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 taken into account. 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 of Sponsored Programs as well as the Office for Research Compliance because 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 generalizable knowledge [45 CFR 46.102(d)].

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: (DHHS): A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information [45 CFR 46.102(f)]. Human Subject (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 individual or a patient.

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 multisite 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 rare 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 on the UA IRB—that UA will defer to a non-UA IRB. However, approval of this type of deferral is extraordinarily rare and will only be considered by the UA Institutional Official (or designee)

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”, http://www.hhs.gov/ohrp/humansubjects/assurance/engage.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 Sponsored Programs 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 Federalwide Assurance. 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.

1.2.4 It is the responsibility of the Vice President for Research, the Director of Research Compliance, and the Director of the Office 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 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: Exempt ion Eligibility Checklist) and the following additional UA IRB requirements:
2.2.1.1 Submit an application 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 an application 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, and 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 a Federalwide Assurance (FWA) or obtain one naming their own IRB or a central IRB.

2.3.6 In rare 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 of 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 all 3 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)];

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

2.4.1.3 The non-UA institution must amend their FWA to list the UA IRB.

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 (i.e., 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 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 a 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 UA IRB will review the material and make a recommendation to UA Institutional Official (or designee) regarding approval.
2.4.4 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 Federalwide Assurance. An agreement is rarely less time consuming than dual IRB review and, in most cases, affords no advantage in terms of human subject protections.

2.5 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 long-term arrangement is extraordinarily rare and 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 PI at UA, 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 Grants and Contracts 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 State whether the activity involves subject recruitment, which began prior to your becoming employed by or enrolled in UA.
2.6 Non-UA Institutions NOT ENGAGED

2.6.1 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:

2.6.1.1 Submit an application 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.

2.6.1.2 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)
3.6 OHRP List of Approved Assurances
3.7 OHRP Assurance Process
3.8 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