Michigan State University
Human Research Protection Program

Subject: Special Considerations

Sub-Topic: Multiple Research Sites

Section: 6-9-F  This policy and procedure supersedes those previously drafted.

Approved by: Vice President of Research and Graduate Studies, 4-4-2007. Revision 1 approved by VP Research & Graduate Studies on 3-9-2008. Revision 2 approved by VP Research & Graduate Studies on 7-22-2011.

Related Sections: 1-3, 2-2-A, 6-7, 11-1-A

This policy applies to human subject research conducted at external sites, which are considered to be locations external to Michigan State University (MSU) (e.g., not on MSU campus, not within an MSU facility, location not under the jurisdiction or control of MSU). There are different requirements based on whether the external site or its employees are engaged in the human subject research conducted by an MSU investigator. The Institutional Review Board (IRB) staff, IRB member, or IRB chair determine whether an external site is engaged in the research using the U.S. Office for Human Research Protection (OHRP) guidance, “Engagement in Research.”

MSU investigators conducting research at external sites that are not considered engaged may be required by the IRB to provide information to the IRB about communication with the site (e.g., letter of permission, contact information), when appropriate.

When an MSU investigator plans to conduct human subject research at an external site(s) that is engaged in the research, communication with the engaged external site(s) is important for the protection of human research subjects. The investigator must provide sufficient information to the IRB about the engaged external sites to enable this communication.

The following are the human subject responsibilities of MSU Principal Investigators (PI) with engaged external sites:

1. Obtain IRB approval from MSU (unless appropriate reliance arrangements are made).
   a. Provide a list of sites external to MSU where research may be performed, e.g., name of hospital, school, or business.
   b. Provide contact information for the PI or administrator at each site (e.g., name, email, telephone) as requested.
   c. Obtain permission to allow research to be conducted at each site as appropriate (e.g., hospital impact statements).
2. Ensure IRB review is obtained at engaged external sites unless appropriate reliance arrangements are made.
   a. When the site has an OHRP Federal Wide Assurance (FWA):
      i. If the local IRB will review the research study, provide MSU IRB with an approval letter(s) from that site, or
      ii. If the institution chooses to rely on the MSU IRB for review, there must be a fully executed Institutional Authorization Agreement. See the Human Research Protection Program (HRPP) Manual 1-3 “Institutional Authorization Agreements” for requirements.
   b. When the site does not have an FWA:
      i. When an MSU investigator works with an external engaged site on a single research study and there is no expectation for that site to do research again or the research is not federally funded or does not otherwise require an FWA, the MSU IRB will work with the MSU investigator to obtain Individual Investigator Agreements for individuals engaged in the research at the external institution. Investigators do not have signatory authority to sign the agreements for MSU. IRB staff will complete this type of agreement if necessary to be signed by the individual who is engaged in research. Contact the IRB staff for more information.
      ii. When an MSU investigator works with an external engaged site on a research study and there is an expectation for that site to do research again and the research is federally funded or otherwise requires an FWA, the site must obtain an FWA.

3. Ensure all investigators and research staff at all sites have required human subjects training and other training as needed. See HRPP Manual 11-1-A “Education: Investigators and Research Staff” for requirements.

4. When appropriate, develop a data safety monitoring plan. See HRPP Manual 6-7 “Data and Safety Monitoring” for requirements.

5. If human tissue, fluid, or cells are transferred to the central site:
   a. Arrange for Material Transfer Agreements.
   b. Arrange for secure and appropriate transport.
   c. Arrange for storage and security.
   d. Develop a confidentiality plan to protect identifiers.

6. If medical records are accessed at performance sites:
   a. Develop an approved HIPAA Authorization Form or obtain Waiver of Authorization.
   b. Work with performance sites to ensure authorization or waiver.

7. Develop plans for data security at all sites.
   a. Physical materials – locked file cabinets, limited access, etc.
   b. Electronic data – passwords, encryption, firewalls, access, etc.
8. Develop a plan for secure data transfer from performance sites to central site.
   a. Transfers of physical materials.
   b. Transfer of electronic data and files.

9. Develop a plan for a secure central database.
   a. Secure data transmission or transportation.
   c. Limited access to identifiable data.
   d. Who has access to data for research purposes and in what form. (e.g., anonymous).

10. Develop a communication plan with all research sites.
    a. Develop a mechanism of reporting and responding to, unanticipated problems, adverse events, and complaints from all sites.
    b. Develop a mechanism of coordinating information and applications for all revision and continuing review applications at all involved IRBs.

11. Develop a management plan with all research sites
    a. Develop plan for management of information that is relevant to protection of subjects, such as interim results.

The IRB staff is responsible for communicating with the engaged external sites in order to:

1. Fulfill requirements stipulated in the formal reliance agreement / memorandum of understanding with the external IRB, e.g., provide copies of relevant IRB determinations regarding approval, continuing review including protocol modifications, interim results, unanticipated problems involving risks to subjects or others, suspensions, terminations, closure, required modifications, reports to government agencies, etc.

The IRB chair or designee is responsible for communicating with the engaged external sites, investigators, and/or IRBs, in order to:

1. Obtain information regarding reports of unanticipated problems, noncompliance, termination or suspension, and emergency use of investigational drugs or devices.

2. Coordinate corrective action plans as necessary.

3. Fulfill any other activity necessary to protect research subjects.

The IRB is responsible for evaluating the communication and management plan, in order to determine whether the plan proposed by the investigator is adequate.
When MSU is a site in a multi-site protocol, but not the lead or coordinating site, the MSU investigators must provide the following information to the MSU IRB:

1. An initial MSU IRB application for the research study.

2. The complete protocol and IRB approval letter from the lead IRB.

3. The portion of the protocol with which the MSU investigators are involved. The MSU IRB will predominantly review the aspects of the protocol with which the MSU investigators are involved, given that the complete protocol has been reviewed and approved by the lead IRB.

4. The MSU PI will provide the MSU IRB with renewal applications, research study information, and provide renewal approval letters from the lead IRB.

5. If subjects are recruited at MSU sites, site specific consent forms, approved by the MSU IRB, are required.

6. The MSU PI is responsible for getting changes that are made at MSU approved by the lead IRB.

**Additional Requirements for Community Research IRB (CRIRB)**

After initial approval of a CRIRB research study, the complete application and documentation package will be forwarded to the IRB(s) for the institution(s) at which the research study is being conducted. Each member representative at the institutions will evaluate the research study and will either allow or not allow the research to be conducted at their institution. This decision will be communicated to CRIRB by returning a signed concurrence agreement via facsimile or email. Investigators may begin gathering data from human subjects only after receiving a signed approval letter from the chair of CRIRB and subsequent concurrence by the designated individual at each performance site. All approvals of renewals and revisions will be sent to the IRB chairs at the performance sites.

**Additional Considerations**

For research studies subject to the requirements of the U.S. Department of Defense, see HRPP Manual 2-2-A “U.S. Department of Defense.”