1.1 Background

1.1.1 Federal regulations require that institutions define several categories of investigator noncompliance, investigate allegations of investigator noncompliance, and report findings of noncompliance to the IRB, institutional officials, and certain federal agencies and department heads.

1.1.1.1 The University of Alabama defines **Noncompliance** as any failure of an investigator to follow (a) federal regulations, state laws, or institutional policies relevant to human subjects research, or (b) the requirements and determinations imposed by the University of Alabama (UA) IRBs.

1.1.1.2 **Minor Administrative Noncompliance** is an occasional/isolated instance of noncompliance that does not affect the rights and welfare of participants or put participants at risk of harm. Examples include a single instance of failure to submit a continuing review application to the IRB in time to prevent the lapse of study approval or failing to sign a protocol application as required.

1.1.1.3 **Serious Noncompliance** is non-compliance that affects the rights and welfare of participants or that may put participants at risk of harm, whether involuntary, careless, reckless, or intentional. (These terms represent an ascending order of seriousness.) The noncompliance may represent failure to comply with federal law/regulations, Alabama law, the ethical principles of the Belmont Report, and/or UA IRB policies, procedures, and determinations.

**Continuing Noncompliance** is multiple or repeated instances of noncompliance, particularly after written notice from the IRB that the investigator must take or must not take a certain action, thus suggesting a pattern of behavior or an unwillingness to follow IRB direction. The multiple or repeated instances of noncompliance may occur on one protocol or on more than one protocol and may occur simultaneously over a period of time. Instances of continuing noncompliance may also be judged as serious. Although continuing noncompliance may consist in principle of minor administrative forms of noncompliance, the IRB may regard multiples of such events as indicative of lax conduct by the investigator and may term them serious. For example, an investigator who fails to renew or formally close more than two studies may be considered to be in continuing noncompliance and incur penalties such as the refusal of ORC to accept more applications from the investigator or his/her students for a specified period of time.
1.1.1.4 An **Allegation of Noncompliance** is an unproven assertion of noncompliance made by an informant, IRB chair or member, or Research Compliance staff member against an investigator which will be investigated by the IRB.

1.1.1.5 The **alleging party** is the author of an assertion of noncompliance.

1.1.1.6 A **Finding of Noncompliance** is a decision by the IRB that an allegation of noncompliance is in fact true. A finding of noncompliance exists because of clear evidence from an investigation in light of clear evidence, an admission by the investigator that noncompliance has occurred, or an investigation of an allegation has determined the allegation to be true. The finding shall be reported in accordance with IRB procedure and corrective or disciplinary actions may be imposed on the investigator.

1.2 Policy Statement.

1.2.1 It is the policy of the University of Alabama that any person with knowledge or suspicion of investigator noncompliance, including the investigator, shall report an allegation of noncompliance to the Office for Research Compliance, IRB chair, an IRB member, a Research Compliance Specialist (RCS) or the Director of Research Compliance (DRC).

1.2.2 No actions shall be taken against any person who files an allegation of noncompliance in good faith. Allegations may be filed anonymously. Confidentiality of an identified alleging party shall be preserved to the extent possible.

1.2.3 The IRBs shall establish procedures for detecting (discovering), investigating, and reporting investigator noncompliance and determine immediate actions needed to protect participants.

1.2.4 **Examples of noncompliance** include but are not limited to:

1.2.4.1 Failure to obtain informed consent or inadequate procedures for obtaining informed consent from human subjects;

1.2.4.2 Conducting human subjects research without an IRB-approved protocol or exemption;

1.2.4.3 Inadequate supervision of research that involves potential risks to subjects and others;

1.2.4.4 Conducting research, including enrollment of subjects, when a UA IRB approval has expired or has been suspended or terminated;

1.2.4.5 Initiating changes to the research protocol without prior IRB approval unless the change is necessary to eliminate apparent immediate hazards to the subject;

1.2.4.6 Failing to adhere to the conditions of approval of a protocol as specified by a UA IRB, including timely response to IRB requirements for revision or resubmission, continuing review, or study closure;
1.2.4.7 Starting research under a protocol before meeting the conditions required by an IRB and receiving an IRB notification of approval;

1.2.4.8 Failing to take IRB or institutionally required human subjects protection training;

1.2.4.9 Enrolling more subjects than approved by an IRB;

1.2.4.10 Failing to have research participants sign a new consent form when new and relevant risks are discovered or failing to provide this new information to participants;

1.2.4.11 Altering an IRB-approved consent process or document or an IRB-approved recruitment process without prior IRB approval.

1.2.5 Examples of serious noncompliance include but are not limited to:

1.2.5.1 One or more instances of conduct defined above as noncompliance that exposes subjects or others to risks of harm that are not an inherent part of the approved research protocol

1.2.5.2 Conduct defined as noncompliance above, even though subjects or others have not been exposed to risks of harm not inherent in the approved protocol, where the IRB finds no mitigating circumstances;

1.2.5.3 More than two administrative withdrawals of approved protocols by the IRB;

1.2.5.4 Misrepresentation of information related to the human subjects research protocol or performance of the research;

1.2.5.5 Conducting non-exempt research without IRB approval;

1.2.5.6 Making substantive changes to a previously approved protocol without IRB approval;

1.2.5.7 Failing to report serious adverse events;

1.2.6 The IRBs shall educate investigators about the nature of noncompliance.

1.2.7 Investigators who believe that the IRB has erred in its finding of noncompliance may submit a written request asking the IRB to reconsider. The report should clearly indicate the facts or the interpretation in dispute, providing supporting evidence where applicable. The decisions of the IRB regarding whether or not to reconsider and if so, to change or retain its original finding shall be final and cannot be overruled by other university officials.

1.2.8 Allegations dealing with such behavior as falsification of data shall be considered as academic misconduct and shall be subject to that University policy and procedure.

1.2.9 The DRC and IRBs shall monitor the nature of investigator noncompliance as an aid to improving routine post-approval monitoring of protocols, the process of monitoring
for cause, and for investigator education about compliance. Such improvements may become part of a quality improvement plan.

1.3 Objective

1.3.1 Implementation of this policy will ensure maintenance of the integrity of the UA program to protect human research participants and that the UA IRBs are compliant with federal regulations and AAHRPP standards for accreditation.

1.4 Responsibility.

1.4.1 The Vice President for Research is ultimately responsible for this policy. Enabling parties include the Director of Research Compliance, Research Compliance staff, IRB members and chairs, and investigators, research study personnel, research participants, or others who report allegations of noncompliance.

2.0 PROCEDURE

2.1 Submission of Allegations of Noncompliance

2.1.1 A person with knowledge or suspicion of investigator noncompliance, including the investigator, reports an allegation of investigator noncompliance to the IRB office, IRB chair, an IRB member, a Research Compliance Specialist (RCS) or the Director of Research Compliance (DRC).

2.1.1.1 Allegations of noncompliance may also arise from (a) IRB discussions at convened meetings, (b) expedited review, (c) reports from the Manager of Research Compliance, (d) comments, questions, complaints, and concerns submitted through the outreach website; and (e) completed Surveys for Participants in UA-Sponsored Research, also available on the outreach website.

2.1.2 Any medium (phone, e-mail, letter, personal visit, etc.) may be used for report of the allegation. Although no form is required, the report should ideally include:

2.1.2.1 The name of the principal investigator or other person charged with the offense;

2.1.2.2 The study title and IRB number if known;

2.1.2.3 The relationship between the alleging party, the investigator, and the research protocol;

2.1.2.4 A description of the nature of the noncompliance (e.g., enrolling participants in an unapproved study; departing from the IRB-approved recruitment script to minimize the risks and increase enrollment) in sufficient detail that the recipient can understand the problem. (It is understood that some reporters may not be fluent in scientific or IRB terminology).

2.1.2.5 A description of the kind and quantity of evidence to support the allegation;
2.1.2.6 Identification of any possible or known effects on the risks to participants;

2.1.2.7 The date(s) or time period of the noncompliance;

2.1.2.8 Reporters may or may not identify themselves. All allegations will be investigated for substance and seriousness.

2.2 Management of Allegations of Noncompliance

2.2.1 All allegations or admissions of noncompliance are forward to the DRC.

2.2.2 The DRC reviews the allegation and determines whether it is a case of Minor Administrative Noncompliance and whether there is a corrective action that can be readily implemented to prevent recurrence (e.g., notifying the investigator that he has failed to sign the IRB application or to renew or close an approved protocol in a timely manner). If so, a notation will be made on the investigator’s file, the IRB will be informed of the instance, and no further action is needed by IRB.

2.2.2.1 On the occasion of a second instance of minor incompliance, the investigator will receive a letter as above, plus the information that a third instance will be reviewed as a pattern indicating consistent noncompliance.

2.2.2.2 A third instance of minor administrative noncompliance will be reviewed by the IRB as possible persistent noncompliance.

2.2.3 If the DRC determines that the allegation is either serious or continuing, s/he will notify the Chair of the appropriate IRB immediately and direct the manager of research compliance (MRC) to supply the Chair and any persons the chair may designate with all materials pertinent to the allegation (e.g., the approval letter, requirements for revision, consent documents, descriptions of identified risks, etc.). The MRC also reviews the investigator's file for the presence of other instances of noncompliance and reports them, with any descriptive materials, in case such instances may indicate a pattern of continuing noncompliance.

2.2.4 The IRB chair reviews the allegation and determines if immediate action is needed to protect human participants in the research. (That is, at first reading the allegation appears serious and raises major issues of participant risk or abrogation of participants' rights or welfare.) If desired, the chair may consult with the DRC, other members of the IRB or an external consultant about this judgment.

2.2.5 If immediate action is necessary, the IRB chair may suspend the study pending the results of the investigation.

2.2.5.1 The investigator will be notified immediately of the allegation and the decision and instructed to suspend all or specified research activities while the issue of noncompliance is reviewed, consistent with Federal Mandate (45 CFR §46.113). This notification may be made by telephone but will be followed with an appropriate letter. (As these letters are likely to be highly individual, no template letters have been prepared.)
2.2.6 All allegations of misconduct will be investigated, whether made anonymously or not.

2.2.7 If the alleging party provided contact information the chair contacts the alleging party to obtain, verify, or amplify the information contained in the allegation to obtain the elements specified in 2.1.2 above. The alleging party will be told that his remarks are being recorded (written) and will be reported as investigative data. The chair will also use this contact(s) as an opportunity to determine whether the allegation was made in good faith and appears credible. This determination, while subjective and variable across incidents, may be spurred by such evidence as remarks that indicate rancor between the alleging party and the investigator or the presentation of mutually exclusive or inconsistent facts. Any doubts about the substance or circumstances of the allegation become part of the chair’s reports to the IRB.

2.2.8 The IRB chair prepares a letter to the investigator informing him/her of the allegation (if he is not the source of the report), the impending investigation, and of his right to respond to the allegation in writing and to appear before the IRB at the meeting at which the investigative report is acted upon.

2.2.9 The IRB chair initiates monitoring of the study for cause, designating persons (e.g., him or herself, Manager of Research Compliance, IRB members) to perform the investigation and specifies the time period in which it is to be performed and reported upon. See POLICY: Monitoring of Previously Approved Protocols for Cause: Suspension and Termination for procedure. The initial focus of the investigation is on the contents of the allegation but the appointed monitors may expand the investigation to any pertinent circumstances such as those that cast doubt on the good faith of the person making the allegation. The IRB Chair or designee completes FORM: Report of Investigation of Allegation of Noncompliance.

2.2.10 The DRC and the IRB Chair either place the Report of the Monitoring Committee on the agenda of the next scheduled IRB meeting or call a convened meeting to act upon the report.

2.2.11 The IRB chair appoints a primary reviewer to present the allegation and the findings from the monitoring. All IRB members receive all study materials relevant to the allegation and may contribute to the discussion, including the Report of Study Investigation from the monitoring committee and communications between the investigator and IRB.

2.3 Convened IRB’s Review of Allegations of Serious or Continuing Noncompliance

2.3.1 The IRB considers the seriousness of each event in relation to the protection of participants or others and whether the allegations of noncompliance are serious and/or continuing. The IRB’s deliberations may be supplemented by statements from the principal investigator or research team, review of statements in UA and IRB policies and procedures, the Belmont Report, Legal Counsel regarding Alabama law, and the investigator’s IRB file.

2.3.2 The IRB determines (a) whether noncompliance has occurred, (b) whether it is serious and/ or continuing, (c) what corrective or protective actions will be required of the investigator, (d) what follow-up measures will be conducted by Research
Compliance staff and on what schedule to assess investigator compliance with board requirements, and (e) what recommendations, if any, should be made to the Institutional Official regarding reporting of noncompliance to OHRP, the FDA, and any other federal department or agency that funds or supports the research in which the noncompliance occurred. These determinations shall include assessment of whether the time frame for reporting noncompliance was met.

2.3.2.1 All deaths related to the research procedures must be reported immediately or within no more than 48 hours after the death.

2.3.2.2 Events involving unanticipated life-threatening experiences must be reported within 7 calendar days of the investigator’s receipt of the information.

2.3.2.3 All other serious and unanticipated events—short of death or life-threatening experiences—must be reported within 14 calendar days of the investigator’s receipt of the information.

2.3.3 The IRB may also suspect or determine that the noncompliant behavior was actually a case of scientific or academic misconduct. If so, the case will be referred to the Vice President for Research and will be managed under the terms of the UA Policy on Academic and Scientific Misconduct (In revision). NOTE: It is possible that a given case may include both noncompliance and academic/scientific misconduct. For example, falsification of data may increase risk to future research participants or patients. If so, the IRB and the academic division shall each pursue their investigations and inform the other unit of their findings.

2.3.3.1 The IRB minutes reflect the discussion and decisions of the IRB about allegations of noncompliance, any corrective/protective actions required of the investigator, plans for follow-up of investigator compliance with board requirements, and document the discussion about incidents that do not clearly meet the definition of serious or continuing noncompliance.

2.3.3.2 The IRB chair communicates the IRB decisions to the investigator in writing (electronically) within two business days of the board meeting, including the steps needed to be in compliance, the dates by which compliance must be accomplished, and, if relevant, the notification that timely failure to comply may lead to referral to the Vice President for Research/Institutional Official for possible disciplinary action.

2.3.4 Corrective/Protective Actions by IRB Regarding Noncompliance

2.3.4.1 IRB actions related to protocols found to be in noncompliance include:

2.3.4.1.1 Requesting or requiring the investigator to modify the protocol;

2.3.4.1.2 Initiating monitoring of the research or requiring more frequent monitoring of the protocol (more than that required for annual review or routine quality control), possibly including observation of the consent process;
2.3.4.1.3 Requesting or requiring the investigator to modify the consent process or consent documents;

2.3.4.1.4 Requiring the investigator to provide additional information to current and/or past participants or to have participants reconsent to participation;

2.3.4.1.5 Requiring additional training of the investigator and/or study staff;

2.3.4.1.6 Reconsideration of IRB approval;

2.3.4.1.7 IRB refusal to review additional applications from the investigator until administratively withdrawn studies have been formally closed or transferred, or until new re-applications for those studies have been submitted. In case of faculty supervisors of student research, this includes both new applications from them and from their student investigators.

2.3.4.1.8 Suspension of the research;

2.3.4.1.9 Termination of the research;

2.3.4.1.10 Refer the matter for further consideration by the Institutional Official. NOTE: Although the IRB can suspend the research study, only the Institutional Official has the authority to suspend an investigator’s privileges to conduct research.

2.4 Investigator appeal of IRB decision regarding noncompliance

2.4.1 Investigators may appeal an IRB decision about noncompliance by filing a written request for reconsideration with the IRB chair. This request should clearly identify the facts or the interpretation in dispute, providing supporting evidence where applicable. If the study was suspended by the IRB chair, research activity must cease until the outcome of the reconsideration.

2.4.2 The IRB will review all requests for reconsideration and decide whether it will or will not reconsider. Reconsiderations of decisions will at the next scheduled meeting of the IRB.

2.4.3 The decision of the IRB regarding the fact or outcome of reconsideration shall be final and cannot be overruled by other university officials.

3.0 REFERENCES

3.1 45 CFR §46.103(b)(5)(i)

3.2 45 CFR §46.116(b)(5)

3.3 21 CFR §50.25 (b)(3)
3.4 21 CFR §56.108(b)(2)
3.5 OHRP Guidance on Reporting Incidents to OHRP
3.6 DoD: DoDD 3216.2, para 4.10; SECNAVINST 3900.39D.para. 8d(2) and 6k

4.0 RELATED SECTIONS

4.1 University of Alabama Policy on Academic/Scientific Misconduct (Under Revision, December 2008)
4.2 POLICY: Routine Post-Approval Monitoring of Protocols
4.3 POLICY: Monitoring of Previously Approved Protocols for Cause: Suspension and Termination
4.4 POLICY: Reportable Events, Unanticipated Problems, and Adverse Events
4.5 FORM: Report of Study Problem
4.6 GUIDANCE: General Responsibilities of Investigators
4.8 POLICY: Investigator and Staff Response to Participants' Questions, Complaints, and Concerns
4.9 POLICY: Participant and Community questions, Suggestions, Complaints, and Concerns About Research Studies
4.10 POLICY: Closure of IRB Protocols