Marshfield Clinic

IRB Review of Transnational Research

1. SCOPE

1.1. System Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1. Transnational Research (TNR)

- Research in which an investigator is engaged that takes place outside the borders of the USA or its territories.
- Engagement in TNR occurs when a researcher:
  - ◊ directly interacts with an international participant, or their identifiable data for research purposes; or
  - ◊ is responsible for the conduct of the research at an international site
- TNR does not refer to medical tourism, or to a TN study for which Marshfield Clinic or one of its employees simply provides a service.

3. RESOURCE GUIDE BODY

3.1. Background

- Transnational research has provided clinical research with some of its finest ethical moments (e.g. Walter Reed is credited with pioneering the use of informed consent in the early 1900s while conducting studies on the origin of yellow fever in the Caribbean). Unfortunately, there are even more examples of ethically controversial transnational research (e.g. studies on the treatment of HIV/AIDS in sub-Saharan Africa over the last several decades have been described as exploitative). In recent years, transnational clinical research (TNR) has been on the rise. One suspected reason for this rise is that overseas nations have fewer (poorly enforced) regulations, and therefore human subjects research can be conducted there with fewer costs and less "red tape."
- The Office for Human Research Protection (OHRP) within the Department of Health and Human Services (DHHS) has established guidelines to help ensure that foreign nationals who participate in TNR are provided "equivalent protections" to those that apply to participate in stateside trials. This guidance emphasizes the importance of IRB review, a risk/benefit assessment of the research, and voluntary informed consent of subjects in an effort to ensure a standard of protections equivalent to those mandated by 45 CFR 46 is in place for TNR studies at all IRB approved sites.

  Since the original formulation of these OHRP guidelines, researchers have noted that some of the elements are tedious and "of dubious value" to the protection of human subjects. They have advocated for adoption of international research ethics standards which would govern the conduct of research by all signatory members. Such an international standard has been drafted but not widely

adopted. The Council for International Organizations of Medical Sciences (CIOMS) has published the *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, and the OHRP has compiled and regularly updates an *International Compilation of Human Research Standards*. These standards enumerate over 1,000 laws, regulations, and guidelines that govern human subjects research in 104 countries, as well as the standards from a number of international and regional organizations. This Compilation was developed for use by researchers, IRBs/Research Ethics Committees, sponsors, and others who are involved in human subject research around the world. To date, many of the world's developing countries have yet to adopt these standards.

3.2. Guidance

IRB oversight is necessary before an employee of Marshfield Clinic (or an institution for which MCRF IRB is the IRB of record) becomes engaged in TNR.

MCRF responsibility is limited to review of the local researcher's participation in the TNR, unless the researcher is PI of the TNR, or if the MCRF IRB is the IRB of record for the entire investigation. In such cases, MCRF IRB will offer equivalent protections to the participants in the TNR as would be afforded to local research participants. MCRF IRB will apply all policies and procedures relevant to domestic research to the TNR, including but not limited to, initial and continuing review, review of modifications, the handling of complaints, non-compliance and unanticipated problems, and requirements for Federal-Wide Assurance (FWA) for federally sponsored research.

Additional responsibilities specific to TNR for which the PI and the MCRF IRB (as the coordinating IRB) will be responsible shall include (as appropriate):

- ◊ Ensuring that the project undergoes an evaluation by a host-country ethics boards, or equivalent, if at all possible, and that the results of the review are communicated to MCRF's IRB. If an IRB or EC is not available, it would be advisable to utilize local contacts for advice regarding an appropriate review mechanism: perhaps the national ministry of health, or the local university (if one exists), etc. Information regarding the cultural context can be obtained from several sources, including expatriated Americans living in the country, World Health Organization (WHO), etc.
- ◊ Gaining and maintaining familiarity with the country's customs, laws, and culture. This may be accomplished by appointing an individual with such knowledge to the Board, or by obtaining a consultant to assist the Board in keeping current on these issues. OHRP's *International Compilation of Human Research Standards* may also be consulted to gain this knowledge.
- ◊ Ensuring research staff is qualified to conduct research in the proposed country, and that the conduct of the TNR at the proposed site is justified.
- ◊ Ensuring that any unique consent process or language issues are adequately addressed.
- ◊ Ensuring mechanisms for post-approval monitoring are established, when deemed necessary by the IRB.

Principal Investigator (PI) or coordinating researcher responsibilities unique to TNR may include:

- ◊ Providing the IRB with contact information for on-site study personnel.
- ◊ Justifying the conduct of the research at transnational sites, and specifically why a particular location was selected to conduct the research.
- ◊ The researcher (and in turn, the IRB) must be able to demonstrate that they are familiar with and sensitive to the cultural, economic, and/or political conditions in the host country which would alter the risk of harm to participants compared to the same project conducted within the USA.
- ◊ If a language (or other communication) barrier exists, the researcher should describe strategies for overcoming it. This should specifically address Informed Consent.
- ◊ A plan for culturally appropriate post-approval monitoring must be in place.

Note that HIPAA regulations do not apply to TNR unless PHI collected on a foreign subject is being sent to and stored in the USA.

4. ADDITIONAL RESOURCES

4.1. References:

- *Protection of Human Subjects: Interpretation of Assurance Requirements*, DHHS: 71 Fed Reg 10511 (July 7, 2006); http://www.gpo.gov/fdsys/pkg/FR-2006-07-07/html/E6-10511.htm
- DHHS, OHRP, *International Compilation of Human Research Standards* (2013 Edition); http://www.hhs.gov/ohrp/international/intlcompilation/intlcomp2013.pdf.pdf
- International Ethical Guidelines for Biomedical Research Involving Human Subjects Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), Geneva, 2002, http://www.cioms.ch/publications/layout_guide2002.pdf

4.2. Supporting documents available:

- None.

5. DOCUMENT HISTORY

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2.0	
3.0	

6. DOCUMENT PROPERTIES

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