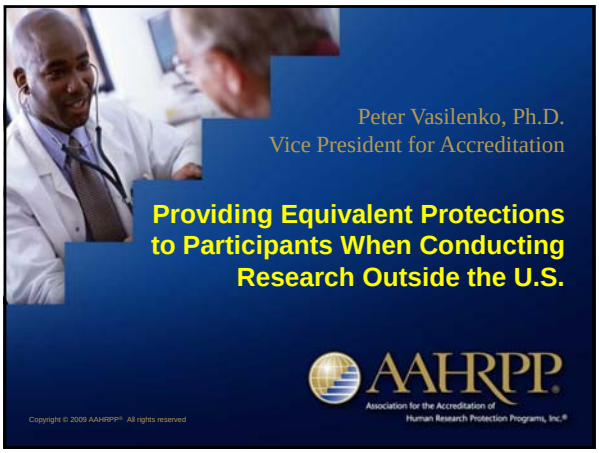


Peter Vasilenko, Ph.D.
Vice President for Accreditation

Providing Equivalent Protections to Participants When Conducting Research Outside the U.S.

AAHRPP
Association for the Accreditation of Human Research Protection Programs, Inc.®

Agenda

- Regulations and Guidance on International Research
- AAHRPP's goal and Standard
- Definition of Equivalent
- Exempt research
- Local research context
- Informed consent
- Research involving children
- Student research
- Clinical Trials
- IRB Considerations, Revisions, Continuing Review and Post-Approval Monitoring
- AAHRPP Expectations

OHRP and International Research

- Applies to DHHS funded research (unless box is unchecked).
- …that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy…
- This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.
- Knowledge of local research context.
- International Compilation of Human Research Protections (2010).

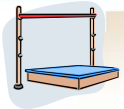
FDA Regulations in International Research

- Applies only to FDA regulated products (drugs and devices).
- Sponsors must follow FDA regulations.
- International sites musts follow ICH-GCP (or FDA).
  - Investigators
  - IRBs or ECs

Other International Guidelines

- International Conference on Harmonization – Good Clinical Practice (E6)
- The Declaration of Helsinki
- International Ethical guidelines for biomedical Research involving Human Subjects (CIOMS)

AAHRPP's Goal



- To raise the bar on international research:
  - Thoughtful, equivalent standards.
  - Based on knowledge of local context.
- Do not over-regulate just because the study is international:
  - Awareness of local laws, customs.
  - Use of flexibility (e.g. waivers).

STANDARD 1-3: The Organization's transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the Organization's principal location while complying with local laws and taking into account cultural context.

Standard I-3 Outcomes

- Researchers provide the same or equivalent protections to human participants in research conducted in other countries.
- When conducting transnational research, Researchers are aware of local laws and cultural context in all locations where the research is conducted and comply with local laws and adhere to cultural norms.
- When reviewing transnational research, IRBs or ECs ensure that equivalent protections are provided to research participants enrolled in research in other countries.
- IRBs or ECs make determinations and decisions based on laws and knowledge of the country in which the research will be conducted.

Equivalent

- Dictionary definition:
  - equal in force, amount, or value; equal in area or volume but not super imposable <a square equivalent to a triangle>
  - like in signification or import**:** having logical equivalence <equivalent statements>
  - corresponding or virtually identical especially in effect or function.
  - having the same solution set <equivalent equations>**:** capable of being placed in one-to-one correspondence <equivalent sets.

Equivalent Protections

- Not necessarily the same.
- But equal in function or effect.
  - The protection of participants in research.
- Respects the autonomy and dignity of all persons.
- Encompasses the principles of respect for persons, beneficence and justice.

Discussion Question

- A physician from the US volunteers in another country's hospital every summer. She wants to bring to that hospital and implement some "best practices" to handle drugs to eliminate medical errors in dispensing and dosing, which are routinely used in US hospitals. She plans on collecting chart data and effectiveness of the practices and presenting and possibly publishing the results.
- The physician asks the US IRB if she needs to submit the project. What should the IRB do?

Exempt Research in International Studies

- Just because a study is being performed in another country, does not automatically exclude it from consideration that it may be exempt.
- A great deal of research in the social and behavioral sciences poses minimal risks to participants and may qualify for exemption, depending upon institutional policy.

Exempt Research in International Studies

- If a proposed study qualifies for exemption, the regulations do not require review at the foreign site where it will be conducted. However, the IRB must determine that the study would qualify for exemption in the country in which it will take place.
- Through consultation with experts, the IRB must ensure that the risk assessment holds true at the foreign site, and that there are no other factors that would disqualify the project from exemption. Thus, knowledge of local context is important even in research which may be exempt.
- Even in exempt research, informed consent, parental permission or child assent may still be ethically appropriate, and/or required under local law.

Discussion Question

- A US researcher plans to conduct education research in two poor schools in Managua, Nicaragua. He wants to compare the success of two first grade (learning-to-read) books, one which is already in use in one school, and the other in use in the second school. He will obtain student reading records at the end of the school year. The researcher applies for an exemption at his home US IRB.
- What should the IRB consider and decide?

Local Research Context

- Researchers must have sufficient knowledge of the local research context to be able to design and carry out research in a way that protects the rights and welfare of the participants and produce viable results.
- The local research context might influence every aspect of the research design.
- The Researcher should demonstrate his or her knowledge of the local context to the IRB, educate IRB members when appropriate, and work with them to resolve issues.
- The IRB, either through its own expertise, consultants, or communication with a local IRB or EC, should become aware of the local context issues relevant to that research project.

Local Research Context

- Laws
- Regulations
- Customs
- Socio-economic factors
- Political factors
- Cultural factors
- Language and literacy

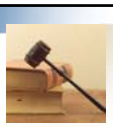
Discussion Questions

- A US graduate student proposes a study in her home Islamic country interviewing wives about feminist issues in their country.
- A US graduate student proposes a study in Iran, his home country, interviewing students about Iran's nuclear program.
- What are the important issues that the researcher and the IRB should know?

Risk

- Research methods that have virtually no risk in the US might have risk when conducted in other countries.
- Questions that may be innocuous in the US could be offensive elsewhere.
- Breach of confidentiality may have dangerous consequences.
- Assuring and maintaining confidentially in other countries may be difficult.
- Danger to the Researcher.

Local Laws or Regulations



- Does the country have laws or guidance related to the protection of human participants?
- Are there other country laws which must be followed and factored into the research?
- What approvals are needed for the research?
  - Biomedical:
    - Ethics committees.
    - Drug approval agency.
  - Behavioral Social Science:
    - Most likely there is not an IRB or EC for social science research.
    - Ministry, local governance approval.

AAHRPP

Local Research Context

- Researchers may need to
  - If not already knowledgeable, become knowledgeable in the local context issues relevant to their research.
  - Consult with community leaders and stake holders who may be able to provide important insights about the local research context, including information about local customs, norms, and laws.
  - Communicate and coordinate with local IRBs or ECs as well as work with their home IRB.
  - Develop local collaborative relationships to assist in the approval, design, and conduct of the research.

AAHRPP

Local Approval and Individual Consent

- Different cultures have different authority structures for approval and consent.
  - Should be honored.
  - May test your views on autonomy.
  - May be coercive.
  - May present ethical and logistical challenges.
  - Real or perceived conflict with US regulations.

AAHRPP

Local Research Context Examples

- An ethnographer conducting research in a village in Northern Togo needed clearance, first, from the Togolese government's Ministère de la Recherche Scientifique; then, from the Préfet of the canton in northern Togo; then, from the Chef (chief) du Canton, the Chef du Village, and the Chef du Quartier. Then the researcher secured the consent of the participants.
- In Israel, the Spokesperson's Unit of the Ministry of Defense must process all requests to interview Israeli soldiers.

Source: CITI Training Module

AAHRPP

Informed Consent

- The investigator must design a consent process that honors local custom.
- However, another individual's permission should not substitute for an participant's voluntary informed consent unless that consent process has been waived by an IRB or equivalent local ethics committee.

AAHRPP

Required Elements of Disclosure

- A statement that the study involves research
- The purposes of the research
- The expected duration of the subject's participation
- Procedures, including the identification of any procedures which are experimental
- Reasonably foreseeable risks, if any
- Potential benefits, if any, to participants
- Alterative procedures, if any
- Confidentiality of records
- Compensation for research-related injury
- Contact information for answers to questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the participant
- A statement that participation is voluntary

AAHRPP

Explanation of Research

- Should be provided in a context understandable to people in that culture
- Say you are growing corn in two fields. Example 1: On one field you put manure, on the other nothing. After harvest, you compare your yield. This is like comparing a person who is getting medicine with one who is not (placebo)…
  - example developed by Professor Paul Ndeble - Malawi

Contact Information

- It might be appropriate to have a local contact identified by the investigator in consultation with the community and the IRB.
- Contact should be fluent in the appropriate languages.
- Is putting an e-mail or phone number in the consent document realistic?

Language Issues

- Consent is best obtained using the language that is most familiar to the prospective participant.
- Some languages are not written.
- Sometimes, people speak a language but not be able to read or write it.
- There might not be any translations of important words like “placebo” or “randomization.”
- Copies of the translated consent documents and instruments, including verification of the accuracy of the translations.

Interpreters

- Ideally, the researcher or research team is fluent in the local language.
- If not, the investigator might seek collaborators or hire assistants who are fluent.
- A third option is to hire interpreters.
  - In a small population, the relationship between the interpreter and the participants must be considered.
  - The interpreter mighty exert undue pressure or influence, selection bias.
  - Interpreter might not relay information in a clear and unbiased manner. E.g. leave out information they believe is unpleasant or culturally inappropriate.
- In addition to the consent process, fluent researchers or interpreters should be available to answer questions, address complaints, or relay instructions throughout the conduct of the study.

Discussion Question

- A research study in a rural town in Cambodia involves educating people about sexually transmitted diseases. The researcher is using an approved consent document in the native dialect. A potential participant say he is happy to participate, but will not sign any documents.
- What does the researcher do?

Documentation of Consent

- Illiterate
- May be culturally inappropriate to ask for a signature
- Legalistic
- Government
- Something to be feared – giving up rights
- Indicate lack of trust

Alternate Consent Procedures

- Use of short form and witness.
- Use of pictures, video, computers.
- Alternate forms of documentation (e.g. thumbprints).

Waiver of Documentation of Consent

- **The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.**
- **The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality**

International Research involving Children

- What is the age of majority?
- What is the relationship between parents and their children in that country?
- What is an acceptable and effective parental permission process?
- What is an acceptable and effective child assent process?
- Are there laws pertaining to orphans?

Discussion Question

- A US researcher proposes a study in an African country interviewing 16-17 year olds living on the streets.
- What are the important issues that the researcher and the IRB should know?

Discussion Question

- A US researcher proposes a study in an African country on using computers to provide AIDS information to 10-15 year olds with HIV. The family receives 2 days of food staples for the child's participation. They request a waiver of child assent, saying that in this culture the child would never go against the parents wishes and it would be dangerous for the child to do so.
- What does the IRB need to know and what should it do?

Who should review?

- US IRB only:
  - Paternalism.
  - Local IRB does not
- Local IRB only:
  - US IRB would rely on local IRB.
  - Does the IRB meet AAHRPP standards.
- Both US and Local IRB review:
  - Communication.
  - Resolve differences.

•Our regulations are better
•Our committee is better
•We care more about participants
•We know what we are doing
•We know what is best for you
•We have to be in control

Communication and Coordination with Local IRBs or ECs

US IRB

- Oversight of their investigator and grant/contract.
- Accredited.
- May have international resources available.
- Often paternalistic.
- Lack of local context.
- Lack of communication.

Local IRB

- Might not be as rigorous.
- Might have different ethical viewpoints.
- It is their country/organization.
- Growing in sophistication.
- Expertise in local context.
- E-mail, international phones, use of Internet.

AAHRPP

Discussion Question

- A researcher in Malawi is studying malaria in children. If a child dies, the consent process includes permission for an autopsy. The autopsy includes the removal and examination of the eyes, an essential issue in malarial research. The US IRB want the removal of eyes in the consent, but the Malawi EC does not, because they see this as important research for their community and parents might not want to participate because stealing eyes is associated with witches.
- What should the US IRB do?

AAHRPP

Western Values vs. Local Country Values

- Signed consent.
- Literate or educated vs. Illiterate or uneducated.
- Individual vs. group.
- Autonomy of the individual.
- Dangerous or inappropriate questions.
- Beliefs (e.g. witches).

AAHRPP

Student Research Abroad

- Require knowledge of the country.
- Oversight from advisor.
  - Frequent communication.
    - Phone
    - E-mail

AAHRPP

Clinical Trials

- Standard of care.
- Providing medical care:
  - Coercion.
  - Therapeutic misconception.
- After the study is over.

AAHRPP

Additional Information to Provide the IRB for International Research

- Information about where the research will be conducted (location/performance site).
- Information about the investigator's knowledge of the local research context, including the current social, economic, and political conditions.
- Whether local IRB or EC approval is available and required.
- What country or local approvals are needed.
- Whether there are any additional risks subjects might face as a result of the population being studied and/or the local research context. How the risks will be minimized.
- The language(s) in which consent will be sought from subjects and the research will be conducted, as well as whether the investigator is fluent in this language, or whether a interpreter will be used. Copies of the translated informed consent documents and instruments, including verification of the accuracy of the translation(s).
- Information on how the investigator will communicate with the IRB while in the field.
- If a student, information on how the advisor will communicate with the student and oversee the research.

42 AAHRPP

IRB Considerations

- The investigator may present, and the IRB approve contingencies:
  - Although signed consent is submitted there is a possibility some people are illiterate.
  - For cultural or political reasons, someone may agree to be in the study but refuse to sign the consent form.
  - Consent in several languages or dialects.
  - Pool of interview questions.

Continuing Review

- The local IRB or EC may not conduct continuing reviews.
- The US IRB should conduct continuing review:
  - Changes that were made.
  - Changes that need to be made.
  - Consent issues.
  - Problems and solutions.

Revisions to Research

- Allow researcher to make minor revisions in the field and inform the IRB afterwards.
- Communication with the IRB:
  - E-mail
  - Internet
  - International cell phones

Post-Approval Monitoring of International Research

- Continuing review.
- Communication with local IRB or EC.
- Remote audits.
- On-site audits.
- A post-approval monitoring program should be commensurate with the size of the Organization's international research program.

Discussion Question

- A major university has a 5-year old ongoing collaborative research program in an African county, which includes investigator initiated disease-specific research, intervention trials, as well as minimal risk behavioral and educational research. The program involves several university faculty and foundation grants.
- What type and amount of post-approval monitoring processes are appropriate for this research program.

AAHRPP Expectations for International Research - 1

- Policies and procedures for reviewing international research:
  - Ensuring appropriate expertise and knowledge through IRB membership or consultants.
  - Confirming the qualifications of the researchers and research staff.
  - Initial review, continuing review, and review of modifications
  - Post-approval monitoring

AAHRPP Expectations for International Research - 2

- Policies and procedures for reviewing international research:
  - Knowledge of local laws
  - Consent process and other language issues.
  - Handling of complaints, non-compliance, and unanticipated problems involving risk to participants or others.
  - Communication and coordination with local IRBs or ECs when appropriate.

AAHRPP Expectations for International Research - 3

- All policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate...
- …with modifications appropriate based on local law, culture and customs.

AAHRPP Expectations for International Research - 4

- Site visits will include
  - Reviewing records for international projects
    - Full board, expedited, and exempt
    - Bio-medical and social science
  - Interviewing researchers and research staff that are involved in international research
  - Interviewing IRB members and staff about reviewing international research.

AAHRPP Expectations for International Research - 4

- Record review will look for documentation of:
  - Knowledge of local context
  - Consideration, discussion, and determinations for relevant international issues.
  - Translations of consent forms
  - Documentation of approval from local IRBs or ECs as appropriate.
  - Communications with local IRBs or ECs as appropriate.

Discussion Questions from Audience