1.0 POLICY

1.1 Background

1.1.1 The University of Alabama, UA investigators and research staff, and the UA IRBs equally share the responsibility for the protection of human research participants as required by local, state, and federal laws, and as set forth in The Belmont Report. As a means of quality improvement and evaluation of protection of human subjects and compliance, the IRBs monitor previously approved research routinely and for cause.

1.1.2 Monitoring for Cause means an IRB monitoring activity initiated because of information, a complaint, or an allegation that a serious noncompliant action is occurring in an approved study or that an investigator is demonstrating continuing noncompliance.

1.1.3 Noncompliance is 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. Noncompliance may be minor administrative, serious, and/or continuing.

1.1.3.1 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, such as 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 an IRB application. A single instance of this category is managed clerically by the Director of Research Compliance and does not stimulate consideration of this policy.

1.1.3.2 Serious noncompliance affects the rights and welfare of participants or puts them at risk of harm and may be involuntary, careless, reckless, or intentional.

1.1.3.3 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.

1.1.4 Federal regulations require that the IRB have the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to participants. Suspensions and terminations represent actions by the IRB to
temporarily or permanently withdraw approval for some or all research procedures. IRBs should have policies and procedures for suspending or terminating previously approved research.

1.1.5 **Suspension** refers to an action by IRB to temporarily withdraw approval for some or all research procedures by the principal investigator or other personnel pending further action by the IRB. The suspension may be in response to a planned or unplanned sponsor or investigator-imposed suspension, findings of a routine post-approval monitoring, or to complaints, specific study events reported by the investigator or others, or allegations of noncompliance. (See Statement 1.2.3 for complete list of triggers for monitoring.)

1.1.6 **Termination** refers to an action initiated by the IRB to withdraw permanently approval for some or all research procedures by the principal investigator or other personnel.

1.1.7 This policy deals only with monitoring for cause and to possible cases of serious or continuing noncompliance. See POLICY: Allegations and Findings of Noncompliance for management of Minor Administrative Noncompliance. See POLICY: Routine Post-Approval Monitoring of Approved Protocols for management of post-approval monitoring for quality assurance/improvement purposes (not “for cause”).

1.2 Policy Statement.

1.2.1 It is the policy of the University of Alabama IRB that all currently approved research is subject to modification or change in approval status, as deemed necessary by the UA IRB to protect human research participants, ensure investigator compliance, and comply with federal regulations and accreditation recommendations.

1.2.2 All complaints or concerns about a study shall be investigated by the IRB and a determination made about whether or not the complaint or concern is justified and whether suspension or termination is appropriate.

1.2.3 Triggers for investigation for cause and possible suspension or termination include but are not limited to:

1.2.3.1 Planned or unplanned suspensions or terminations by the investigator or study sponsor;

1.2.3.2 An externally initiated complaint (OHRP, FDA, Sponsor) of potential protocol violations or regulatory non-compliance;

1.2.3.3 An internally initiated complaint or concern (a participant, family member, research staff member) or a completed Survey of Participants in UA-Sponsored Research that raises a question, complaint, or concern;

1.2.3.4 A discovery by the investigator of potential additional risks;
1.2.3.5 Reports from Data Safety Monitoring Boards;

1.2.3.6 IRB deliberations about the proposal or an investigator history of poor adherence to UA or IRB policies and procedures;

1.2.3.7 Serious or continuing noncompliance by the investigator with federal regulations, IRB policies, or IRB requirements;

1.2.3.8 Reports of serious unsatisfactory practices from a routine post-approval monitoring team;

1.2.3.9 Inappropriate involvement of human subjects in research, e.g., subjects are participating without giving informed consent; studies that have not been reviewed or approved by the IRB are underway;

1.2.3.10 Abridgement or inhibition of the rights or welfare of participants;

1.2.3.11 New information regarding increased risk to human participants.

1.2.3.12 Reports from any source of unusual morbidity or mortality.

1.2.4 The IRB has the authority to suspend approval for all or parts of an approved study while it gathers additional information about the complaint or concern or to suspend approval before investigation of a complaint if it sees a possibility of serious harm to participants.

1.2.5 Following investigation the IRB has the authority to inform investigators that all or parts of an approved study are terminated. In most cases termination follows suspension but serious or persistent noncompliance with IRB requirements or the occurrence of unusual morbidity or mortality may mean that a study could be terminated immediately.

1.2.6 The IRB shall maintain written procedures for assuring prompt reporting to the IRB, appropriate institutional officials, sponsoring agencies, and the department.

1.2.7 When necessary the IRB shall report complaints or concerns about a study to the Vice President for Research/Institutional Official (IO). The IO shall notify the study sponsor, the Office for Human Research Protections (OHRP), and the Food and Drug Administration (FDA) as appropriate.

1.2.8 If the investigation supports the validity of the complaint/concern, the IRB may require termination of the study, certain modifications of design or procedures, increased frequency of monitoring, and notification, withdrawal, or follow-up of enrolled participants.

1.2.9 If investigation does not support the complaint/concern as valid, the IRB will immediately notify investigator that the study may return to active status.

1.2.10 All UA employees (investigators, faculty, research personnel, and non-research staff) and UA students are responsible for reporting known or suspected violations.
of local, state, or federal laws; UA and IRB policies; scientific misconduct; noncompliance; or increased or unusual risk to research participants to the Vice President for Research, Director of Research Compliance, or an IRB chair or member. The initial report of a complaint/concern should always be made to a UA official or university-affiliated person.

1.2.11 The identity of those who report possible violations of good ethical or legal practice shall be protected to the fullest extent possible.

1.3 Objective.

1.3.1 Implementation of this policy ensures that the rights and welfare of human research participants are protected, that IRB policy and requirements are followed, and that the University of Alabama is in compliance with federal regulations and accreditation standards.

1.4 Responsibility.

1.4.1 The Vice President for Research/Institutional Official (IO) is ultimately responsible for this policy. Enabling parties include the Office for Research Compliance, the IRB chairs and members, investigators and their staff, and professional or lay persons who raise concerns about the conduct of a research study.

2.0 PROCEDURE

2.1 Planned Investigator or Sponsor-Initiated Suspensions

2.1.1 If the investigator or study sponsor reports a planned suspension of activities at a certain point (for example, to perform a preliminary data analysis), the Director of Research Compliance (DRC) or the IRB chair notifies the IRB that the protocol is suspended while the planned action is completed. Upon completion of the action, the investigator will report the results to the IRB and request any needed modifications of the protocol.

2.2 Unplanned Investigator or Sponsor-Initiated Suspensions or Terminations

2.2.1 If an investigator or sponsor reports suspension because of new risks to participants, the IRB receives the report and decides whether to keep the study open pending new information or requests for modification of the protocol or whether to suspend it also.

2.2.2 If an investigator or sponsor reports that the study is terminated, the Director of Research Compliance (DRC) places the report on the IRB agenda and informs IRB that the study has been terminated.

2.3 Receipt of External Complaints or Concerns (All Sources Other Than Investigator or Sponsor)
2.3.1 Complaints or concerns will be accepted by any medium (telephone, e-mail, a completed FORM: Report of a Complaint or Concern about a Research, a letter to the DRC or other university-affiliated person, website).

2.3.2 The DRC will initiate tracking of the response to the complaint using FORM: Response to Complaint or Concern about Research Study and reviewing the concern/complaint, noting the level of review given the study and whether the concern/complaint involves risks to human participants.

2.3.3 Complaints or concerns about studies originally approved as exempt will be managed by the DRC, who will report findings and resolution at the next convened meeting of the IRB.

2.3.4 For studies given expedited review, the DRC and the appropriate IRB Chair will manage the concern/complaint and report findings to the IRB.

2.3.5 For studies given full board review, the DRC will notify the investigator that there has been a complaint and notify the IRB Chair of the need for the full board to review the concern/complaint. Depending on the seriousness of possible increased risks to participants, the IRB Chair may decide to suspend all or part of the study pending investigation, call a convened meeting of the board, or present the complaint/concern at the next regularly scheduled meeting of the board. If the IRB chair suspends part or all of the study, the suspension is reported to and reviewed by the convened IRB.

2.3.6 The board reviews the complaint/concern and decides how to proceed. Options include:

2.3.6.1.1 Asking the investigator to provide additional information before monitoring the study;

2.3.6.1.2 Instituting an investigative monitoring committee that may include the DRC and/or a Research Compliance Manager, the IRB Chair, one or two members, and if deemed desirable, a consultant.

2.3.7 The investigation will be planned, using FORMS “Checklist for Post-Approval Monitoring of Expedited and Full Board Protocols” and “Report of Complaint or Concern About a Research Study” if available.

2.3.8 The IRB Chair or designee contacts the investigator regarding available dates and times that reflect the seriousness of the complaint/concern and the availability of the monitors. In general the interval between contacting the PI and the monitoring visits will be between 24 and 96 hours (1-4 days). The PI need not be present for the visit but another investigator or the study/project director must be.

2.3.9 The monitoring committee visits the study.

2.3.9.1 If the committee finds no major deviations, serious noncompliance, or serious increased risks to participants, the monitors will complete a report of the visit within five working days that includes the FORM: Report of a Study Investigation by a Monitoring Committee and the completed checklist and forward the report to
the Director of Research Compliance and the IRB chair. The IRB chair will present this report to the IRB at the next scheduled meeting.

2.3.9.2 If the investigation finds evidence of major deviations from protocol, serious noncompliance, or serious increased risks to participants, the monitoring committee shall complete a report within 48 hours of its visit and forward the report to the Director of Research Compliance and the IRB Chair. The IRB Chair may seek external consultation, order increased monitoring, discuss the matter with a called or scheduled meeting of the IRB, or suspend the study until after a convened meeting.

2.3.9.3 A number of actions may be recommended by the IRB. These include but are not limited to suspension or termination of some or all of the research activities in the reviewed study and any approved studies closely related to it. The IRB may require the investigator to modify the approved protocol, submit interim reports on a specified frequency, notify participants about new study procedures or risks, follow up participants to monitor possible harm from the study, and inform the research staff of changes in procedures, retraining them if necessary, and implementing closer supervision of their activities.

2.3.9.3.1 When study approval is suspended or terminated, the IRB or the person ordering the suspension or termination:

2.3.9.3.1.1 Considers actions to protect the rights and welfare of currently enrolled participants;

2.3.9.3.1.2 Considers whether procedures for withdrawal of enrolled participants took into account their rights and welfare. [e.g., making arrangements for medical care off a research study, transfer to another investigator, and continuation in the research under independent monitoring.]

2.3.9.3.1.3 Considers informing current participants of the termination or suspension;

2.3.9.3.1.4 Has any adverse events or outcomes reported to the IRB.

2.3.9.4 The DRC or IRB chair prepares a report using FORM: Report of Study Investigation.

2.3.9.5 The DRC communicates the report and decision to:

2.3.9.5.1 The Vice President for Research/Institutional Official (always);

2.3.9.5.2 If appropriate, other University officials such as the Provost, the IRB member from University Legal Counsel, the Dean of the principal investigator’s school or college, and the department chair or program head;

2.3.9.5.3 The supervising professor (if the study is student research);

2.3.9.5.4 The complainant, if known and if a response was requested, and if the DRC decides a report is needed.
2.3.9.5.5 The Office for Sponsored Programs (when study is externally funded);

2.3.9.5.6 Any federal department that has oversight due to funding, conduct, or assurance, including but not limited to OHRP, FDA, NIH, DOD, and DOE within 30 days.

2.3.9.5.6.1 The Institutional Official reports to OHRP. In the IO’s absence, the Director of Research Compliance will do so.

2.3.9.5.6.2 If OHRP is likely to learn of the event before completion of a decision as to whether the event is reportable, the Director of Research Compliance and IRB Chair will provide OHRP with a preliminary report that describes the situation, indicates the current state of review of the event by the IRB, and a time frame for a final follow-up report.

2.3.9.6 The investigator immediately complies with the requirements of IRB as described in the report.

2.4 Enforcement and Discipline

2.4.1 The IRB may specify more frequent monitoring of the study by compliance personnel; direct observation of certain study activities such as consenting or data collection sessions; contacts with current or former participants to verify that specified changes have been made or that data collection has ceased; or other measures deemed necessary to assess compliance with recommendations from the monitoring committee.

2.4.2 Investigator failure to implement IRB-required changes in the research may lead to disciplinary action such as loss of investigator privileges or employment.

2.4.3 Research staff who fails to report continued violation of IRB-required changes may be subject to institutional discipline such as loss of employment on this or other research studies or being reported to OHRP.

2.4.4 A record of the complaint/concern, the monitoring report, and investigator compliance with IRB requirements will be placed in the investigator’s folder. This information will be used to identify patterns of noncompliance or more serious noncompliance with IRB requirements.

2.4.5 The university must report to AAHRPP within 48 hours after the university or any research (if the research is notified rather than the university) becomes aware of: 1) any negative action taken by a government oversight office, including, but not limited to OHRP determination letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA restrictions placed on IRBs or investigators. Organizations outside the US must report any sanctions taken by their country regulatory agencies, 2) any litigation, arbitration, or settlements initiated related to human research protections, 3) any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the university’s HRPP.
3.0 REFERENCES


3.2 OHRP Guidance on Reporting Incidents to OHRP

3.3 OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects of Others and Adverse Events

3.4 FDA Information Sheets: Continuing Review after Study Approval.

4.0 RELATED SECTIONS

4.1 POLICY: Routine Post-Approval Monitoring of Approved Protocols

4.2 POLICY: Allegations and Findings of Noncompliance

4.3 FORM: Report of a Complaint or Concern About a Research Study

4.4 FORM: Survey of Participants in UA-Sponsored Research

4.5 FORM: Checklist for Post Approval Monitoring of Expedited and Full Board Protocols

4.6 FORM: Report of A Study Investigation by a Monitoring Committee