1.0 POLICY

1.1 Background.

1.1.1 Federal Regulations (45 CFR 46.114 and 21 CFR 56.114) and AAHRPP require policies and procedures for communication among IRBs, when appropriate, for research conducted at multiple sites (e.g., multi-site clinical trials, epidemiology studies, or educational surveys).

1.1.2 When an investigator plans to conduct research at sites external to the organization and those sites are engaged in the research, provisions for IRB review of the research at each engaged site must be considered. For example, an investigator might conduct research at nursing homes, schools, or community-based organizations, where these sites would meet the definition of “engaged in research”. This document describes the steps in defining the responsibilities of each IRB and to communicate with each IRB.

1.1.3 Investigators who plan to conduct research at non-engaged sites external to UA must also follow this policy for such research.

1.1.4 Multi-site research often involves the Office for Sponsored Programs, as well as the Office for Research Compliance, because of the need to manage awards.

1.1.5 Key Definitions

1.1.5.1 Research: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizeable knowledge [45 CFR 46.102(l)].

1.1.5.2 Clinical Investigation: In FDA regulations, any experiment that involves a test article and one or more human participants and is one of the following: (1) Subject to requirements for prior submission to the FDA; (2) Is not subject to requirements for prior submission to the FDA but the results are intended to be submitted later or held for inspection by the FDA as part of an application for a research or marketing permit; (3) Does not include experiments subject to 21 CFR §58, regarding non-clinical laboratory studies.

1.1.5.3 Human Subject:

1.1.5.3.1 Per DHHS: A living individual about whom an investigator (whether professional or student) conducting research: (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [45 CFR 46.102(e)(1)].
1.1.5.3.2 Per FDA: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient [21 CFR 50.3].

1.1.5.4 **UA Research Activity:** Any human subject research activity that is supported with UA funds or by funds awarded/contributed to UA and/or is conducted using UA facilities, personnel/students, research subjects, data or other non-public resources.

1.1.5.5 **Non-UA Institution:** An institution (or an employee or agent of the institution) that is not under the authority of UA and is located within the United States or a United States territory. Examples include clinics, schools, other universities, consulting firms, or other institutions where activities include interaction or intervention with human subjects and/or the collection or analysis of identifiable data. Non-UA facilities that are located outside the United States may include a variety of entities, including government agencies, non-governmental organizations (NGOs), corporations, and organizations of indigenous peoples.

1.1.5.6 **Engaged in Research:** A non-UA institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d)-(f)].

1.1.5.7 **Non-Engaged in Research:** A non-UA institution is not engaged in human subjects research if it is not intervening or interacting with living individuals for research purposes and not obtaining individually identifiable private information for research purposes.

1.1.6 **Applicability:** This policy applies to any UA research activity involving human subjects (regardless of source or plans for funding) that involves a non-UA institution, whether or not the non-UA institution is engaged in research and to independent investigators (not acting as employees or agents of another institution) involved in UA human research, and to UA investigators leading or collaborating in international research done in one or more countries besides the United States. Specific procedures and IRB requirements for these circumstances are described below.

1.1.7 Investigators conducting international research should also see GUIDANCE: International Research.

1.2 **Policy Statement**

1.2.1 The University of Alabama bases its policy for multi-site studies on the terms of the UA Federalwide Assurance (FWA) as follows:

1.2.1.1 If UA is the prime awardee under a federal grant, contract, or cooperative agreement (supporting research to which the FWA applies), then UA will ensure that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved assurance for the protection of human subjects;

1.2.1.2 If UA is the coordinating center for federally conducted or supported research (to which the FWA applies), then UA will ensure that all collaborating institutions engaged in such research operate under an appropriate OHRP-approved assurance for the protection of human subjects; and

1.2.1.3 Regardless of the source of sponsorship, all investigators must follow additional requirements of the non-UA institution (including additional IRB review, if required).
1.2.1.4 As with single-site studies, investigators may request exempt or expedited status for their applications. However, the UA IRB may upgrade the level of review based on the level of risk and other factors.

1.2.1.5 In some cases UA will consider a request from a non-UA institution to review the application – it will “defer” to the UA IRB. Justifications in this case are considered only where the risk level is low or when UA personnel oversee research activities at the non-UA institution.

1.2.1.6 Investigators may request that a non-UA IRB review on behalf of the UA IRB – that UA defer to a non-UA IRB, although this type of deferral is less common.

1.2.1.7 UA administration will not approve an IRB authorization agreement (Deferral 1.2.1.5; use of a non-UA IRB, 1.2.1.6) without a favorable recommendation by the UA IRB.

1.2.1.8 Investigators are directed to the OHRP Guidance Document, “Engagement of Institutions in Research” at https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html. If questions remain, the investigator should:

1.2.1.8.1 Contact the sponsor or program director if the research is federally funded, and/or:

1.2.1.8.2 Contact the UA Office for Research Compliance or the Director of Research Compliance. [Note that a telephone conversation often does not fairly represent the entire scope of the research activity. If questions remain about whether a non-UA institution is engaged in the research, the investigator may be requested to submit a written IRB protocol for consideration].

1.2.2 It is the responsibility of the principal investigator to: (1) plan for the involvement of non-UA institution(s) in UA human research AND (2) obtain ALL necessary permissions and documents in accordance with the UA FWA. In addition, the principal investigator must be prepared to (1) ensure that adequate resources will be available at the non-UA institution to conduct the research safely and effectively in full accordance with the approved protocol; (2) ensure that all persons interacting with human subjects and/or their identifiable data are adequately trained in the protection of human subjects, regardless of their employment status with UA; (3) make every effort to ensure that any non-UA institution whose IRB is reviewing research that is associated with UA is registered with the U.S. Office for Human Research Protections; (4) ensure that the UA IRB receives complete reports of all IRB-reportable events occurring both at UA and at the non-UA institution; (5) ensure the consent documents fairly and accurately represent the involvement of UA in the research and the decisions of all responsible IRBs reviewing the research.

1.2.3 It is the responsibility of the IRB to review requests for the involvement of non-UA institutions and determine the path that: (1) ensures optimal human subject protections and (2) represents controlled institutional risk.

1.2.3.1 When the investigator is the lead investigator of a multi-site study, the IRB evaluates whether the management of information that is relevant to the protection of participants is adequate.

1.2.4 It is the responsibility of the Vice President for Research, the Director of Research Compliance, and the Director of Sponsored Programs to monitor this policy and facilitate agreements.

1.3 Objective
1.3.1 When implemented, this policy and procedure will provide guidance to investigators doing multi-site research and to UA IRBs reviewing such research, and will ensure UA compliance with its FWA.

1.4 Responsibility.

1.4.1 The Vice President for Research and Economic Development is ultimately responsible for this policy. Enabling parties include principal investigators, the IRBs, the Director of Sponsored Programs, and the Director of Research Compliance.

2.0 PROCEDURE

2.1 The investigator should determine the roles each institution will serve in the research project:

2.1.1.1 Is UA the prime awardee under a federal grant, contract, or cooperative agreement? OR, is UA the coordinating center for federally conducted or supported research?

2.1.1.2 If either is true, is the non-UA institution engaged in the research project or not? (See Key Definitions in Background).

2.1.1.2.1 Follow the procedures below for Engaged or Non-Engaged institutions, as appropriate.

2.1.1.3 If NEITHER is true, this policy is not relevant except as an informational guide.

2.2 Non-UA Institutions ENGAGED, Exempt Research

2.2.1 Investigators planning to work with Non-UA institutions that are engaged in human subject research activity eligible for or to be considered for exempt status must meet the usual UA IRB requirements for exempt research (See POLICY: Exempt Review and FORM: Exemption Eligibility Checklist) and the following additional UA IRB requirements:

2.2.1.1 Submit a protocol for UA IRB review and approval. Identify only institutions that have agreed to participate. Include in the research synopsis a description of their role in the human subjects research, adequacy of the facility (in order to ensure human subject safety in the case of an unanticipated emergency), responsibilities of their agents/employees, and oversight that you will be providing in order to ensure adequate and ongoing protection of the human subjects.

2.2.1.2 Obtain a written letter of permission from an authorized individual at the non-UA institution that authorizes the PI to perform activities at that location and include it with the IRB application.

2.2.1.3 Follow any additional requirements of the non-UA institution including additional IRB review if required.

2.3 Non-UA Institution, ENGAGED, Expedited and Full Board Reviews

2.3.1 Submit a protocol for UA IRB review and approval. (For expedited research, see also POLICY: Expedited Research). Identify only institutions that have agreed to participate. Include in the research synopsis a description of their role in the human subjects research, adequacy of the facility (in order to ensure human subject safety in the case of an unanticipated emergency), responsibilities of their agents/employees, protection of the human subjects.

2.3.1.1 State whether or not this is a multi-site study in which you are the lead investigator.

2.3.1.2 If YES, describe the management of information obtained in multi-site research that might be relevant to the protection of human subjects, such as (a) unanticipated problems involving risks to subjects or others, (b) interim results, and (c) protocol modifications.
2.3.2 In the case of more than one IRB reviewing the research, every effort should be made to develop a single consent document that fairly and completely represents the decisions of each IRB involved and that explains the involvement of each institution. **UA strongly recommends that a single consent document be given to the research participant, whenever possible.** The consent form must name the UA PI.

2.3.3 Obtain a written letter of permission from an authorized individual at the non-UA institution that authorizes the PI to perform activities at that location and include with the IRB application.

2.3.4 Follow any additional requirements of the non-UA institutional including additional IRB review if required.

2.3.5 If the research project involves a direct federal award to UA (or application for such), OHRP requires that the non-UA institution have an FWA or obtain one naming its own IRB or a central IRB.

2.3.6 In some cases, it may not be practical for the non-UA institution’s IRB to review the research and they plan to 'defer' to the UA IRB. If this is the case, the PI must contact OSP to begin the agreement process between UA and the non-UA Institution (which must have or obtain an FWA). Historically, justifications are only considered in this case where the risk level is low or UA personnel oversee research activities at the non-UA institution. See 2.4 below for details of the deferral procedure.

2.3.7 In certain instances a federally sponsored protocol may describe collaborations with unnamed investigators or institutions who will be engaged in the research in a one-time, short-term capacity. In this rare case, the investigator should contact the Office for Sponsored Programs, which, together with the Director of Research Compliance, will coordinate a plan for compliance that ensures maximized protections for the research participants.

### 2.4 Deferral Process (request for the UA IRB to review on behalf of a non-UA institution)

2.4.1 UA may permit the non-UA institution to defer to the UA IRB if both of the conditions below are met:

2.4.1.1 The research must involve no greater than minimal risk. (If the research involves greater than minimal risk, the principal investigator/research staff must be either conducting the research activities or directly supervising the research activities of the employees/agents of the non-UA institution); **and**

2.4.1.2 A written agreement must be negotiated between UA and the non-UA institution (as a formal documentation of deferred responsibilities).

2.4.2 To request that an agreement for deferral be considered, the PI should contact the UA OSP as soon as possible and begin preparing a written request that includes the elements described below. The written request should be submitted with the UA IRB application including:

2.4.2.1 A statement of whether the proposed human research activity involving a non-UA institution is conducted under the direct supervision of the UA PI/research staff as part of their UA employment responsibilities. Describe the level of UA PI oversight of the research activities conducted at the non-UA institution.

2.4.2.2 Identification of the source(s) of all funding (e.g., grantor, donor of unrestricted gifts, contracting agency, UA departmental funds, non-UA institutions funds) and a statement about which institution is managing the funds (i.e., UA, Non-UA Institution).

2.4.2.3 A description of the investigator’s understanding of the local research context (including any laws relevant to the study being reviewed by the IRB) or how the knowledge will be obtained (i.e., use of consultants).
2.4.2.4 A statement of whether or not the non-UA Institution has an FWA. If so, provide the FWA number and effective dates.

2.4.2.5 An assessment of whether the non-UA institution has adequate resources to conduct the research and a description of those resources.

2.4.2.6 If the research is ongoing at another institution (such as in the case of a multi-center study) provide a report on research results to date and summary of all unanticipated problems and/or serious adverse events and other reportable adverse events.

2.4.3 The relying institution provides the UA IRB with management plans for investigators and research staff when a conflict of interest exists.

2.4.4 The UA IRB will review the material and make a recommendation to UA Institutional Official (or designee) regarding approval.

2.4.5 UA administration will not approve an IRB authorization agreement without a favorable recommendation by the UA IRB. The principal investigator should be aware that the agreements process requires additional effort and required paperwork at the Federal level in accordance with the terms of the UA FWA. An agreement is rarely less time consuming than dual IRB review and, in most cases, affords no advantage in terms of human subject protections.

2.4.6 The UA IRB makes available relevant IRB records, including but not limited to minutes, approved protocols, consent documents, and other records that document the IRB’s determinations to the relying institution upon written request.

2.4.7 The UA IRB will determine on a case-by-case basis whether to process the addition of a new research site(s) as a separate protocol or modification to a previously approved protocol.

2.4.7.1 The request to add a new research site may be processed via expedited or convened IRB review and is considered a minor modification if it does not increase the level of risk or burden to participants or affect the previous review category. This determination is also based on the UA IRB’s assessment of the qualifications of the new study personnel and facilities available to support the safe conduct of the research. [Please also see UA IRB Policy: Modifying Approved IRB Protocols and Guidance: Minor Changes to Approved Protocols.]

2.4.8 For all non-UA institutions, the UA IRB reviews issues involving participant complaints, protocol deviations, and all unanticipated problems involving potential risk to participants or others. The UA IRB addresses and reports such events and notifies non-UA investigators and institutions of its corresponding decisions and actions (including suspension or termination of IRB approval) in accordance with UA IRB policy and as communicated in the written agreement between the institutions. [See Participant and Community Questions, Suggestions, Complaints, and Concerns About Research Studies; and Allegations and Findings of Noncompliance for additional information.]

2.4.9 Relevant policies regarding Human Research Protection Program (HRPP) staff and investigators/research staff are readily available on the UA Office for Research Compliance (ORC) website (http://ovpred.ua.edu/research-compliance/institutional-review-board-irb/). The ORC posts timely updates on the website and communicates these via its listserv. UA investigators forward applicable ORC updates to collaborators at relying institutions.

2.4.10 The UA IRB provides contact information for ORC, the IRB, and Research Compliance Officer to investigators and research staff to provide to their participants in the event they have questions or want to express concerns or convey suggestions regarding the IRB. This information is also included on all UA consent documents.

2.5 Requests for a Non-UA IRB to review on behalf of UA (UA IRB defers to Non-UA IRB)
2.5.1 Approval of this type of arrangement will only be considered by the UA Institutional Official (or designee) when both of the following conditions are met:

2.5.1.1 The research began at another institution, prior to employment of the UA investigator, and remains active only at that other institution **AND**

2.5.1.2 Any funds supporting the research remain under the control of the non-UA institution.

2.5.2 To request that an agreement for deferral be considered, the PI should contact the UA OSP as soon as possible and begin preparing a written request that includes the elements described below:

2.5.2.1 The name of the institution that would provide the IRB oversight for this research and its FWA number, expiration date, and IRB registration number(s).

2.5.2.2 A statement of whether the proposed human research activity that causes the non-UA institution to be engaged in the research will be conducted under the direct supervision of the UA PI/research staff.

2.5.2.3 A statement of whether the activity involves UA property or facilities (e.g., outpatient clinics) and which one(s).

2.5.2.4 A statement of whether the proposed activity involves the use of UA patients (including tissues, medical information, or other UA non-public information) for research purposes.

2.5.2.5 Identification of all sources of funding.

2.5.2.6 Identification of the institution and division that is managing the funds (i.e., UA Contract & Grant Accounting, or Non-UA Institution).

2.5.2.7 For persons currently employed part-time outside UA, indicate what part of the research is being conducted at UA and what part is being conducted at the other institution.

2.5.2.8 If this activity began at another institution, indicate the name of that institution and the date of original and most recent IRB approval (at that institution). Please explain if this is a different institution than that noted above.

2.5.2.9 A statement of whether the activity involves subject recruitment that began prior to becoming employed by or enrolled in UA.

2.5.3 The UA IRB reviews issues involving participant complaints, protocol deviations, and all unanticipated problems involving potential risk to participants or others. The UA IRB addresses and reports such events and notifies non-UA investigators and institutions of its corresponding decisions and actions (including suspension or termination of IRB approval) in accordance with UA IRB policy and as communicated in the written agreement between the institutions. [See Participant and Community Questions, Suggestions, Complaints, and Concerns About Research Studies; and Allegations and Findings of Noncompliance for additional information.]

2.5.4 The UA ORC provides UA investigators with information regarding:

2.5.4.1 The requirement to conduct additional reviews (such as scientific review or conflict of interest review) prior to review by the external IRB, and when appropriate, the process to communicate the results of this review to the external reviewing IRB.

2.5.4.2 The requirement to provide the reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB’s determination prior to IRB review.

2.5.4.3 Whom investigators/research staff should contact at UA to obtain answers to questions, express concerns, and convey suggestions when using a non-UA IRB for review.

2.6 **Respective Responsibilities of Institutions When Sharing Oversight of Research**
2.6.1 The UA IRB requires that a written agreement (i.e., IRB authorization/reliance agreement) is established when it enters into a relationship with another institution (e.g., UA defers to another institution or UA serves as the IRB of record). The written agreement describes which institution (reviewing or relying) is responsible for the following:

2.6.1.1 Providing education to investigators and research staff.
2.6.1.2 Conducting scientific review.
2.6.1.3 Ensuring concordance between any applicable grant and the IRB protocol.
2.6.1.4 Reviewing potential non-compliance, including complaints, protocol deviations, and results of audits:
   2.6.1.4.1 Identifying which institution is responsible for deciding whether each allegation of noncompliance has a basis in fact.
   2.6.1.4.2 Identifying which institution’s process is used to decide whether each incident of noncompliance is serious or continuing.
2.6.1.5 Obtaining management plans for investigator and research staff when a conflict of interest exists.
   2.6.1.5.1 If the relying institution maintains responsibility for this issue, the management plan must be provided to the IRB in a timely manner prior to the decision by the IRB.
2.6.1.6 Managing organizational conflict of interest related to the research.
2.6.1.7 Continued oversight of active studies until closure or a mutually agreed upon transfer of the studies in the event a reliance agreement is terminated.

2.6.2 When following DHHS and FDA Regulations and Requirements: The UA IRB requires that a written agreement is established when it enters into a reliance agreement with another institution (e.g., UA defers to another institution or UA serves as the IRB of record). The written agreement defines which institution (reviewing or relying) is responsible determining the following:

2.6.2.1 Whether the relying institution applies its FWA to some or all research, and ensuring the IRB review is consistent with requirements in the relying institution's FWA.
2.6.2.2 Which institution is responsible for obtaining any additional approvals from DHHS when the research involves pregnant women, fetuses, and neonates; children; or prisoners.
2.6.2.3 Which institution is responsible for reporting serious or continuing non-compliance; unanticipated problems involving risks to participants or others; and suspensions or terminations of IRB approval.
   2.6.2.3.1 Reporting may be done by the reviewing IRB, the relying institution, or jointly, but must be defined in the written agreement.

2.6.3 When following the NIH Policy on Single IRB Review: For studies that fall under the NIH Single IRB policy (i.e., awardees and participating sites in the U.S.), the UA IRB requires that a written agreement is established when it enters into a reliance agreement with another institution. The written agreement:

2.6.3.1 Describes the process for entering into an authorization agreement or reliance agreement which documents respective authorities, roles, responsibilities, and communication between the reviewing and relying institutions.
   2.6.3.1.1 Defines who is responsible for managing authorization agreements.
2.6.3.2 Describes the process to ensure IRB approval is obtained when the institution is responsible for a multi-site research study outside the U.S. that is not required to follow requirements for single IRB review.
2.6.3.3 Describes the process used by the awardee institution to ensure authorization agreements are in place and that documentation is maintained.

2.6.3.4 Describes which institution is responsible for meeting additional certification requirements, such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.

2.6.3.5 Describes the process to document the rationale for not relying upon a single IRB review in accordance with NIH policy on exceptions from single IRB review.

2.6.4 When Relying Upon Non-AAHRPP Accredited IRBs: The UA IRB may choose to defer IRB review and oversight to an institution that is not accredited by AAHRPP under the following conditions:

2.6.4.1 The research involves no greater than minimal risk.

2.6.4.2 The non-UA institution must have an OHRP-approved FWA and OHRP-registered IRB. Under the terms of the FWA, the non-UA institution asserts that it complies with the federal regulations governing human subjects research and follows the basic ethical principles and guidelines for protecting the rights and welfare of research participants.

2.6.4.3 A written agreement outlining institutional responsibilities must be negotiated between UA and the non-UA institution.

2.6.4.4 The UA IRB may review the protocol and materials approved by the non-UA institution and request additional information as necessary.

2.6.4.4.1 The extent of the UA IRB’s evaluation of the review conducted by the non-AAHRPP accredited IRB may vary depending upon the level of risk to participants in the research.

2.6.5 Ancillary Reviews: Some human subjects research may require review by institutional committees other than the IRB (e.g., biosafety, radiation safety, recombinant DNA research, human stem cell research, financial conflict of interest). Whenever ancillary reviews are warranted, the non-UA/external IRB must notify UA in writing in a timely manner about the following:

2.6.5.1 The results or findings of the ancillary review in a timely manner.

2.6.5.2 Any circumstances when the external review must take into account additional regulatory requirements, such as those of the U.S. Department of Defense and Department of Justice.

2.6.5.3 Any additional education requirements for investigators when ancillary review is required.

2.7 Non-UA Institutions NOT ENGAGED

2.7.1 Investigators planning to work with Non-UA institutions that are not engaged in the human subject research activity must meet the following additional UA IRB requirements:

2.7.1.1 Submit a protocol for UA IRB review and approval and include in the research synopsis a description of their role in the human subjects research, adequacy of the facility (in order to ensure human subject safety in the case of an unanticipated emergency), responsibilities of their agents/employees, and oversight that you will be providing in order to ensure adequate and ongoing protection of the human subjects. Identify only institutions that have agreed to participate.

2.7.1.2 Obtain a written letter of permission from an authorized individual at the non-UA institution that authorizes the PI to perform activities at that location and include with the IRB application.
3.0 REFERENCES

3.1 45 CFR 46.101-102

3.2 45 CFR 46.114

3.3 21 CFR 56.114

3.4 45 CFR 46.102(d)-(f)

3.5 DoD: SECNAVINST 3900.39D 6f


3.7 OHRP List of Approved Assurances

3.8 OHRP Assurance Process

3.9 OHRP Registration of an Institutional Review Board (IRB)


4.0 RELATED SECTIONS

4.1 GUIDANCE: International Research

4.2 POLICY: Exempt Review

4.3 POLICY: Expedited Review

4.4 GUIDANCE: IRB Application Guide