



Institutional Review Board

University of Missouri-Columbia

Standard Operating Procedure

Off -Site Research

## Off -Site Research

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## 1.0 Purpose

To describe the procedures for coordination of Institutional Review Board (IRB) research review and oversight for University of Missouri (UMC) research involving human subjects conducted at off-site locations or at multiple sites.

## 2.0 Scope

### GENERAL DESCRIPTION

Off-site research activities are subject to special procedures for coordination of research review and may involve more than one IRB responsible for research oversight. In these cases, UMC has established additional procedures to define the responsibilities of each IRB, coordinate communication among responsible IRB committees, and manage information obtained in off-site or multi-site research to ensure protection of human subjects. In coordinating off-site research reviews, the IRB staff, in consultation with the Assistant Vice Chancellor for Research and UMC Legal Counsel, if needed take into consideration the source of funding for the research activity, federal regulations, specific sponsor regulations governing human research protections, and institutional policy.

The UMC IRB requires additional information and documentation for research that meets the definition of off-site research. Institutional policies apply to all off-site research involving human subjects regardless of funding source including all non-externally funded off-site research involving human subjects such as educational and other survey research.

In addition, UMC may enter into formal agreements with other facilities which are not legal entities of UMC to provide research review (i.e., to act as the relied-upon IRB), to rely on other institutions for research review, or to cooperate in review. UMC enters into these types of arrangements through a Memorandum of Understanding, IRB Authorization Agreement, or contract with the institution(s) in question.

### **3.0 Policy/Procedure**

#### **PROCEDURES**

##### *Types of Off-Site Research and Associated Requirements*

##### Research Involving Non-UMC Performance Sites: Cooperative Research

1. The PI must address the following information at the off site institution:
  - Agreement of the facility's administration for the investigator to conduct the study at that site;
  - Review of the project by facility personnel with respect to issues of appropriateness for its human subjects population and adequacy to perform the research procedures as approved by the UMC IRB (i.e., the facility has the appropriate equipment and personnel to conduct the research and/or store and dispense investigational drugs in a manner reviewed and approved by the UMC IRB);
  - If applicable, assurance that personnel from the facility who collect data are responsible for implementing the research following IRB approved procedures. The facility administrator is responsible for including written confirmation that facility personnel have the appropriate expertise to carry out the research procedures as reviewed and approved by the UMC IRB; and
  - If applicable, assurance that personnel from the facility who collect data have appropriate training in the protection of human subjects.

2. For cooperative research projects, it is determined whether an off-site facility is “engaged” in research according to the guidance outlined in the Office for Human Research Protections (OHRP) Engagement Memo by considering the nature of the involvement of off-site personnel in implementing research procedures and/or collecting data at the site.
3. If the off-site non-UMC facility is “engaged” in research, it is determined whether the off-site facility requires an assurance mechanism. (See the section on *Negotiation of Federal Assurances for Collaborating Institutions* for details.)
4. A cooperative research site “engaged” in research which has its own non-UMC IRB is responsible for conducting the research review for that site and providing the PI with appropriate documentation to submit to the UMC IRB. This documentation includes the Federalwide Assurance (FWA) number for all federally funded research and the non-UMC IRB approval letter.
5. A cooperative research site that is “engaged” in research and which does not have its own IRB may need to establish one (or contract with a “for-hire” IRB) prior to its participation in the research. The cooperative site should register its IRB with the OHRP/Food and Drug Administration (FDA) as instructed by those agencies, if appropriate.
6. In cases in which research undergoes joint IRB review at UMC and at the non-UMC institution, an IRB Authorization Agreement is usually not necessary unless required by the sponsor. Staff evaluates each situation on a case-by-case basis.
7. In some cases, however, the off-site facility may enter into an agreement allowing the facility to rely on the UMC IRB to review, approve, and provide continuing oversight of the off-site research. These circumstances may include but are not limited to the following: research that is not greater than minimal risk; or research involving non-UMC institutions that do not have an IRB and are not the type of institution that would typically establish an IRB (e.g., a school system). UMC may also serve as the relied-upon IRB if the PI of the study is a UMC employee and he/she conducts the study at an off-site facility. In such cases, the off-site facility may be asked to sign an IRB Authorization or Individual Investigator Agreement to abide by the decisions and determinations of the UMC IRB in the conduct of the research. (See the section on *Negotiation of IRB Authorization Agreements for Collaborating Institutions* for details.)
8. The Assistant Vice Chancellor for Research in conjunction with the Associate Vice Chancellor of research and UMC Legal Counsel if necessary makes the final determination whether the UMC IRB will serve as the relied-upon IRB.
9. UMC may also agree to defer responsibility for IRB review to a non-UMC institution’s IRB under limited circumstances. To defer responsibility, the non-UMC IRB must have an approved FWA. Other criteria taken under consideration when determining whether or not UMC will defer responsibility to another IRB include whether or not that institution is

accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), and/or whether the cooperating institution is willing to sign an agreement in which it assures UMC that it complies with the same federal regulations for the protection of human subjects. Examples of circumstances in which UMC may defer IRB review may include cases where: the funding agency requires it; the UMC employee role is limited, such as data analysis only; the research began at another institution prior to employment of the investigator at UMC and remains active only at the other institution (and any funds supporting the research remain under the control of the non-UMC institution); and/or the research is not greater than minimal risk. The two institutions may sign an IRB Authorization Agreement, if appropriate.

10. For less than minimal risk studies, the Assistant Vice Chancellor for Research or designee may make the final determination as to whether UMC IRB will defer review and oversight responsibilities to another IRB. For greater than minimal risk studies, the Assistant Vice Chancellor for Research, Associate Vice Chancellor of Research and, if appropriate, with UMC Legal Counsel, makes the final determination as to whether the UMC IRB will defer review and oversight responsibility to another IRB.
11. In cases where the UMC IRB relies on another non-UMC IRB, the PI ensures that research activity does not begin prior to UMC IRB review and approval of the documentation for each study site, as appropriate. Documentation may be in the form of IRB approval from the non-UMC IRB, verification of federally assigned assurance numbers, and/or a letter of cooperation from the facility administrator, as appropriate.
12. The PI coordinates with project personnel at the off-site locations to initiate any required off-site research review.
13. IRB staff assists the PI in identifying required documentation on a case-by-case basis and maintain copies of all documentation from each off-site facility in the study file.
14. When the UMC IRB conducts research reviews for off-site facilities, as appropriate to the agreement and in accordance with its standard policies and procedures for research review and oversight, the IRB ensures sufficient knowledge of local research context for the off-site location as detailed in the section on *IRB Knowledge of the Local Research Context*.
15. The PI submits documentation of approvals for off-site research in the initial submission to the UMC IRB or as it becomes available and may authorize research to start at a site once the UMC IRB approves the protocol. IRB staff maintains this information in e-compliance.

#### **Research Projects Involving Multiple Sites Where UMC is the Lead Site/Lead Investigator**

1. If UMC is the lead site in a multi-site study or the UMC investigator is the lead investigator, the PI provides additional information to the UMC IRB to ensure ongoing communication among the participating IRBs and sites. The UMC investigator submits the following information along with the IRB application:

- For each non-UMC site, a contact name and contact information (e.g., phone or e-mail) and name of individual who is responsible for such contact;
  - For each non-UMC site, a letter from the appropriate administrator granting permission for the investigator to conduct the research at its site;
  - For each non-UMC site with an approved FWA, the non-UMC site's FWA number;
  - For each non-UMC site, the relied upon IRB and appropriate documentation as needed (if joint review, a copy of the non-UMC site's IRB approval letter).
2. Additionally, the UMC investigator must submit to the IRB a written plan for the management of information that is relevant to the protection of human subjects, such as reporting unanticipated problems, protocol modifications, and interim results from all participating sites.

*See Guidance Multi-Site Research*

**Research at Geographically Separate Off-Site Location with No Cooperating Institution/Facility/Organization**

1. In the IRB application, the PI provides the necessary information, as appropriate, on the subject populations, the cultural context, and the languages understood by the human subjects.
2. If the IRB membership does not have the appropriate expertise to conduct the review, IRB staff and/or the PI assists the IRB in identifying cultural consultants. (See procedures outlined in the Initial Full Review, Expedited Initial Review, and IRB Member and Conflict of Interest SOPs.) The PI may supply the name of an appropriate consultant in the IRB application.
3. Cultural consultants may review consent forms, provide verifications of translations, and provide guidance on the impact of the research on subjects and the impact of the culture on the research to be conducted.

**Research at Geographically Separate UMC-Owned Site with Non-UMC Employees**

1. IRB staff assists the PI in determining whether the non-UMC employees will actively participate in the implementation of research procedures or will obtain individually identifiable private data about human subjects for research purposes. If the non-UMC employees are engaged in the research, then the UMC human research protection policy applies to those personnel. They must complete the appropriate human subjects' protection training, and the PI lists them as study personnel in the IRB application.
2. The PI provides the IRB the necessary information, as appropriate, on the subject populations, the cultural context, and the languages understood by the human subjects.

3. If the IRB does not have the appropriate expertise to conduct the review, IRB staff and/or the PI assists the IRB in identifying cultural consultants. (See the procedures outline in the Initial Full Review, Expedited Initial Review, and IRB Member and Conflict of Interest SOPs.) The PI may supply the name of an appropriate consultant in the IRB application.

### **Sites Operating under a Formal Agreement with the University of Missouri IRB**

1. UMC may enter into a formal agreement to serve as the relied-upon IRB for a single off-site facility, which is not a legal entity of UMC, by signing a Memorandum of Understanding, contract, or other official written agreement. Unlike the IRB Authorization Agreement, which applies to single projects, a formal agreement provides for ongoing IRB oversight of some or all of the research involving human subjects at the off-site facility.
2. In these cases, the formal agreement outlines the relationship between the institutions and documents the authority granted to the institution to serve as the relied-upon IRB for the off-site facility.
3. Sites operating under a formal agreement must file their own individual assurance with the OHRP and list the appropriate UMC IRB committee(s) as the designated IRB on the assurance. The Signatory Official for each institution signs all formal agreements. The Associate Vice Chancellor of Research serves as the Signatory Official for UMC.
4. The terms of the formal agreement specify appropriate human subjects education and training resources for investigators at the cooperating site as well as education and training for UMC IRB members pertaining to IRB knowledge of the local research context, including distinct subject populations (i.e., veterans, non-English speaking populations, etc.) See the section on *IRB Knowledge of Local Research Context* for additional details.
5. The Office of Research and IRB Office maintains a record of current formal agreements on file.

### *Negotiation of Federal Assurances for Collaborating Institutions (Applicable to Federally Funded Research)*

1. The institution is responsible for ensuring that all performance sites and investigators engaged in its federally supported research involving human subjects operate under an appropriate OHRP or other federally approved assurance. In general, institutions affiliated solely through professional or collaborative arrangements apply to OHRP for their own assurance. OHRP offers a number of different assurance mechanisms, including the FWA, Individual Investigator Agreement, and IRB Authorization Agreements. If a federal agency that is not a division of the DHHS supports the research, there may be additional requirements. IRB staff determines these additional requirements on a case-by-case basis with the sponsoring agency.

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2. Off-site facilities determine the appropriate assurance mechanism with assistance from the OHRP based on such issues as the funding source, nature of the research, ownership of the performance site, and affiliation of the individuals collecting the data.
3. The PI assists performance sites without an IRB which are “engaged” in research in obtaining the appropriate assurance and IRB approvals. The IRB advises the PI throughout the process, as appropriate.
4. Off-site facilities submit an application for an assurance to the OHRP and designate an institutional Signatory Official with authority to represent and commit the entire institution and all of its components to a legally binding agreement. If the Signatory Official is not legally authorized to represent an entity, it may not be covered under the assurance.
5. In some cases, an institution may operate under another institution’s assurance with the approval of the supporting agency. In such cases, UMC may enter into a formal IRB Authorization Agreement with the collaborating institution for review, approval, and continuing oversight of the research in question. (See *Negotiation of an IRB Authorization Agreement with Collaborating Institutions* for more information.)
6. The institution’s assurance may also cover independent investigators who are not an employee of the institution only in accordance with a formal written agreement of commitment to relevant human subject protection policies and IRB oversight. The institutions may formalize such agreements under the sample OHRP Individual Investigator Agreement or by a commitment agreement developed by the institutions. The institution entering into the commitment agreement maintains the agreement on file and submits copies to OHRP upon request.

### *Negotiation of an IRB Authorization Agreement with Collaborating Institutions*

1. Cooperative research studies involving multiple institutions may rely on cooperative review. In such cases, participating IRBs enter into a written cooperative review agreement identifying the specific IRB designated to provide review and detailing the respective responsibilities of the IRB and each institution under the review agreement.
2. Under an IRB Authorization Agreement, both institutions agree that one institution is responsible for providing IRB review and the second will rely on the other for IRB review for a single specified project. IRB Authorization Agreements list the federal assurance number for each institution, designate the specific project to which the agreement pertains, and specify that the agreement applies to no other research projects.
3. The Authorized Officials for both institutions must approve the agreement in writing. The UMC Associate Vice Chancellor of Research or the Assistant Vice Chancellor for Research as his designee, signs all IRB Authorization Agreements as the Signatory Official for UMC under its assurance. Both institutions maintain an IRB Authorization Agreement on file and agree to submit the document to OHRP upon request.

4. The IRB which agrees to review studies conducted at another institution (primary IRB) has the responsibility for initial and continuing review of the research. The primary IRB takes into account the required criteria for approval, the applicable regulations (e.g. 21CFR 50 or 56), the facilities and capabilities of the other institution, the measures to be taken by the participating institution to ensure compliance with the IRB's determinations, and community attitudes or local research context, as appropriate. (See the section on *IRB Knowledge of Local Research Context* for additional information.)
5. The primary IRB under an IRB Authorization Agreement is responsible for conveying approvals to all participating sites, either directly to the IRB or through the respective PI.
6. In cases in which UMC relies on another designated IRB under an IRB Authorization Agreement, the PI, with assistance from the IRB, is responsible for providing information to the non-UMC IRB assuring sufficient consideration of local research context for the UMC component(s) of the study.
7. When the UMC IRB relies on a non-UMC IRB for review of research under an IRB Authorization Agreement, it agrees to abide by the decisions and determinations made by the non-UMC IRB.
8. Likewise, individual investigators agree to abide by those same decisions and determinations and may not modify or alter the research protocol without prior written approval of the non-UMC IRB.
9. The PI sends all required reports directly to the non-UMC IRB with copies to the UMC IRB, as appropriate.
10. Additional information on the negotiation of subaward agreements for off-site sponsored research may be found in the Office of Sponsored Projects Administration/IRB/ Coordination SOP.

#### *IRB Knowledge of Local Research Context*

1. In accordance with OHRP guidance, when the UMC IRB serves as the relied-upon IRB for another institution or when the research involves distinct subject populations (non-English speaking populations, veterans, etc.), the UMC IRB ensures that it possesses or obtains sufficient knowledge of the local research context even when the IRB is geographically removed from the off-site research location.
2. The PI supports the IRB in understanding the local research context by providing the IRB necessary information, as appropriate, on:
  - The anticipated scope of the off-site facility's research activities;
  - The types of subject populations likely to be involved;



- The size and complexity of the institution;
  - Institutional commitments and regulations;
  - Applicable law;
  - Standards of professional conduct and practice;
  - Method for equitable selection of subjects;
  - Method for protection of privacy of subjects;
  - Method for maintenance of confidentiality of data;
  - Languages understood by prospective subjects;
  - Method for minimizing the possibility of coercion or undue influence in seeking consent;
  - Safeguards to protect the rights and welfare of vulnerable subjects.
3. In cases where the UMC IRB conducts non-local review, members must have sufficient knowledge of the community from which the subjects are drawn to ensure protection of subject rights and appropriateness of the consent process for the subject population. In addition, the IRB must be sensitive to community laws and mores. The IRB may ensure the necessary expertise and knowledge to make appropriate determinations regarding the local research context through one or more of the following activities, as appropriate to the level of risk and in accordance with OHRP guidance and FDA regulation:
- Personal knowledge of the local research context on the part of one or more IRB members, such knowledge obtained through extended direct experience with the research institution, its subject populations, and its surrounding community;
  - Review of the proposed research by representatives from the facility or by one or more ad hoc or cultural consultants with knowledge of the local research context. Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review, either physically or through audiovisual or telephone conference, when participation is deemed warranted by the consultant(s) or any one member of the IRB;
  - Systematic reciprocal documented interchange between the IRB and elements of the local research context through periodic visits to the research site by one or more IRB members/IRB staff or University representatives in order to obtain and maintain knowledge of the local research context; periodic discussion with appropriate consultants knowledgeable about the local research context; interaction with one or more designated institutional liaisons; and/or review of relevant written materials;
  - Appointment of an IRB member from the community in question.
4. IRB staff assists the PI in addressing the requirements for information on the local research context upon request.
5. IRB staff assists the IRB in identifying appropriate consultants and distributing appropriate review materials pertaining to the local research context to IRB members, as appropriate.
6. IRB staff maintains documentation in the database and the study file of the local research context and the measures taken to ensure sufficient IRB knowledge of that context.

7. The IRB includes the name and toll-free contact information for an IRB contact in the consent document for non-local IRB review or designates an individual at the research site to serve as the contact to relay reports to the IRB.
8. In the minutes of the meeting or in the IRB file, IRB staff or the IRB reviewer documents the procedures used to ensure that the IRB adequately considered community attitudes.

## **REFERENCES**

Office for Human Research Protections (OHRP)

Engagement Memo

Terms of the Federalwide Assurance of Protection for Human Subjects

IRB Knowledge of Local Research Context Guidance

Sample Unaffiliated Investigator Agreement

Food and Drug Administration (FDA)

Cooperative Research Guidance

Non-Local IRB Review Guidance

21 CFR parts 50 and 56

45 CFR 46.114

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