1.0 POLICY

1.1 Background

1.1.1 Federal Regulations (45 CFR Part 46, 21 CFR Part 56) and AAHRPP require institutions to evaluate their research programs so that risks to human subjects are identified, minimized, and reasonable in relation to any anticipated benefits and to maintain adequate documentation of its activities. Risks may be physical, social, economic, psychological, or legal. Benefits may take the form of therapy, education, information, resources, or empowerments and may accrue to participants or their community.

1.1.2 IRBs are to give special attention to risks and benefits with participants from vulnerable populations, defined as persons with some characteristic that presents special issues for their inclusion or exclusion in research or their treatment within a study. They may be especially prone to coercion, undue influence, or stigmatization or have some limitation or incapacity that is not part of normal growth and development that interferes with their ability to understand their role, risks, or benefits in a research study and to give truly informed consent.

1.1.3 Vulnerable populations addressed in the federal regulations are pregnant women, fetuses, non-viable neonates, neonates of uncertain viability, prisoners, children, mentally disabled persons, and economically or educationally disadvantaged persons. However, the elderly, the terminally ill, the physically handicapped, cognitively impaired persons, persons with HIV/AIDS, members of some racial and ethnic minorities, employees, members of the Armed Forces, patients in emergency rooms, homeless people, refugees, members of communities unfamiliar with modern medical concepts, and students are other groups that may be considered vulnerable within the context of research protocols by an investigator or an IRB. The determination of a vulnerable population is highly context-dependent--both investigators and IRBs may identify prospective participants as vulnerable populations. Investigators must justify the inclusion or exclusion of such persons from research and explain how the vulnerable characteristic will be addressed to protect human subjects. IRBs must evaluate the appropriateness of sample characteristics or size and the adequacy of protection for vulnerable participants.
1.1.4 Persons may fall into more than one category of vulnerability. For example, a prisoner may be a child or a pregnant woman. Investigators must address all sources of vulnerability.

1.1.5 Some members of vulnerable populations will have guardians or legally authorized representatives (LARS) who must figure prominently in obtaining informed consent.

1.1.6 Investigator or staff conflict of interest may constitute a risk to human participants by adversely affecting their protection in terms of the criteria for IRB approval or the integrity of the research.

1.1.7 This policy deals with the general topic of evaluating and minimizing risk in research populations. See Related Section for other policies on particular vulnerable populations (students, children, prisoners, pregnant women, fetuses, and neonates), evaluating prospects' comprehension of research explanations, obtaining informed consent, and conflict of interest.

1.2 Policy Statement

1.2.1 IRB membership at the University of Alabama will include persons with expertise in selected vulnerable populations routinely reviewed by the IRB (such as children or prisoners), non-scientists, and a non-affiliated community representative. The Office of Research Compliance staff will screen IRB membership applicants for expertise with vulnerable categories to insure that designated representatives are available to review research involving children, prisoners, or other vulnerable populations, as may be required.

1.2.2 A non-scientist must be present at all IRB meetings.

1.2.3 In reviewing research protocols, the IRB will use a reasoned, nuanced approach to evaluating vulnerability and risk protection rather than taking a simple subpopulation or "labeled group" approach. The IRB will review study design to determine if it maximizes the safety of the research participant through appropriate data collection, assessment and monitoring. These evaluations will especially consider populations specified by 21 CFR Part 56 and 45 CFR Part 46 as particularly vulnerable to risks inherent in research. The IRB is authorized to approve research under the guidelines provided by 21 CFR Part 56.111 and 45 CFR Part 46.111 – if:

1.2.3.1 Risks to subjects are minimized,

1.2.3.2 Risks to subjects are reasonable in relation to anticipated benefits,

1.2.3.3 Selection of subjects is equitable,

1.2.3.4 Informed consent will be sought from each prospective subject or subject's legally authorized representative (LAR),

1.2.3.5 Informed consent will be appropriately documented,
1.2.3.6 The research plan, where appropriate, makes adequate provision for monitoring data,

1.2.3.7 There are adequate provisions to protect the privacy of subjects and the confidentiality of the data.

1.2.4 The IRB is responsible for reviewing clinical trials to determine human subject research eligibility, including recruitment and selection procedures.

1.2.5 The IRB may seek consultation to determine that risks to research populations have been adequately identified and addressed.

1.2.6 Investigators shall provide all required or requested information to the IRB for the IRB to make risk determinations.

1.2.7 Addition of an initial or a different vulnerable population to an approved protocol requires submission of FORM: Modification of an Approved Protocol. This may result in changing a proposal approved as Expedited to full board review.

1.2.8 Investigators shall not implement a change in an approved IRB protocol without prior IRB approval, except for correction of spelling or grammatical errors or to address an apparent immediate hazard to a research subject.

1.2.9 Implementation of this policy will ensure the safety of human subjects participating in research by applying a formal and rigorous analysis to identify and minimize the risks inherent in research for all populations.

1.3 Responsibility

1.3.1 The Vice President for Research is ultimately responsible for this policy. Enabling parties include the Director of Research Compliance and Staff, IRB chairs and members, members of the Council of Associate Deans for Research, study investigators, and faculty supervisors of student research.

2.0 PROCEDURE

2.1 Risk identification and Protection.

2.1.1 Study investigators will provide all required or requested information to the IRB for the IRB to make risk determinations, including disclosure and management of the appearance or fact of conflict of interest, and, if appropriate, supplemental forms for specific vulnerable populations. See GUIDANCE: IRB Application Guidelines, and the FORM: IRB Checklist for Reviewers and Investigators on this website for information about writing satisfactory applications and managing study risks.

2.1.2 All research applications must indicate the level of risk associated with the proposed research by describing the scientific context of the study, including:

2.1.1.1 Study methodology
2.1.1.2 The sample, including identification and justification of the use of vulnerable populations
2.1.1.3 Each procedure to which human subjects will be exposed, their frequency and duration
2.1.1.4 Foreseeable risks and their type: physical, psychological, social or economic.
2.1.1.5 Alternate treatments or the withholding of normal treatment
2.1.1.6 Procedures to protect privacy of persons and confidentiality of data
2.1.1.7 Procedures to assess prospects’ understanding of the study and their ability to give informed consent and allow time for questions or reflection about participation
2.1.1.8 Procedures to minimize the risk to human subjects
2.1.1.9 Potential benefits accruing directly to participants (therapy, education, information, resources, etc.), their community, or to society by the acquisition of scientific knowledge. Benefits must not be promised and must seem logically possible or likely. (No stretch of imagination should be required to identify a possible benefit.)
2.1.1.10 Whether the potential benefits outweigh the risks inherent in the research.

2.2 Risk analysis and minimization.

2.2.1 The IRB considers the overall risk level to participants in evaluating proposed research in accordance with the conditions outlined in 45 CFR 46.111(a)(1-7), 21 CFR 56.111 7), as well as the ethical principles outlined in the Belmont Report.

2.2.2 The Research Compliance Specialists will verify that the application is complete and ready for review by the IRB using FORM: Checklist for Completeness of IRB Applications. If it is incomplete, the missing information will be obtained from investigators in time for IRB review.

2.2.3 Using FORM: IRB Checklist for Reviewers and Investigators, IRB members specifically review the application for identifiable risks to research participants and the minimization of those risks. For studies undergoing Full-Board Review at convened meetings, the nature and extent of risk and risk minimization will be specifically discussed. For studies undergoing Expedited Review, reviewers will state agreement with the judgments and actions proposed by the investigator or their own judgment about risk level and adequacy of risk minimization and any additional safeguards to be implemented.

2.2.4 The assessment of the presence of undeclared COI or the effects and management of declared COI on risk to human participants is part of the review of all applications, whether for exempt, expedited, or full board review.
2.2.4 In order to approve the application, the IRB must determine that the proposed research:

2.2.4.1 Has a sound research design [45 CFR 46.111(a)(1)(i) and 21 CFR 56.111(a)(1)(i)].

2.2.4.2 Does not expose subject to unnecessary risks [45 CFR 46.111(a)(1)(ii) and 21 CFR 56.111(a)(1)(ii)].

2.2.4.3 Whenever appropriate, utilizes procedures that are already being performed on the subjects for diagnostic or treatment purposes.

2.2 The IRB also considers the professional qualifications and resources (including time, equipment and support services) of the research team to protect and minimize potential harm to study participants. The IRB will ensure that clinicians involved in the research maintain appropriate professional credentials and licensing privileges.

2.3 Reasonable Risks Relative to Anticipated Benefits.

2.3.1 The IRB will use Form: IRB Checklist for Reviewers and Investigators to assist in identification of risks and determination of whether risks are reasonable in relation to the potential benefits to study participants and to society. The IRB develops its risk-benefit analysis by evaluating the most current information about the risk and benefits of the interventions involved in the research, as well as the reliability of this information, or by seeking consultation. The IRB considers only those risks that result from the research, and does not consider long-range effects (e.g., public policy implications) of applying the knowledge gained in the research [45 CFR 46.111(a)(2) and 21 CFR 56.111(a)(2)].

2.3.2 The nature of risks, strategies of minimizing risks, the risk-benefit ratio, and the presence of vulnerable populations will be considered in deciding whether the application will be approved for one year or less, whether interim reports are required of the investigator, whether the consent process should be monitored, and whether the study should be monitored during the approval period.

2.5 Documenting IRB Decisions About Risks and Risk Minimization

2.5.1 For full board review, the IRB minutes will describe the discussion of risks, risk minimization, risk-benefit ratio, issues related to COI, and conclusions about the protection of vulnerable populations in order to verify that it has effectively addressed risks and risk minimization for every protocol undergoing review.

2.5.2 For expedited review, the reviewers will receive and complete Form: IRB Checklist for Reviewers and Investigator for each protocol. They will complete and return this form with the application face sheet when they recommend.
modifications to the informed consent document or consent procedure or propose additional safeguards if a vulnerable population or COI are involved.

3.0 REFERENCES

45 CFR §46.111(a)(l)
45 CFR §46.111(a)(2); (a) (6)
21 CFR§56.111(a)(l)
21 CFR §56.111(a) (2); 56.111 (a) (6)
The Belmont Report

AIDS/HIV-Related Research: http://www.hhs.gov/ohrp/irb/irb_chapter5.htm

4.0 RELATED SECTIONS

4.1 GUIDANCE: IRB Application Guidelines
4.2 FORM: IRB Checklist for Reviewers and Investigators
4.3 POLICY: Protection of Prisoners in Research (and other policies dealing with specific vulnerable populations)
4.4 FORM: Modification of an Approved Protocol
4.5 POLICY: Informed Consent Process And Documentation
4.6 POLICY: Investigator Assurance of Participant Comprehension
4.7 POLICY: Protection of Human Research Participants’ Privacy and Confidentiality
4.8 GUIDANCE: Alabama Law on Children, Minors, Consent, and Other Research-Related Topics
4.9 POLICY: IRB and Investigator Responsibilities for Applications Involving Declared or Undeclared Conflicts of Interest
4.10 GUIDANCE: Protection of Subjects in HIV/AIDS-Related Research