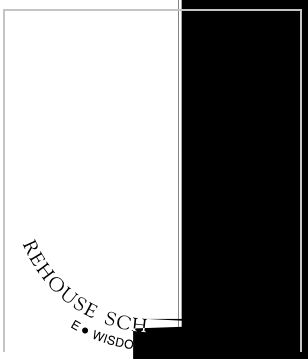

Morehouse Scho

Morehouse School of Medicine
Human Research Subjects Protection Program

Declaration of Institutional Review Board Authority

The Institutional Review Board (IRB), a component of the Human Research Subjects Protection Program of Morehouse School of Medicine, is constituted as required by federal regulations (45 CFR 46.101; 45 CFR 46.107; 21 CFR 56.101; 21 CFR 56.107) and well-respected ethical standards (The Belmont Report) to review and approve all research projects involving human subjects under the direction of the institution, shall have the authority to discharge its duties and responsibilities free from influence or coercion as declared by this document.

The IRB shall have the authority to approve, require modifications in, or disapprove all research activities under its jurisdiction (45 CFR 46.109(a); 21 CFR 56.109(a)). The institution shall not interfere with the deliberations or findings of the IRB. The institution reserves the authority to

medical treatment or emergency medical care to the extent the individual is permitted to do so under

THE IRB APPLICATION/PROPOSAL SUBMISSION AND REVIEW PROCESS

A. INVESTIGATIONAL ACTIVITIES REQUIRING IRB REVIEW AND APPROVAL

Any systematic investigation (*research*, 45 CFR 46.102(d) or *clinical investigation*, 21 CFR 50.3(c); 21 CFR 56.102(c)) involving human subjects (45 CFR 46.102(f); 21 CFR 50.3(g); 21 CFR 56.102(e)), including research development, testing and evaluation, which is designed, in whole or in part, to

a. A complete IRB Initial Protocol Review Application
Send the application to the IRB office via e-mail and forward a copy with all pertinent signatures to the IRB office via mail or internal distribution.

b. Informed Consent/Parental Permission/Assent Form(s)
These documents must reflect IRB format, style and readability standards as described by the templates and discussed further in these guidelines. Each document should have a header or footer indicating the version (such as the date of application for review) of the document. Forward these documents via e-mail along with the application for review.

c. Detailed Research Protocol
The research protocol (grant application or other descriptive document) should include the following information in sufficient detail to convincingly show scientific merit and justification for undertaking the study.

Background
he Objectives of the research project
c

proposal should contact the IRB administrator. The 30 day period allows the IRB to preview the application and provide feedback to investigators so that they may make changes prior to initial review.

2. Application P

1. General Review Criteria: The following criteria are taken into consideration for each protocol review:

a. Review of the Prospective Subject Population

The prospective subject population must be equitable (45 CFR

presents the prospect of **direct benefit** to individual subjects; 46.406 where the research lacks direct benefits to research subjects but is likely to yield generalizable knowledge about the subjectsÕ disorder or condition; and 46.407 - research that is not otherwise approvable but which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health and welfare of children, but only following approval by the Secretary of DHHS.

Further discussion of research-related risk may be found in other sections of these guidelines.

e. Review of Potential Benefits

A benefit is a valued or desired outcome. Benefits associated with participation in research can be classified generally as those that accrue to the subject directly (e.g., improvement of the subject's health status; acquisition by the subject of knowledge considered of value) and those that accrue to society (e.g., additions to the knowledge base). The IRB will review the anticipated benefits to both the subject and to others. In addition, the IRB will consider whether the benefits are maximized to the greatest extent possible through proper protocol design. Therefore, an underlying moral notion of "beneficence" should guide the investigator the design and conduct of the research

Financial or other forms of compensation or incentives are not considered benefits derived from research participation. Although the subject may consider financial compensation a desirable outcome, this fact will not be used in risk/benefit analysis.

f. Risk/Benefit Analysis

There are no strictly applied formulae 0 0 0.24 367.4515 440.76 cm BT 50 0 0 5e

h. Review of Confidentiality

The IRB will review the methods to be used to preserve confidentiality of information. If research data with subject identifiers will be made available to persons other than investigators, members of the research team, sponsors or federal agencies, the IRB will review the justification for sharing this data and determine acceptability of protective measures (45 CFR 46.111(a)(7), 21 CFR 56.111(a)(7)).

Under 45 CFR 164.508(b)(3)(i), the Morehouse School of medicine IRB does not require HIPAA authorizations for use or disclosure of protected health information to be combined with other regulatory requirements regarding informed consent to participate in research.

It is the policy of the IRB to request investigators to use standalone HIPAA authorizations permitting the use and disclosure of individually identifiable health information. The IRB need not approve standalone HIPAA authorizations.

force, fraud, deceit, duress, overreaching or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision."

The legal documentation of informed consent is the consent form signed by both the subject and the investigator. The ethical and, indeed, legal validity of, consent is, however, dependent upon the process of informed consent which requires the investigator to engage in dialogue or negotiation with the prospective subject. The consent form, therefore, should be used by the investigator as an instrument to guide the negotiations with the prospective subject. The informed consent form must embody the elements of informed consent contained in the DHHS and/or other applicable federal, state or local laws or regulations. As presented in Section II of these guidelines and policies, the IRB will review both the consent form and the process of informed consent to ensure the preservation of autonomy of research subjects as well as to ensure adequate documentation of informed consent (45 CFR 46.111(a)(4),(5),(7),(b); 21 CFR 56.111(a)(4),(5),(7),(b))

j. Review of Investigator Qualifications and Research Environment

The IRB will review investigator qualifications to assure the investigator has the appropriate qualifications and training to carry out the procedures described in the research. Investigators and each member of the research team must account for current training in human subjects research as required by the institution. In addition, the IRB may include in its review the adequacy of facilities, funds, equipment

(b)

In verifying information to determine whether unapproved changes have occurred, from sources other than the investigator, the IRB shall make inquiries directed to parties knowledgeable about the specific research protocol. These parties may include but not necessarily be limited to:

a resident research subject advocate

the research sponsor or external review/advisory panel

members of the research team

research subjects

To ensure prompt reporting to the IRB of proposed changes in a research activity; and, to ensure that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval, except when necessary to eliminate apparent immediate harm to subjects (45 CFR 46.103(b)(4)(iii); 21 CFR 56.108(a)(3),(4)), the IRB approval memorandum informs investigators as follows:

ÒAny advertisements, questionnaires or other written materials pertaining to human subjects must be reviewed and approved by the IRB before use in the project. Any changes made in either the protocol or the consent form must be brought to the attention of and approved by the IRB prior to implementation of such changes. If applicable, please bring this approval notice to the attention of the research administrator of any granting agency(ies) to which you have made application for funding. **Promptly notify the IRB of any changes in the protocol or consent process as well as any adverse events, or unanticipated problems to subjects or others as defined and required by current federal regulations and institutional policies.** This approval is issued with the understanding that you have read and agree to comply with all laws and regulations governing the conduct of this research involving human volunteers as well as the institutional

exceptions to informed consent (21 CFR 50.24 Exception from informed consent requirements for emergency research), the IRB shall promptly notify the investigator and the sponsor of the research in the event the IRB determines that it cannot approve the research because it fails to meet the criteria under se

IRB research protocol files are available for inspection and review by members of the IRB.

b. Full Board Review

Proposals that do not qualify for expedited review will be submitted to the full IRB. Following intake and preview, as described above, research protocols requiring full board review are assigned to a primary reviewer. The primary reviewer receives the entire file (including the InvestigatorÕs Brochure, when applicable). Reviewers document their findings and recommendations on the full board review documentation form. All IRB members receive a copy of the application for review and consent/assent documents. The primary reviewer presents findings at the convened meeting and makes a recommendation. The findings are discussed and all comments regarding changes to be made by the investigator and questions to be answered are recorded by the IRB administrator or other person assigned by the chair to record the minutes of the meeting. The primary reviewer, as well as any member of the IRB who wishes, submits a report of IRB protocol review form. Contents of the report form(s) are forwarded to the investigator for required action. In the event the primary reviewer is unable to attend the meeting, review findings and recommendations are forwarded to the IRB office and are presented to the IRB by the chair or a member designated by the chair. Within five to ten work days following the IRB meeting, the investigator will be notified of the IRB's decision concerning the proposal. Reviewed proposals will be assigned to one of four categories:

(1) **Approved:**
Notice of approval is sent to the investigator along with a approved informed consent document (if applicable) that is to be used for enrolling subjects. The investigator may begin the study.

(2) **Approved contingent upon specific minor modifications or clarifications:**
On occasion, the protocol, consent form or other pertinent document may contain minor errors or omiss

by way of the report of IRB protocol review form. The IRB administrator, chairman, vice chairman and/or an assigned member of the IRB may discuss the findings with the investigator to resolve issues raised in the review. Following resolution of issues and concerns raised, the proposal will be brought before the full IRB to complete the review at a subsequently convened meeting.

(4) **Disapproved:**

If a proposal is disapproved, the investigator has the right to respond to the IRB in person or in writing (45 CFR 46.109(d); 21 CFR 56.109(e)) When necessary, the IRB will seek consultation from qualified experts, other IRBs, the Office of Human Research Protections (OHRP) or the Food and Drug Administration (FDA). Every attempt will be made to resolve the identified problem(s). The IRB, however, retains final /F2.0 1 Tf [(E) 0.2 (ve) 0.2 (ry a) 0 s

a continuing review report the IRB will review and approve, if appropriate, continuation of the project for a specified period. Irregularities in reports (e.g., changes or differences noted from protocol or deviations from approved consent) may delay review and re-approval. The IRB will contact investigators to clarify irregularities. If questions and issues remain to be addressed following explanation by the investigator, the IRB will delay the review and verify the information through sponsors or other parties who should be knowledgeable about the research in question. When a project is terminated or is otherwise completed, the investigator must immediately notify the IRB in writing and submit a closing report. The IRB will inform investigators of any further requirements regarding the project.

7. Reporting Proposed Changes in a Research Protocol or Changes in the Informed Consent Document or Informed Consent Process

previously approved research require full board review or may be processed by expedited review considering and justifying the expedited review category(ies) using the reference ÒCategories of Research That May be Reviewed by the Institutional Review Board (IRB) through an Expedited Review ProcedureÓ (45 CFR 46.110; 21 CFR 56.110) as published in 63 FR 60364-60367, November 9, 1998, currently in effect and as may be amended.

Minor changes to previously approved research (45 CFR 46.110; 21 CFR 56.110) will be reasonably determined in the context of the research and may include but not necessarily be limited to: clarifications of risks so long as any new risks do not elevate risk factors beyond greater than minimal, changes in personnel, modest changes in subject compensation for participation, changes in sequence of scheduling, addition or elimination of procedures that do not elevate risk factors beyond greater than minimal, changes that improve the risk/benefit ratio, and any changes that improve the understanding of informed consent.

If a change in protocol is relatively minor (e.g., change in the sequence of follow up visits, change in personnel), it is not necessary to have the subject sign a revised consent form or an addendum to the consent form. If, however, the change is not minor (e.g., addition of an intervention not addressed in the original consent form or

The IRB recognizes the difficulty in defining adverse events and unanticipated problems that would require reporting as contemplated in current regulations. Therefore, the IRB will consider any current guidance or agency directive addressing reporting of adverse events and unanticipated problems.

Not all adverse events are unanticipated problems and not all unanticipated problems in research are necessarily adverse events that elevate risks to subjects or others. The term ÒadverseeventÓ is not found in the federal regulations controlling the conduct of human subjects research; however, it is the most commonly used expression intended to convey harm or injury in the context of human subjects research. The three most familiar federal regulations (45 CFR Part 46, and 21 CFR Parts 50 and 56) governing the conduct of human subjects research use the expression Òunanticipated problems involving risks to subjects or *others*Ó (emphasis added). The regulations do not define Òunanticipated problemsÓ or ÒothersÓ or what associated risks or severity of harm may give rise to unanticipated problems that would require ÒpromptÓ reporting to the IRB, appropriate institutional officials, and the department or agency head of HHS or the FDA.

There are, however, expressions in the regulations that may be reasonably interpreted as adverse events and/or unanticipated problems giving rise to risks to subjects or others. The terms described below are assumed to establish an interpretation of the term Òunanticipated problemsÓ requiring reporting as directed by the regulations. The common rule, 45 CFR 46, considers risks to include disclosure of private information that could reasonably place research subjects at risk of criminal or civil liability, or be damaging to

The IRB will forward on-site adverse event reports and its recommendations on such to the Office of Sponsored Research Administration within 5 working days following receipt of the report from the investigator.

56.108(b)(1)(2)(3), 45 CFR 46.113; 21 CFR 56.113). The IRB must also consider laws and regulations of the State of Georgia as may be applicable in the context of human research subjectsÕ protection. State laws that regulate professions as well as laws regulating administration and uses of drugs and controlled substances, e.g., as found under Title 43 Ð Professions and Businesses, Title 16 Ð Crimes and Offenses (includes the Georgia Controlled Substances Act and the Dangerous Drug Act), Title 24 Ð Evidence (includes confidentiality of research data), and Title 31 Ð Health (includes medical consent to treatment and surgery), are of particular relevance to human subjects research.

The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with applicable federal, state or local regulations or laws, or the IRBÕs requirements as set forth in its policies (45 CFR 46.113, 21 CFR 56.113). The IRB shall have authority to suspend or terminate approval of research that has been associated with unexpected serious harm to human research subjects or others (45 C FR 46.113, 21 CFR 56.113). The IRB shall have authority to observe, or have a third party observe, the consent process and the research (45 CFR 46.109(e), 21 CFR 56.109(f))

Any incident of non-compliance with federal policy or IRB guidelines should be reported in a timely manner (refer to 2.a., below) to the IRB. Non-compliance with IRB requirements is a violation of MSMÕs Federal-Wide Assurance and the federal regulations for the protection of human subjects. Non-compliance may result in suspension or termination of IRB approval. All incidents of non compliance reported or otherwise coming to the attention of the IRB will be brought also to the attention of appropriate department/unit heads, the Office of Sponsored Research Administration.

1. Interpretation of Federal Policy on Noncompliance and IRB Actions

Noncompliance is reasonably int 0.2 (s). q 0.24 0 0 0.24 72.51992 341.88 cm BT het (r

2. How Reports or Notices of No

Within 2 working days of issuing an order for suspension or withdrawal of IRB approval, the IRB will forward a preliminary written report to the investigator describing the reasons for issuing a suspension or withdrawal of approval. A copy of the report will be forwarded to the Office of Sponsored Research Administration. The investigator must respond to the IRBÕs determination within 5 working days of the date of suspension or withdrawal of IRB approval. The investigator must describe a course of action to correct noncompliance.

Following analysis of the investigatorÕs response and proposed course of action, within 2 additional working days, the IRB will determine whether the matter has been resolved and reinstate approval or whether the suspension or withdrawal of approval should remain in effect. In cases where the IRB determines that matters pertaining to 45 CFR 46.103; 21 CFR 56.108 have not resolved and the IRB continues the order for suspension or withdrawal of approval, the IRB will inform appropriate institutional officials to report the action taken to the agencies identified in I.E.3.b., below, as may be applicable to the case in question.

b. The IRB considers the person responsible for the Office of Sponsored Research Administration to be the appropriate institutional official to be notified and responsible for reporting to federal agencies as required by regulations. Reports sent by the Office of Sponsored Administration should include the following information:

For serious or continuing noncompliance:

- the MSM location, unit, department, etc., in which the research is conducted and the name of the person in charge of that location
- the title of the research project and/or grant proposal in which the noncompliance occurred, including any identifying research project numbers assigned by the IRB or sponsor/granting agency
- the name of the principal investigator(s)
- a detailed description of the noncompliance
- actions the institution is taking or plans to take to address the noncompliance (e.g., stop the study, require further education on humans subjects research and applicable regulations/guidelines, suspend research activities, suspend the investigator, suspend subject enrollment until noncompliance is addressed, conduct random audits of the study, etc.)

For suspension or termination of studies:

- the MSM location, unit, department, etc., in which the research is conducted and the name of the person in charge of that location
- the title of the research project and/or grant proposal suspended or terminated via suspension or withdrawal of IRB approval or through administrative authority, including any identifying

research project numbers assigned by the IRB or sponsor/granting agency
- the name of the principal investigator(s)
- a detailed description of the reas

subjects is anticipated. Reviews involving these categories of vulnerable subjects include research of any nature unless the research is determined by the IRB to be exempt under the provisions of 45 CFR 46.101(b).

Food and Drug Administration Categorization of Drug Risks to Fetus

Category A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm appears remote.
Category B	Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).
Category C	Either studies in animals have revealed adverse effects on the fetus (teratogenic, embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available. **Drugs should be given only if the potential benefit justifies the potential risk to the fetus.**
Category D	**There is positive evidence of human fetal risk**, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

Category X

IRB will review research involving this category of vulnerable subjects in compliance with additional safeguard requirements to include composition of the IRB as described under 45 CFR 46.304 and review and documentation of additional IRB duties as described under 45 CFR 46.305 considering permissible categories of research described under 45 CFR 46.306. The review and documentation process for research involving epidemiological studies on prisoners, the IRB will consider waiver of 45 CFR 46.305(a)(1)and(2) as described in the FR Vol. 68, No. 119, 6/20/03, 36929-36931, effective June 20, 2003. For purposes of reviewing research involving prisoners, the IRB considers a person who is incarcerated or under detention of a police power authority to be a prisoner. A person who is on parole or on probation is not considered to be a prisoner subject to the requirements of this subpart. In determining the risks to subjects in this category, the IRB will apply the definition of minimal risk as described in 45 CFR 46.303(d).

In the event a subject becomes a prisoner at some time subsequent to enrollment in research, the investigator must send a report to the IRB, within a reasonable time of such notice having come to the attention of the investigator. The report must include a plan describing how the research will be brought under Subpart C compliance as to prisoner research subjects. The plan will detail why it is in the best interest of prisoner subjects to continue in the research and to what extent the informed consent process must be changed. The plan must detail how prison authorities will allow access to the prisoners in a manner that preserves the best interest of the prisoners as well as the context of the research. If the investigator determines that it is in the best interest of prisoner subjects not to continue in the research or prisoner research subjects decide autonomously to withdraw from the study, the investigator must describe a procedure addressing the orderly or safe withdrawal of prisoner subjects from the research activity and any follow-up intended to take place after a subjectÕs participation terminates.

3. Children Involved as Subjects in Research

This category of human subjects research requires additional protections as described under 45 CR 46 Subpart D and 20 CFR 50 Subpart D, as well as ÒOHRP Guidance on Protections for Children as Research Subjects,Ó 31 August 2005; or as may be amended subsequently by OHRP SecretaryÕs Advisory Committee on Human Research Protections, Appendix B (pertaining to research involving children under 45 CFR 46.404; 405, and 406), November 25, 2005. The IRB will review research involving this category of subjects in compliance with additional safeguards and protections taking into consideration the exception of exemption at 45 CFR 46.101(b)(2) as described under ¤46.401(b). The IRB will review and document its findings in satisfaction of the conditions of all applicable sections expressed in 45 CFR 46.403 and 21 CFR 50.50 and approve

guardian permission and assent processes are discussed further under Section II of these guidelines and policies.

For the purpose of IRB review of research in this category of subjects, the terms minor and child will be considered to be synonymous and the legal status of minor or child will be identified according to current federal and state law. Generally, in the State of Georgia, a person under 18 years of age is considered a minor for transactions involving health care. The State of Georgia does not have an emancipated minors act.

4. Other Categories of Potentially Vulnerable Persons

The IRB considers the following factors in determining whether additional protections may be required:

- Employees
- Students at any level of education
- Economic status
- Education level
- Physical or medical disability/.88 cm BT (bi) 992 507.48 cm BT 50 0 0 50 0 0 T

SECTION II

Informed Consent

45 CFR 46 Protection of Human Subjects
21 CFR 50 Protection of Human Subjects

REQUIRED ELEMENTS AND PROCESS OF INFORMED CONSENT
and
ASSENT OF MINORS

A. INFORMED CONSENT REQUIREMENTS/ELEMENTS

The purpose of this section is to assist the investigator by providing guidance on how to construct and obtain valid informed consent, and assent where appropriate in the case of minors, from prospective research subjects. The IRB informed consent requirements are based on current DHHS and FDA regulations (45 CFR 46.116, 46.117 and as applied in subsequent sections; 21 CFR 50 Subpart B), Principle I of the Nuremberg Code and applicable principles as enumerated in the World Medical Association Declaration of Helsinki. To this end, any member of the IRB may be contacted for advice on writing informed consent documents.

1. General Requirements of Informed Consent

Under the provisions of 45 CFR 46.116 and 21 CFR 50.20, unless provided elsewhere in these respective federal regulations and policies, an investigator may not involve a human subject in research without first having obtained the legally effective informed consent of the subject or the subjectÕs legally authorized representative. As to exceptions regarding informed consent in either the DHHS or the FDA regulations and policies, Morehouse School of Medicine does not

considered research-related benefits. As contemplated by this element, ÒothersÓ may be interpreted as persons similarly situated that may benefit from the research at some time in the future.

(4) a disclosure of alternative appropriate procedures or courses of treatment, if any, that might be advantageous to the subject. Included in this element would be a statement that the subject may

administration of drugs, the frequencies of occurrence may be expressed as a percentage or other meaningful description as may be published in medical or prescribing literature. Description of risks should not be understated. The most commonly reported risks should be described as well as risks that rarely occur but may pose serious threats to the subject should they occur. A description of risk factors should include those risks which may be expressed as:

- Physical harms to the subject or others
- Disclosure of information that could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjectsÕ financial standing, employability, or reputation.
- Disclosure of information that may damage a subjectsÕ relationships to others such as family members or spouses.
- Disclosure of information that may have a widespread negative social impact on a particular group or race/ethnicity.

(2)

(1) the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (1) public benefit or service programs; (ii) procedures for obtaining benefits

2. Documentation of Informed Consent

a. General Requirements

As required by 45 CFR 46.117(a) and 21 CFR 50.27(a), unless the IRB finds and documents exceptions noted below, consent must be documented by the use of a written form approved by the IRB and signed and dated by the subject or the subjectÕs legally authorized representative. Although not required by regulation, the IRB requires the signature and date of the person responsible for obtaining

A copy of the short form and a copy of the summary shall be given to the subject or the subjectÕs representative.

The following is an example of a short form written consent. This sample was derived from current f

The following form is suggested as a written summary form to be approved by the IRB:

c. Witness Requirements/Guidance

Other than the federal regulatory requirements cited above, the IRB may recommend a witness to the informed consent process where the IRB finds either in full-board or expedited review that a witness to the

regulatory requirements, the IRBÕs recommendation of witness to the consent process may apply whether or not the informed consent process involves a comprehensive written document or is presented orally to the subject as described above.

The witness must directly observe the consent process and not merely be present during the signing of the document. The witness should be an impartial adult who has no interest in the research project and who cannot be unfairly influenced by the investigator or members of the research team. Ideally, the witness would be a person unaffiliated with the project or the investigatorÕs academic department or research unit of the institution. However, a member of the research team who serves as a clinical monitor or is otherwise a research subject advocate may act as a witness to the informed consent process

In no event may the investigator or other person authorized to conduct the informed consent process serve as the witness to the informed consent process.

The investigator may petition the IRB, with appropriate justification, that this requirement unfairly burdens the conduct of the research and that a member of the research team should be allowed to act as a witness to the consent process. Justification for this allowance should explain how the research team memberÕs interest or involvement in the research would not bias his/her role as witness to the consent process.

d. Signed Consent Form Waiver

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all of the subjects, if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from breach of confidentiality.

(45 CFR 46.117(c)(1))

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (45 CFR 46.117(c)(2); 21 CFR 56.109((c)(1)).

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research (45 CFR 46.117(c)(2); 21 CFR; 21 CFR 56.109(b).

The IRB will carefully examine requests for signed consent form waivers

information. The IRB will consider the nature of the information, protective measures taken to protect confidentiality as well as the degree of harm that may result from breach of confidentiality.

C. THE PROCESS AND DOCUMENTATION OF ASSENT OF MINORS AND PERMISSION OF PARENT(S) OR GUARDIAN(S)

1. Assent Process

Legally, children cannot give consent on their own behalf. In the context of research, the terms children and minors are used interchangeably. The permission of their parent(s) or a legal guardian is, therefore, required before children can participate in any non-exempt (and some exempt) research projects. In the State of Georgia, a minor attains majority at age 18 or upon marriage. Pregnancy does not confer majority status. A minor may, however, with IRB approval, legally consent on his/her own behalf (as a mature minor) if the research involves a treatment for which a minor's consent is permissible under applicable law (e.g., use of contracept

Verbal assent may be appropriate in some circumstances. Investigators must clearly describe in IRB applications for review why a verbal assent process is appropriate and how it will be documented. In cases where verbal assent is approved by the IRB, the IRB will require the investigator to prepare a script to be read to the minor subjects. The parent(s)/guardian(s) shall receive a copy of the script with a written acknowledgement from the investigator as to the investigatorÕs formed belief and judgment that the minor understands the nature of the research.

In cases where the IRB finds and documents that a waiver of assent is appropriate, the IRB will require the investigator to prepare a description of the research, written at the appropriate reading level of minor subjects, to be given to the subjects as well as a copy to be given to the parent(s)/guardian(s) as part of their permission process.

Any assent process approved by the IRB expires as indicated on notice of approval documentation or upon any minor subject attaining the age of majority while participating in research. Any minor attaining the age of majority (18 years old) while participating in research must consent to continue as an adult.

2. Regulatory Requirements - the DHHS

a. Research not involving greater than minimal risk

ÒRisksÓ in this category of subjects is interpreted as those risks normally encountered during the daily life of average, healthy children living in safe environments or equivalent to the risks associated with the performance of routine physical or psychological examinations or tests (OHRP

(1) The risk is justified by the anticipated benefit to the subjects (45 CFR 46.405(a)).

In reference to the SACHRP document cited above, the IRB considers the likelihood that the benefit will actually materialize, the anticipated magnitude of the benefit, and the degree to which anticipated benefits are at least as or superior to available alternative approaches, if any exist. The IRB shall base its assessment on sound scientific evidence provided by the investigator in the research protocol. Any procedures, tests or methods to be employed relative to anticipated benefit must be justified as an integral part of the research design and cannot be performed on speculation or the potential for a serendipitous beneficial outcome.

(2) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by alternative approaches (45 CFR 46.405(b)).

The IRB shall carefully examine research procedures to determine whether the investigator has justified non-beneficial procedures as vital to the conduct of the research and that the parental permission document clearly explains the nature and rationale for such procedures. In cases where multiple procedures are proposed, the IRB shall assess each procedure individually as well as collectively to determine a reasonable relationship vital to the success of the research proposed.

In this case, assent of the child and the permission of one parent or legally authorized representative shall be sufficient, unless the IRB finds and documents that, in the best interest of the child, the permission of both parents, if reasonably feasible, should be obtained (45 CFR 46.405; 408(b)).

c. Research involving greater than minimal risk and no prospect of *direct*

factorsidentified as minimizing risks. The term ÒconditionÓ is interpreted by the SACHRP guidance described above to refer to specific physical, psychological, developmental, or social characteristics known to negatively affect childrenÕs health or well-being or to increase their risk of developing a health problem in the future.

(2) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social , or educational situations (45 CFR 46.406(b)).

In this context, ÒcommensurateÓ means *similar* to those interventions or procedures that children with the condition or disorder, as a class, have or are expected to experience. However, ÒcommensurateÓ does not justify any level of risk beyond a minor increase over minimal risk. For example, a procedure or intervention that would present an unfair burden to the subject would be considered one that elevates the risk level above what is permissible in this code section. Commensurability is to be judged by what the parent/child believes is commensurate in the childÕs particular circumstance. The risk assessment criteria remain as described under II.C.2.a. & b. above and must be justified in the protocol as being met and applicable for the study under review. The investigator must convincingly propose the interventions or procedures to be used in the study are similar to those that children with the condition or disorder, as a class, have or are expected to experience (SACHRP guidance, cited above).

(3) The intervention or procedure is likely to yield generalizable knowledge about the subjectÕs disorder or condition which is of vital importance for the understanding or amelioration of the subjectÕs disorder or condition (45 CFR 46.406(c)).

ÒVital importanceÓ is interpreted to mean clear and significant scientific evidence that procedures or interventions intended in the research are likely to yield generalizable knowledge that would contribute to understanding the etiology, prevention, diagnosis, pathophysiology, amelioration or treatment of a condition or disorder (SACHRP guidance cited above).

Clear and significant evidence, although subjective, must be deliberated by the IRB in order to reach a valid conclusion as to whether this criterion has been met. The IRB shall consider whether the scientific evidence demonstrates a substantially more likely than not probability that the research would result in generalizable knowledge to meet the standard of this code section.

Under this risk category, assent of the child and permission of <u>both</u> parents must be obtained unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent

The IRB may suggest consultation with a suitable individual knowledgeable about the research context and the rights and welfare of children.

f. Documentation of parental permission.

Permission by parents or guardians shall be documented in accordance with and to the extent required for informed consent (45 CFR 46.117) as described in these guidelines under II.B.2. (45 CFR 46.408(b)).

g. Documentation of assent.

When the IRB determines that assent is required, it shall also determine whether and how assent must be documented. (45 CFR 46.408(e))
A person who commences in research under the legal status of being a minor must provide consent to continue as a subject in research upon becoming an adult (generally, on their 18th birthday).

h. Waiver of assent.

3. Regulatory Requirements - the FDA

a. Clinical investigations not involving greater than minimal risk.

For purposes of reviewing and approving research involving clinical investigations in this category, the IRB will find and document adequate provisions for solicitation of assent of the children and permission of their parents or guardians (21 CFR 50.51). The determination and description of risk involved in this category of research is the same as described under II.C.2.a. in these IRB guidelines and policies.

In this case, assent of the child and the permission of one parent or child's legally authorized representative shall be considered sufficient (21 CFR 50.55(e)(1)). The SACHRP document referenced above provides examples of procedures considered as standards that meet the definition of minimal risks. The FDA regulations define minimal risk as : "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or

For purposes of reviewing and approving research involving clinical investigations in this category in which more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring

(a) The clinical investigation involves no more than minimal risk to the subjects (21 CFR 50.55(d)(1));

(b) The waiver will not adversely affect the rights and welfare of the subjects (21 CFR 50.55(d)(2));

(c) The clinical investigation could not be practicably carried out without the waiver (21 CFR 50.55(d)(3)); and,

(d) Whenever appropriate, the subjects will be provided with additional pertinent information after participation (21 CFR 50.55(d)(4)).

i. Wards

Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 21 CFR 50.53 or 50.54 only if such clinical investigations are:

(1) Related to their status as wards (21 CFR 50.56(a)(1)); or

(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards (21 CFR 50.56(a)(2)).

If the research is approved under 21 CFR 50.56(a), the IRB must require appointment of an advocate for each child who is a ward (21 CFR 50.56(b). The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in *loco parentis* (21 CFR 50.56(b)(1)). One individual may serve as advocate for more than one child (21 CFR 50.56(b)(2)). The

- Physical or medical disability/compromise
    - Mental capacity/compromise:
        - Cognitive impairment/mental disease
        - Influence of medication
    - Sensory impairment/sight/hearing
- Relationship between investigator and subject
-

(1) Any adult, for himself, whether by living will or otherwise;

(1.1) Any person authorized to give such consent for the adult under a health care agency complying with Chapter 36 of Title 31, the 'Durable Power of Attorney for Health Care Act';

(2) In the absence or unavailability of a living spouse, any parent, whether an adult or a minor, for his minor child;

(3) Any married person, whether an adult or a minor, for himself and for his spouse;

(4) Any person temporarily standing in loco parentis, whether formally serving or not, for the minor under his care; and any guardian, for his ward;

(5) Any female, regardless of age or marital status, for herself when given in connection with pregnancy, or the prevention thereof, or childbirth;

(6) Upon the inability of any adult to consent for himself and in the absence of any person to consent under paragraphs (2) through (5) of this subsection, the following persons in the following order of priority:

(A) Any adult child for his parents;

(B) Any parent for his adult child;

(C) Any adult for his brother or sister; or

(D) Any grandparent for his grandchild.

(b) Any person authorized and empowered to consent under subsection (a) of this Code section shall, after being informed of the provisions of this Code section, act in good faith to consent to surgical or medical treatment or procedures which the patient would have wanted had the patient understood the circumstances under which such treatment or procedures are provided.

Considering the AlzheimerÕs AssociationÕs recommendations for institutional review boards and investigators, the IRB provides the following directives:

a. Description/Nature of Research and Capacity Assessment

The investigator will describe in the application for IRB review the following:

(1) The rationale for the inclusion of cognitively impaired research subjects, including why it may be in the best interest of the subjects to participate.

(2) The process through which subjectÕs cognitive capacity is assessed and documented.

(3) A risk/benefit analysis of the proposed research

(4) A description of the process for allowing potential subjects to provide affirmative acknowledgement to participate and how the investigator may determine when the subject declines participation regardless of the LARÕs point of view.

b. Description of LAR

The investigator will provide the following information in the application for IRB review:

(1) The relationship of the LAR to the subject that will be considered appropriate to allow proxy consent in the context of the research.

(2) The role of designated caregivers in cases where the LAR is not the subjectÕs caregiver.

(3) The process for assessing the LARÕs basis of knowledge of the potential subject with

continuation in the study in cases where the subject regains capacity at any time during the research.

e. The IRB Review Process

In its review and evaluation for approval of research involving cognitively impaired adult subjects, the IRB shall adopt the categories and stipulations for approval of research described under II.C.2 & 3., above as applicable to this category of research subjects. In the case of research in cognitively impaired adults, the designated LAR substitutes for "parent(s) or guardians" as described in the context of research involving children.

E. HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT OF 1996 – "HIPAA"

Under the HIPAA privacy regulations, 45 CFR 164.508(b)(3)(i), the Morehouse School of Medicine IRB does not require HIPAA authorizations for use or disclosure of protected health information to be combined with other regulatory requirements regarding informed consent to participate in research. It is the policy of the IRB to request investigators to use stand-alone HIPAA authorizations permitting the use and disclosure of individually identifiable health information. The IRB need not approve stand-alone HIPAA authorizations.

The IRB defers to the responsibility of each covered entity under 45 CFR 160 and 164 to comply with use and disclosure requirements, including waivers and uses

1. The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based upon, at least, the presence of the following elements;

   a. An adequate plan to protect the identifiers from improper use and disdosure;

   b. An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and,

   c. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;

2. The research could not practicably be conducted without the waiver or alteration; and,

3. The research could not practically be conducted without access to and use of the protected health information.

4. A description of the protect

A. ORGANIZATION

The IRB is administratively positioned in the Office of Research Development under the Office of the Dean & Senior Vice president for Academic Affairs. The institutional signatory official for the IRB is the Vice President & Associate Dean for Sponsored Research Administration. The IRB is a standing committee of the Academic Policy Council (Bylaws of the Faculty, October 30, 1998, Article V, Section 4, K.). Policies and procedures relating to IRB functions reflect requirements of current federal regulations (45 CFR 46, 21 CFR 50, 21 CFR, 56, 45 CFR 164), advisory memoranda of federal agencies, laws of the State of Georgia, and Morehouse School of Medicine institutional policies.

B.

The IRB meets once a month at regularly scheduled dates and times. Meeting frequency may change depending upon institutional circumstances and requirements. Meeting dates and times are well publicized. The chair of the IRB, or in his/her absence the IRB administrator or vice chair, may convene called meetings as necessary to conduct urgent business. Matters of pecuniary interest are not considered reasons sufficient to convene called meetings. Investigators submitting protocols are not requested to attend meetings unless deemed essential to the deliberations. Investigators who may also be members of the IRB are excused from deliberations and the voting process of their protocols submitted for review.

At the commencement of each convened meeting, the IRB administrator, chair, vice chair or a member designated by the chair shall confirm the assembly of an appropriately configured quorum to conduct business. Minutes of meetings shall be recorded by the administrator, chair, vice chair or a member designated by the chair. Administrative office staff may assist in recording IRB minutes.

Protocols requiring full-board review are presented by the primary reviewer; and, when a secondary reviewer has been assigned, the secondary reviewer provides input as well. Upon conclusion of their presentation, the reviewers make a recommendation based upon their findings. Each member present is then allowed an opportunity to ask questions, raise issues, and make comments. The IRB chair will provide the committee with information from members who could not make the meeting but who submitted input to the IRB office. Following close of discussion, the person chairing the meeting asks the reviewer to make a motion. A motion may be made to approve, to table action pending further considerations, or to disapprove the research study. Upon a motion made and seconded, the chair calls for the question, provided there is no further discussion requested, votes are cast by a show of hands. Unless otherwise indicated by

2. Protocol Review Management

As detailed in I.B and C, of these guidelines and policies, reviews are expected to be completed in a timely manner. In no case, however, will time constraints override the importance of careful and complete review processing. Timeliness of reviews depends upon completeness and clarity of material submitted for review as well as the complexity of the research under review. Primary and secondary reviewers fill out review checklists and documentation forms as well as forms requesting responses from investigators. Reviewers may direct their questions and comments to investigators with copies to the IRB office or the

4. Protocol Modifications and Other Communications

Protocol amendments and other research-related communications are reviewed by the IRB administrator or chair and managed according to review guidelines described in appropriate sections of these guidelines and policies. Investigators are on notice not to commence research modifications without prior approval from the IRB unless justified for reasons necessary for the safety and welfare of research subjects.

5. Administrative Authority