduct of research and a meaningful consent process according to the standards of the local culture. When use of a formal informed consent form has been waived, full disclosure to participants is required; i.e., all information as specified in the federal regulations and by WSU policy. A written statement containing the content of this disclosure should accompany the research application.

Special attention should be given to local customs and to local cultural and religious norms when drafting written informed consent documents or when proposing alternative consent formats. The HIC requires consent forms (or oral consent scripts) to be written at a level that will be understood by the study participants.

*For studies that are **no more than minimal risk***, when English is not the study participant's language, all informed consent/assent documents submitted to the HIC must include the original English version and a translation done in the participant's language.

*For studies that are **greater than minimal risk***, when English is not the study participant's language, all informed consent/assent documents submitted to the HIC must include the original English version, a translation done in the participant's language, and a back translation into English done by someone fluent in both languages and independent of the research with any analyses done when the versions are compared. If using a *certified translator*, a back translation is not required. This assures the HIC that the information in the translated versions of the informed consent documents is the same as the English version.

If the participant is unable to read, then a Short Form consent/assent version with the above translations should be submitted, with a summary of the research in both languages.

Informed consent/assent form templates, including the Short Form consent, are available on the WSU HIC website.

Additional Considerations

Avoidance of coercion – When international research is planned, every effort must be taken to ensure that participation is truly voluntary and that there is no potential for coercion. When making payments in goods, local currency, or services, the amount of the payment should be explained on the HIC application in terms of U.S. currency standards as well as the local economic standards. For example, if a person is to be paid in goods that far surpass anything that would be commonly available to that participant, that could be interpreted as coercion to participate in the study. Similarly, if the amount of local money that is paid to the participant is out of proportion to their normal income, the same holds true. (See HIC Policy/Procedure “Compensation for Research Participation” for additional guidance.)

Safety plan – There must be a safety plan in place if the research is to take place in an area of the world that is politically unstable or where the safety and well being of the participant, PI and his/her research staff, or the research data may be in jeopardy. The safety plan may include documented permission from the local authorities to conduct the study.

Institutional review and oversight – The PI should recognize that WSU IRB review of an international research project may be a lengthy process. In certain instances, review by institutional officials as well as IRB review will be required. It is advisable that the researcher consult the HIC early in the planning stages of the proposed research.

Training in Protection of Human Participants in Research – As with all research conducted through WSU, mandatory online CITI training must be completed. This includes all key personnel from the proposed international site who may be involved in the conduct of the research. Training for the international members of the research team can be done via a local program, if available, or (if accessible) they can log on directly to the CITI website and with the assistance of a translator complete the required training. Verification of the content of the training, as well as satisfactory completion of the training must be submitted prior to HIC approval. NOTE: This training is in addition to any specific research protocol instructions that the investigator may provide to research personnel recruited from the local research site(s).

For research sponsored by the DoD – The investigator must follow all local laws, regulations, customs, and practices.