22.0 COORDINATION of IRB REVIEW and OVERSIGHT CONDUCTED at OFF-SITE LOCATIONS or MULTIPLE SITES

22.1 OBJECTIVE

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

22.2 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, HU 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 Office of Research Regulatory Compliance (ORRC) staff, in consultation with the Associate Vice President (AVP) for Regulatory Research Compliance (RRC) and HU Legal Counsel, takes into consideration the source of funding for the research activity, federal regulations, specific sponsor regulations governing human research protections, and institutional policy.

The HU 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.

The IRB application available from ORRC staff includes instructions to investigators describing specific institutional and regulatory requirements for obtaining IRB approval of off-site research. ORRC staff advises investigators on meeting the requirements, as appropriate.

In addition, HU may enter into formal agreements with other facilities which are not legal entities of HU 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. HU enters into these types of arrangements through a Memorandum of Understanding, IRB Authorization Agreement, or contract with the institution(s) in question.

22.3 DEFINITIONS

The term *off-site research* designates research conducted at performance sites that are not owned or operated by HU, at non-HU sites that are geographically separate from HU, or at sites that do not fall under the HU IRB's authority.

Cooperative research is defined as research conducted in cooperation with and at a performance site of an institution or facility that is not affiliated with HU or that does not fall under the HU IRB's authority. An off-site institution or facility may be domestic or international and may or may not have its own IRB.

22.4 RESPONSIBILITY

Execution of SOPP: Principal Investigator (PI)/Study Personnel, HU IRB, ORRC Staff, Associate Vice President for Regulatory Research Compliance, HU Legal Counsel, recipients of subaward agreements to conduct research involving human subjects.

22.5 PROCEDURES

22.5.1 Research Involving Non-HU Performance Sites: Cooperative Research

- The PI arranges for the off-site facility administrator to submit a letter on the facility's letterhead stationery addressing the following information:
  - 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 HU 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 HU 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 HU IRB; and
  - If applicable, assurance that personnel from the facility who collect data have appropriate training in the protection of human subjects.

- For cooperative research projects, the PI determines 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. The ORRC assists the PI in making this determination, as appropriate.

- If the off-site non-HU facility is "engaged" in research, the PI determines, with ORRC assistance, whether the off-site facility requires an assurance mechanism (See the section on *Negotiation of Federal Assurances for Collaborating Institutions* for details).

- A cooperative research site “engaged” in research which has its own non-HU IRB is responsible for conducting the research review for that site and providing the PI with appropriate documentation to submit to the HU IRB. This documentation includes the Federal Wide Assurance (FWA) number for all federally funded research and the non-HU IRB approval letter.

- 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.

- In cases when research undergoes joint IRB review at HU and at the non-HU institution, an IRB Authorization Agreement is usually not necessary unless required by the sponsor. ORRC staff evaluates each situation on a case-by-case basis.

- In some cases, however, the off-site facility may enter into an agreement allowing the facility to rely on the HU 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-HU 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). HU may also serve as the relied-upon IRB if the PI of the study is an HU 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 HU IRB in the conduct of the research (See the section on *Negotiation of IRB Authorization Agreements for Collaborating Institutions* for details).

- The AVP for RRC, in consultation and, if appropriate, HU Legal Counsel, makes the final determination whether the HU IRB will serve as the relied-upon IRB.

- HU may also agree to defer responsibility for IRB review to a non-HU institution’s IRB under limited circumstances. To defer responsibility, the non-HU IRB must have an approved FWA. Other criteria taken under consideration when determining whether or not HU 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 HU that it complies with the same federal regulations for the protection of human subjects. Examples of circumstances in which HU may defer IRB review may include cases where: the funding agency requires it; the HU employee role is limited such as data analysis only; the research began at another institution prior to employment of the investigator at HU and remains active only at the other institution (and any funds supporting the research remain

under the control of the non-HU institution); and/or the research is not greater than minimal risk. The two institutions may sign an IRB Authorization Agreement, if appropriate.

- For less than minimal risk studies, the AVP for RRC, the ORRC Director, or designee may make the final determination as to whether HU IRB will defer review and oversight responsibilities to another IRB. For greater than minimal risk studies, the AVP for RRC, in consultation with the ORRC and, if appropriate, with HU Legal Counsel, makes the final determination as to whether the HU IRB will defer review and oversight responsibility to another IRB.

- In cases where the HU IRB relies on another non-HU IRB, the PI ensures that research activity does not begin prior to HU 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-HU IRB, verification of federally assigned assurance numbers, and/or a letter of cooperation from the facility administrator, as appropriate.

- The PI coordinates with project personnel at the off-site locations to initiate any required off-site research review.

- ORRC 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.

- When the HU 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.

- The PI submits documentation of approvals for off-site research in the initial submission to the HU IRB or as it becomes available and may authorize research to start at a site once the HU IRB approves the protocol. ORRC staff maintains this information in the ORRC database and the study files.

22.5.2 Research Projects Involving Multiple Sites Where HU is the Lead Site/Lead Investigator

- If HU is the lead site in a multi-site study or the HU investigator is the lead investigator, the PI provides additional information to the HU IRB to ensure ongoing communication among the participating IRBs and sites. The HU investigator submits the following information along with the IRB application:
  - For each non-HU 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-HU site, a letter from the appropriate administrator granting permission for the investigator to conduct the research at its site;

- For each non-HU site with an approved FWA, the non-HU site's FWA number;
- For each non-HU site, the relied upon IRB and appropriate documentation as needed (if joint review, a copy of the non-HU site's IRB approval letter).

- Additionally, the HU 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.

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

- 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.

- If the IRB membership does not have the appropriate expertise to conduct the review, ORRC 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 Consultant Conflict of Interest SOPPs). The PI may supply the name of an appropriate consultant in the IRB application.

- 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.

22.5.4 Research at Geographically Separate HU-Owned Site with Non-HU Employees

- ORRC staff assists the PI in determining whether the non-HU 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-HU employees are engaged in the research, then the HU human research protection policy applies to those personnel. They must complete the appropriate human subject protection training, and the PI lists them as study personnel in the IRB application.

- 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.

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

22.5.5 Sites Operating under a Formal Agreement with the Howard University IRB

- HU 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 HU, 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.

- 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.

- Sites operating under a formal agreement must file their own individual assurance with the OHRP and list the appropriate HU IRB committee(s) as the designated IRB on the assurance. The Signatory Official for each institution signs all formal agreements. The AVP for RRC serves as the Signatory Official for HU.

- 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 HU IRB members pertaining to IRB knowledge of the local research context, including distinct subject populations (i.e., veterans, non-English speaking populations, etc.).

- The ORRC maintains a record of current formal agreements on file.

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

- 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 Department of Health and Human Services (DHHS) supports the research, there may be additional requirements. ORRC staff determines these additional requirements on a case-by-case basis with the sponsoring agency.

- 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.

- The PI assists performance sites without an IRB which are “engaged” in research in obtaining the appropriate assurance and IRB approvals. The ORRC advises the PI throughout the process, as appropriate.

- 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.

- In some cases, an institution may operate under another institution’s assurance with the approval of the supporting agency. In such cases, HU 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).

- 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.

22.5.7 Negotiation of an IRB Authorization Agreement with Collaborating Institutions

- 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.

- 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.

- The Authorized Officials for both institutions must approve the agreement in writing. The HU AVP for RRC signs all IRB Authorization Agreements as the Signatory Official for HU under its assurance. Both institutions maintain an IRB Authorization Agreement on file and agree to submit the document to OHRP upon request.

- 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. 21CRF 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).

- 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.

- In cases in which HU relies on another designated IRB under an IRB Authorization Agreement, the PI, with assistance from the ORRC, is responsible for providing information to the non-HU IRB assuring sufficient consideration of local research context for the HU component(s) of the study.

- When the HU IRB relies on a non-HU IRB for review of research under an IRB Authorization Agreement, it agrees to abide by the decisions and determinations made by the non-HU IRB.

- 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-HU IRB.

- The PI sends all required reports directly to the non-HU IRB with copies to the HU IRB/ORRC, as appropriate.

- Additional information on the negotiation of subaward agreements for off-site sponsored research may be found in the Research Administrative Services/IRB/ORRC Coordination SOPP.

22.5.8 IRB Knowledge of Local Research Context

- In accordance with OHRP guidance, when the HU 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 HU 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.

- 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.

- In cases where the HU 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, *including local and tribal 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/ORRC 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.

- ORRC staff assists the PI in addressing the requirements for information on the local research context upon request.

- ORRC staff assists the IRB in identifying appropriate consultants and distributing appropriate review materials pertaining to the local research context to IRB members, as appropriate.

- ORRC 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.

- The IRB includes the name and toll-free contact information for an ORRC 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.

- In the minutes of the meeting or in the IRB file, ORRC staff or the IRB reviewer documents the procedures used to ensure that the IRB adequately considered community attitudes.

22.6 REFERENCES

Office for Human Research Protections (OHRP)
Engagement Memo
Terms of the Federal-Wide 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