

UNIVERSITY OF MISSISSIPPI MEDICAL CENTER

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Policies And Procedures of the University of Mississippi Medical Center's Institutional Review Boards (IRBs)

Mission Statement

One component of the University of Mississippi Medical Center's mission is to expand the body of basic and applied knowledge. The Institutional Review Board, a federally mandated committee charged with overseeing all research projects involving human participants, helps to further this research mission and fulfills its charge by:

- Reviewing all proposed research involving human participants, to protect the rights and welfare of research participants.
- Ensuring compliance with Federal, State, and University requirements.

Introduction

The University of Mississippi Medical Center (UMMC) and its IRBs are committed to following the letter and spirit of the human research participant protection regulations and guidance to ensure the integrity of the IRB decision-making process. Federal research regulations set forth an IRB's authority to oversee research involving human participants. They mandate that an IRB "shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities" subject to the regulations [45 CFR 46.109(a)][21 CFR 56.109(a)]. Further, the IRB "shall conduct continuing review of research" annually or more often when appropriate [45 CFR 46.109(e)][21 CFR 56/109(f)]. The IRB also has the authority "to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects" [45 CFR 46.113][21 CFR 56.113].

These regulations specify both the IRB's composition (inclusion of scientists, and at least one nonscientist and one unaffiliated member) and the criteria for IRB approval of research, among other requirements. In exercising this federal regulatory authority to review, approve, and provide continued oversight of research, the IRB communicates its decisions regarding research to investigators and to the institution.

Importantly, the IRB must exercise independence as the entity authorized to oversee research involving human participants. Federal regulations specify that if an IRB disapproves research, no one within an institution may overrule that decision and allow the research to go forward [45 CFR 46.112][21 CFR 56.112]. Research that has IRB approval may, however, be subject to further institutional review if appropriate.

The independence of IRB decisions has taken on added importance given heightened attention to potential conflicts of interest that an institution or its investigators may have. Department of Health and Human Services (DHHS) guidance recommends that institutions consider several measures to protect research decisions from financial ones within an institution, including establishing measures to foster the IRB's independence. Accordingly, all investigators and research personnel are subject to UMMC's Code of Conduct and Conflicts of Interest Policy ("Policy on Commercial Relationships"). The UMMC system for handling conflicts of interest is based on self-reporting. Self-reporting forms are required to be completed by investigators and research personnel annually. (The time of reporting and the definition of the year to be reviewed will be determined by the COI official and/or the COI Committee.) The disclosure form will be accessible through the Annual Compliance Training site, and can be completed during that training session. Once completed, disclosure forms are returned to the Office of Compliance. The COI Committee will review disclosures to determine whether a conflict of interest reasonably appears to exist. The COI Committee will identify and resolve the conflict of interest or the appearance of a conflict of interest, or concern, or establish conditions for management of the conflict or concern, and report the resolution to the Investigator, employee, IRB, IACUC, the Office of Research, Grants and Contracts, Institutional officials, state and federal officials, research sponsor(s), and/or publication editors, as determined appropriate by the COI Committee.

Investigators must also disclose conflicts of interest (financial and otherwise) to the IRB. If a conflict is identified or a situation raises concern, the information will be forwarded to the COI Committee and the Office of Research. Approval for the proposed research will not be granted until the conflict or concern has been resolved or conditions for management of the conflict or concern have been established.

Voting members of UMMC's IRBs are also required to disclose conflicts of interest and recuse themselves from participating in the discussion and vote on research activities with which they have a conflict of interest as defined in UMMC's conflict of interest policy. IRB members may, at the request of the IRB, provide information about the research prior to leaving the room for the discussion and the vote on the research.

I. AUTHORITY

UMMC's IRBs derive their authority from the UMMC's Vice Chancellor for Health Affairs. The responsibility for the protection of the rights and welfare of human research participants is shared by the Institution and the Investigators conducting the research.

II. SCOPE OF AUTHORITY

UMMC's IRBs are responsible for the review and approval of all research involving human participants that is conducted at UMC and its affiliates, as listed in its FWA. Review by UMMC's IRBs is required when:

- The research is sponsored by UMMC;
- The research is conducted by or under the direction of employees or agents of UMMC in connection with their institutional responsibilities;
- The research is conducted by or under the direction of any employee or agent of UMMC using any property or services of UMMC; or
- The research involves the use of UMMC's private information to identify or contact participants.

UMMC's IRBs are also responsible for the review of innovative diagnostic and therapeutic activities that involve human research participants, research involving deceased individuals that would otherwise meet the definition for research involving human participants, and research activities that qualify for exemption from the Common Rule as outlined in 45 CFR 46.101(b)(1-6).

UMMC's IRBs have the authority to:

- determine exemptions from 45 CFR 46;
- approve, require modifications in (to secure approval of), or disapprove research activities involving human participants;
- require progress reports from investigators;
- oversee the conduct of research;
- require a third party to observe the consent process;
- suspend or terminate approval of a study;
- place restrictions on a study;
- request a directed audit by UMMC's Office of Compliance; and
- conduct reviews and inquiries regarding research activities as needed to obtain information necessary for the fulfillment of the institutional responsibilities outlined in the OHRP-approved FWA.

UMMC's IRBs and relevant ancillary committees or departments must approve all human research activities prior to initiation of the research. The decision of UMMC's IRBs to disapprove human research cannot be overruled by any other

institutional body or individual(s); however a Principal Investigator (PI) may ask that the decision be reconsidered by submitting a request in writing directly to the Chairperson of the IRB that disapproved the research. The request will be scheduled for review at a convened meeting of the IRB that disapproved the research initially, and the Principal Investigator will be invited to attend the meeting.

A. Relationship of Other Institutions to UMMC's IRBs

Institutions outside UMMC may rely on UMMC's IRBs if there is an executed IRB Authorization Agreement (or Inter-Institutional Amendment) in effect between the institution and UMMC's IRBs. The decision of whether to rely on UMMC's IRBs for review of a particular protocol is made jointly by the Chairperson of UMMC's IRB and the Chairperson of the collaborating institution's IRB. Both must agree that it is acceptable to rely upon UMMC's IRB for initial and continuing review of the research in accordance with the terms and conditions of the Agreement or Amendment. When acting as the IRB of record, UMMC's IRB sends copies of IRB correspondence to the site responsible PI and designated institutional representatives. Copies of relevant portions of IRB Minutes are provided to the designated institutional representative, upon written request.

III. ETHICAL PRINCIPLES

UMMC's IRBs are guided by the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, generally known as the "Belmont Report", as well as UMMC's institutional policies.

IV. DEFINITION OF HUMAN RESEARCH

For the purposes of this policy, *human research* encompasses the following definitions:

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)].

Human subject or human research participant means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the research participant or the research participant's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and research participant.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the research participant is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human research participants [45 CFR 46.102(f)(1)(2)].

Clinical investigation means any experiment that involves a test article and one or more human research participants and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the Act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical studies.

The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous. [21 CFR 56.102(23)(c)].

V. RESPONSIBILITIES

A. The Institutional Official

UMMC has an approved Federal Wide Assurance (FWA) on file with the Office for Human Research Protections (OHRP), Department of Health and Human Services (DHHS). The FWA has been signed by an individual with the legal authority to represent the institution. This individual is referred to as the Institutional Official (IO). The IO understands the institution's responsibilities under the FWA, assures the protection of human research participants, and assures that the designated IRBs are knowledgeable about the local research context and will comply with the terms of the FWA. The FWA has been approved by OHRP and is updated as required, and as necessary when information changes.

The IO is responsible for:

- Setting the “tone” for an institutional culture of respect for human research participants;
- Ensuring effective institution-wide communication and guidance on human research issues;
- Ensuring that investigators fulfill their responsibilities;
- Facilitating participation in human research education activities; and
- Serving as a knowledgeable point of contact for OHRP.

Administratively, the IO is responsible for:

- Appointing IRB Chairpersons;
- Providing the IRB with necessary resources and staff; and
- Supporting the authority and decisions of the IRB.

B. Department Chairpersons

The department chairperson is responsible for ensuring that the PI is qualified by training and experience to conduct the proposed research. In addition, the chairperson is responsible for ensuring that the PI has sufficient resources and facilities to conduct the proposed research. For each protocol submitted to the IRB for approval, the department chairperson must certify that she/he accepts responsibility for assuring adherence to federal and state research regulations and institutional policies governing the protection of human research participants, including applicable institutional credentialing requirements. Department chairpersons are also required to fulfill the annual IRB education requirements.

C. Investigators

Primary responsibility for protecting the rights and welfare of human research participants rests with the principal investigator (PI). The PI must be a full time faculty/staff member, or be a resident, research fellow, trainee, or student with a faculty sponsor. For each protocol submitted to the IRB for approval, the PI (and the faculty sponsor, where applicable) must certify that she/he accepts responsibility for assuring adherence to applicable federal and state research regulations and Institutional policies relative to the protection of the rights and welfare of participants enrolled in the research.

PIs must be qualified by training and experience to conduct the research and must be in compliance with UMMC’s Conflicts of Interest Policy. The PI’s department chairperson or his/her designee must review and sign the submission to the IRB. The department chairperson’s signature on the IRB submission signifies that the PI has the necessary qualifications to be the PI for the study.

When the research involves the administration of a drug or use of a device for research purposes, the PI must be a licensed physician. Exceptions to this requirement will be made only on a case-by-case basis where there are licensed physician co-investigators and with the approval of the department chairperson. PIs may delegate some responsibilities to appropriately qualified co-investigators and research staff. Co-investigators and research staff must be qualified by training and experience to perform these responsibilities and must be in compliance with UMMC's Conflicts of Interest Policy.

All investigators and research staff must successfully complete the Collaborative IRB Training Initiative (CITI) program, or an equivalent program designated by the IRBs, before participating in the conduct of human research, and must successfully complete the CITI refresher course each year, or an equivalent program designated by the IRBs, to continue to conduct human research. In addition, PIs must sign an Investigator's Assurance for each human research study she/he is conducting, and agree to fulfill all responsibilities as identified in the Investigator's Responsibilities appended to each approval letter sent to the PI.

D. The University of Mississippi Medical Center's Institutional Review Boards

The IRBs are responsible for the review and oversight of human research and the development of human research policies and guidelines. Investigators and the research community are informed of new institutional human research policies and guidance in general or directed mailings. Institutional human research policies, guidance documents, and forms, as well as links to relevant state and federal regulations and guidance are available on UMMC's IRB website.

The University of Mississippi Medical Center is responsible for ensuring that its IRBs have adequate resources and facilities to meet institutional and regulatory requirements. IRB review activity and program resources and facilities, including staffing, equipment, and space, are evaluated at least once a year to prepare annual budget requests.

UMMC's IRBs are registered with DHHS/OHRP. The IRB registrations are updated and submitted to OHRP as required, and as needed when there are any changes to the membership of the IRBs. The IRBs are responsible for the review and oversight of research involving human participants conducted at or sponsored by UMMC and its affiliates, regardless of the source of funding. The IRBs exercise their responsibilities for the protection of human research participants with autonomy and without regard to possibly conflicting institutional interests. The policies and procedures described herein and the IRB guidance documents apply to the operations of each institutional IRB.

E. The University of Mississippi Medical Center's Office of Compliance

The Office of Compliance is responsible for assisting the institution and investigators in fulfilling their responsibilities for research involving human participants through compliance with Federal and State regulations governing human research and for promoting an environment in which research involving human participants will be conducted according to the highest standards. The Office of Compliance accomplishes these goals through on-site assessments, review of self-assessments completed by investigators, and education. The Office of Compliance is responsible for and has the authority to:

- Perform quarterly audits of the IRB;
- Perform random, routine reviews of any study that has been approved by the UMMC IRBs; and
- Conduct directed (for-cause) audits at the request of UMMC's IRBs or the Institutional Official.

F. The University of Mississippi Medical Center's Office of Research

The University of Mississippi Medical Center's Office of Research has the authority to review and execute research agreements with federal agencies and foundations on behalf of UMMC. Staff review all research agreements with federal, state and foundation or non-profit sponsors. Institutional review, including review by the Staff Attorney and the Department of Compliance, ensures that all terms of the award are in compliance with institutional policies. Designated individuals within the Office of Research have the authority to approve research proposals and to execute research agreements on behalf of the institution. Proposals and agreements presented for institutional signature have the approval of the academic department chairperson as indicated by a signed UMMC Transmittal Sheet. UMMC's Office of Research staff may consult with other UMMC departments to address complex contractual issues.

The Office of Research has the authority to negotiate and execute clinical research agreements with industry sponsors on behalf of UMMC. The clinical research agreement includes provisions whereby the sponsor agrees to abide by all applicable federal, state and local laws and regulations. The sponsor, through the Principal Investigator, must obtain IRB approval prior to initiation of the research and must report promptly to the investigator any findings that could (1) affect the safety of volunteers participating in the research; (2) affect the willingness of volunteers to continue participating in the research; or (3) alter the IRBs approval to continue the study. The agreement also addresses ownership

of the study data, the investigator's right to publish the results, indemnification by the sponsor, governing law, payment terms, confidentiality, privacy, termination, and other related issues.

G. Research Participants

Research participants are encouraged to contact the Chairpersons of UMMC's IRB if they wish to speak with someone not directly involved in the research. The research consent form template includes the telephone number of the IRB Office for participants to call if they wish to discuss their rights as a research participant, concerns about the research, or a complaint about the research.

VI. MANAGEMENT OF THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER'S INSTITUTIONAL REVIEW BOARDS

A. Management and Support Staff

Human research activities are overseen by the Director of the IRB who reports to UMMC's Associate Vice Chancellor for Research. The Director is responsible for overseeing the IRBs, as well as for interacting with the IRB chairpersons, the Office of Compliance, investigators and research leadership. UMMC's IRBs are supported by the following administrative staff:

- Education Specialist;
- IRB Specialists and Coordinators;
- Administrative Support Staff.

B. IRB Chairpersons

1. Selection of Chairperson

The Chairpersons are selected and appointed by the Institutional Official. Chairpersons are generally selected from among experienced members of the IRBs, and as such are familiar with regulatory requirements and ethical considerations. There are no term limits placed on length of service. The Chairpersons are provided with orientation and training by the IRB Director and are encouraged to attend at least one IRB-related regional or national conference every two years.

2. IRB Chairperson Responsibilities

IRB Chairpersons are responsible for:

- presiding at IRB meetings during which review of initial, continuing, and modifications of research activities involving human research participants is conducted;
- conducting review of initial, continuing, and modifications of research activities involving human research participants that may be approved through the expedited review procedure;
- reviewing (and approving) modifications required by the IRB at convened meetings to secure approval;
- determining exempt status of research involving human research participants;
- participating in the development of policies and procedures for research involving human participants;
- fulfilling annual continuing education requirements, including attendance at conferences, workshops, seminars, or lectures pertaining to research involving human volunteers; and
- performing other activities, as needed, to fulfill institutional responsibilities set forth in the FWA or at the request of the Institutional Official.

C. Comments and Suggestions from the Research Community

Open communication between the research community and UMMC's IRB Office is encouraged and welcomed. Investigators and members of the research community may suggest improvements in any aspect of the human research protection program by submitting suggestions in writing, by email, or by telephone to the Director, Chairpersons of the IRBs, or Institutional Official. Suggestions will be considered by the above, and/or appropriate IRB administrative staff, and responded to by one of the above or his/her designee.

D. Complaints from the Research Community

Investigators and members of the research community may submit in writing or by email complaints about any aspect of the human research protection program to the IRB Director, Chairpersons, or Institutional Official. Complaints will be reviewed by the IRB Director and Chairperson(s), and when relevant, the Director of the Office of Compliance. The IRB Chairperson may appoint an ad

hoc committee to review the complaint and report findings and recommendations. Serious complaints may be referred to the Institutional Official, who may at his/her discretion appoint an ad hoc committee to review the complaint and report findings and recommendations, if any, to the IO and Associate Vice Chancellor for Research for further consideration and/or implementation.

E. Complaints from Research Participants

Every UMMC IRB-approved consent form provides research participants with the telephone number of the IRB office if she/he wishes to speak to someone not directly involved in the research. Written or telephone complaints from research participants are handled by the IRB Director, Office of Compliance Director, or one of the IRB Chairpersons. UMMC's IRB staff provides the research participant or his/her representative with a safe and confidential means to discuss research-related concerns with someone unaffiliated with the research protocol. The IRB staff makes reasonable efforts to protect the identity of the research participant and not release his/her name in any communication with the investigator or others unless permission to do so has been given or there is a safety issue requiring disclosure. The IRB staff may involve others, as necessary, in the resolution of the concern or complaint, including, but not limited to the Principal Investigator (or his/her representative), Patient Accounts, Accounts Payable, the Chairperson of the IRB overseeing the research, and the Office of Compliance. The IRB Chairperson or IRB Director may involve the Principal Investigator's Department Chairperson, the Office of the General Counsel, Risk Management, and the Institutional Official if the concern or complaint involves serious allegations about the manner in which the research is being conducted.

F. Allegations of Regulatory Noncompliance or Scientific Misconduct

Allegations of regulatory noncompliance are managed by UMMC's IRBs as described elsewhere in this policy. Allegations of scientific misconduct are referred to the Office of Compliance and the Institutional Official for fact finding and further action as required. Misconduct means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scholarly and scientific community for proposing, conducting, or reporting research. Misconduct does not include honest error or honest differences in interpretations or judgments of data.

VII. MEMBERSHIP OF THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER'S INSTITUTIONAL REVIEW BOARDS

A. Composition

Each IRB is composed of at least 5 members with varying backgrounds to promote complete and adequate review of research activities commonly conducted at the institution. The membership includes individuals with the necessary experience and expertise and knowledge of the local research context to review the scope of biomedical and behavioral research conducted at UMMC. Members include both men and women and members of minority groups. Designated alternates are used.

The membership includes:

- physicians;
- scientists;
- nurses;
- pharmacists;
- at least one member who is unaffiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution; and
- at least one member whose primary concerns are in nonscientific areas, such as lawyers, ethicists, and clergy.

The membership roster and IRB registration information are updated as required, and as needed when membership changes. The revised IRB registration is submitted to the Office for Human Research Protections (OHRP) as required by the institution's FWA. The membership of the IRBs is reviewed at least annually to determine if the membership includes individuals with varying backgrounds and the experience and expertise needed to review the scope of biomedical and behavioral research conducted at UMMC. As needed, or upon request, the IRB Office will compile information about research protocols reviewed at convened meetings (full board review) to assess the scope of biomedical and behavioral research reviewed by the IRBs. The report may include institution, department and division, as well as special populations, such as pregnant women and fetuses, prisoners, children, and individuals with impaired decision-making capacity.

B. Recruitment and Selection of Members

Physician-scientist members are recruited by the Associate Vice Chancellor for Research and the Chairpersons of UMMC's IRBs through the department chairpersons. Affiliated and non-affiliated individuals who are interested in serving on an IRB may self-refer or be referred by current IRB members. New members are recruited as needed to ensure that the membership of each IRB includes individuals with varying backgrounds and the necessary experience and

expertise to review the scope of biomedical and behavioral research conducted at UMMC. In addition, new members are recruited as needed to replace the experience and expertise of members who resign, and to provide additional experience and expertise needed to review new research programs. Members are selected based on reputations for fairness, objectivity and commitment to exercise faithfully their responsibilities for protection of research participants in human research, according to the guiding principles, and relevant federal and state regulations. There are no term limits placed on length of service.

C. Member Orientation/Education and Training

New members must successfully complete the Collaborative IRB Training Initiative (CITI) program. The Chairpersons of the IRBs and IRB Director provide new members with an overview of the UMMC IRB review process and governing regulations. Once the member has completed the education program and orientation, the member is added as a voting member to the IRB. The IRB roster is updated and the updated IRB registration is sent to OHRP. Institutional policies, IRB policies and procedures, IRB guidance documents, IRB review worksheets, and other information relevant to IRB members, as well as links to the Belmont Report, and federal and state regulations are on the IRB website. Printed materials are provided upon request. All IRB members receive copies of the Institutional Review Board Member Handbook, continuing educational materials, articles, and IRB-related publications, and new guidance documents from FDA, OHRP, or other governing agencies, and updates on recent FDA, OHRP, and ORI findings. IRB members are invited to attend the annual national PRIM&R/ARENA HRPP Conference.

D. Responsibilities of IRB Members

Voting members are responsible for initial, continuing review, and amendments of all research activities involving human volunteers scheduled for review at the convened meeting of the IRB and for considering:

- ethical and scientific issues;
- the appropriateness of the study population;
- the appropriateness of the methods of recruitment and process for obtaining informed consent of participants;
- the risks and anticipated benefits to participants, as well as the importance of the knowledge that may reasonably be expected to result;
- the adequacy of the study design and methods of data analysis;
- the adequacy of procedures used to monitor the data and participant safety;
- the adequacy of procedures used to protect confidentiality and privacy; and
- the accuracy and completeness of information in the consent form as well as the reading level and presentation of the information.

Voting members (or their alternates) are expected to attend at least 3/4 of the scheduled IRB meetings. Attendance records are reviewed annually. The IRB Director and Chairpersons will consider removal of voting members who have not met this obligation during the past year or the addition of an alternate voting member with similar experience and expertise.

E. IRB Members and Conflicts of Interest

Voting members of the IRBs are required to self-identify conflicts of interest and recuse themselves from participating in the discussion and vote on research activities with which they have a conflict of interest as defined in UMMC's Conflicts of Interest Policy. When members recuse themselves, they must leave the room for the discussion and vote on the research, except to provide information at the IRB's request prior to the discussion and vote. Recusals are documented in the Minutes of the meeting.

VIII. FUNCTIONS OF THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER'S INSTITUTIONAL REVIEW BOARDS

UMMC's IRBs are responsible for:

- determining exemptions from 45 CFR 46 in accordance with 45 CFR 46.101(b)(1-6);
- conducting initial and continuing review of research activities and amendments, including scientific review;
- determining that risks to research participants are minimized;
- determining that risks to research participants are reasonable in relation to anticipated benefits;
- determining that selection of research participants is equitable;
- determining that informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and, when applicable 21 CFR 50.25;
- determining that informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and, when applicable, 21 CFR 50.27;
- determining that when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants;
- determining that when appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data;
- determining that, when some or all of the participants are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect vulnerable participant populations (i.e., pregnant women,

- human fetuses and neonates, prisoners, and children) in accordance with 45 CFR 46 Subparts B, C, and D and, when applicable, 21 CFR 50 Subpart D;
- determining which device studies pose significant vs. non-significant risk, in accordance with guidance provided by the FDA;
 - determining which studies require review more often than annually;
 - determining which studies need verification from sources other than the investigators that no material changes have occurred since previous IRB review;
 - reporting in writing the findings and actions of the IRB to the investigator and the institution;
 - ensuring prompt reporting to the IRB of changes in research activities;
 - ensuring that changes in approved research are not initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the research participant; and
 - ensuring prompt reporting to the IRB, appropriate institutional official, OHRP and the FDA of (1) unanticipated problems involving risks to participants or others, (2) serious or continuing noncompliance with regulations governing research involving human participants or the requirements of the IRB; and (3) suspension or termination of IRB approval.

IX. OPERATIONS OF THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER'S INSTITUTIONAL REVIEW BOARDS

IRB review of human research activities is conducted either at a convened meeting of a quorum of the membership of one of the IRBs, including at least one physician/scientist and at least one member whose primary concerns are in nonscientific areas, or through the expedited review procedure as authorized in 45 CFR 46 as amended. Whether the IRB review is conducted at a convened meeting or through the expedited review procedure, the review encompasses the application form and all documents and materials submitted to the IRB for review.

A. Initial and Continuing Review

The IRBs have developed forms for IRB submissions. Investigators are required to submit relevant forms and documents for IRB review to the IRB Office. Submission requirements are outlined in the IRB Initial Application and Continuing Review Instructions. Submissions are checked for completeness by the IRB staff and scheduled for full board review or, as appropriate to the research activities, referred to the IRB Chairperson for expedited review, or for determination of exemption. Human research protocols are scheduled for review based on the order in which they are submitted; however the IRBs reserve the right to schedule protocols for review based on the experience and expertise of the membership of a particular IRB, or reschedule the protocol as necessary due to availability of members.

1. Exemptions from 45 CFR 46

The IRBs are responsible for determining whether research involving human participants is exempt from the requirements of the Common Rule as outlined in 45 CFR 46.101(b)(1-6), as quoted below:

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- (2) Research involving the use of education tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
- (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if: (i) The human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subject.
- (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

The exemptions do not apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization, subparts B and C. The exemption 45 CFR 46.101(b)(2) does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

The IRB Chairperson is responsible for reviewing and determining whether the research is exempt from 45 CFR 46. As part of this review, the IRB Chairperson will consider whether informed consent can be waived and whether there are adequate provisions to protect the privacy of research participants and maintain the confidentiality of the data. The IRB Chairperson may use a review checklist to indicate whether or not the research is exempt from review. If the IRB Chairperson determines that the research is exempt from the requirements of 45 CFR 46, continuing review will not be required unless changes are made to the research that exceed the parameters of the exemption and require subsequent IRB review. The IRB Chairperson may request additional information from the PI to make the determination. If the research does not meet the criteria for exemption, the protocol is returned to the PI and must be resubmitted for review through the expedited review procedure or by full board review at a convened meeting of the IRB, as appropriate to the research activities.

Investigators are notified in writing that the research is exempt from further IRB review and that they may not make changes to the research activity without first notifying the IRB office to determine whether the changes are within the parameters for exemption. If the research no longer meets the criteria for exemption, the investigator must resubmit the research for review by the IRB at a convened meeting or through the expedited review procedure, as appropriate.

IRB members are informed of all research activities deemed exempt through the meeting agenda. The meeting agenda lists all new research activities deemed exempt and is distributed with the meeting materials for the next convened IRB meeting.

2. Expedited Review Procedure

New and ongoing research activities that present no more than minimal risk to human participants and involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110, as quoted below:

Minimal risk means that 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 psychological examinations or tests [45 CFR 46.102(i)].

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increase the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

(8) Continuing review of research previously approved by the convened IRB as follows: (a) where (i) the research is permanently closed to the enrollment of subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Research in any of these categories may require review at a convened meeting of the IRB if the circumstances of the proposed research involve more than minimal risk. The expedited review procedure may not be used where identification of the research participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the participant's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that the risk related to invasion of privacy and breach of confidentiality is no greater than minimal. In addition, the expedited review procedures may not be used for classified research involving human participants.

The IRB Chairperson is responsible for reviewing and determining whether the research is eligible for review through the expedited review procedure. The IRB Chairperson follows a form listing the expedited review categories published in the Federal Register at 63 FR 60364-60367 to document that the research is minimal risk and the applicable expedited review categories. The IRB Chairperson also assures that the consent form includes the basic elements of informed consent, or approval of a waiver or alteration of informed consent. If the proposed research is not eligible for review through the expedited review

procedure, the IRB Chairperson refers the research protocol for full board review at a convened meeting of the IRB.

The IRB Chairperson may approve, require modifications to secure approval or defer action pending receipt of additional information from the PI. The IRB Chairperson may not disapprove a study through the expedited review procedure; protocols can only be disapproved by the IRB at a convened meeting. The IRB Chairperson may elect to have another voting member of the IRB with special expertise review the research through the expedited review procedure. The IRB member is provided with all of the information provided to the IRB for review and follows the procedure for expedited review as described in this policy. The IRB member must comply with UMMC's Conflicts of Interest Policy and decline to review if a conflict exists.

When the IRB Chairperson or member designee requires modifications to secure approval or defers action pending receipt of additional information, the PI is notified in writing of the required modifications or additional information required for review. The PI is asked to submit a point-by-point response and revised documents to the IRB within 30 days of the review date. If no response is received, the PI is notified in writing of the outstanding response and given an additional 15 days to respond. Unless there are extenuating circumstances, the protocol is withdrawn from further review at the end of the 45-day period if the PI has not submitted a response. When received, the IRB Chairperson or member designee reviews the PI's response, including revised documents, and indicates whether the modifications have been made as requested and whether the protocol can be approved. The IRB Chairperson or member designee may continue to request additional modifications or information until the protocol is approved or referred for full board review at a convened meeting of the IRB.

IRB members are informed of all research activities approved by expedited review through the meeting agendas. The meeting agenda lists all new and ongoing research approved through the expedited review procedure and is distributed with the meeting materials for the next convened IRB meeting.

3. Full Board Review (Convened Meetings)

(a) Meeting Dates UMMC's IRB meeting dates and times are determined by the end of each year for the following year. Members are informed of the meeting schedule prior to the end of the year in order to reserve the dates and times on their calendar. The meeting dates and submission deadlines are posted on the IRB website.

(b) Quorum Research activities that cannot be reviewed through the expedited review procedure are reviewed at a convened meeting of a quorum of the membership of the IRB, including at least one physician/scientist and at least one

member whose primary concerns are in nonscientific areas. A *quorum* is defined as more than one-half the voting membership.

(c) Determining Attendance and Assigning Reviewers The IRB Chairperson or his/her designee reviews the agenda and assigns reviewers to each protocol. When making reviewer assignments, consideration is given to the scientific area or discipline, the study population, and study procedures, and the experience and expertise of the members attending the meeting. A primary and secondary reviewer system is used. The IRBs reserve the right to reschedule protocols for review based on the experience and expertise of the members attending the IRB meeting. Prior to each convened meeting, members are asked if they will attend the meeting. This is necessary to determine whether the requirement for quorum will be met.

(d) Use of Consultants [46.107(f)] Although rarely needed because of the depth and breadth of the membership on the IRBs, consultants may be used to supplement or provide expertise not available on the IRBs. When needed, potential consultants are identified by the IRB Chairperson in consultation with experts in the scientific area or discipline. Consultants are subject to UMMC's *Conflicts of Interest Policy* and must confirm that they have no conflict of interest. If the consultant agrees to review the research and the consultant has no conflict of interest, she/he is provided with all of the forms and documents submitted for review to the IRB. Consultants are asked to attend the meeting to present their findings relative to the scientific merits of the study and risks and benefits to research participants, and to answer questions; however, if the consultant is unavailable to attend the meeting, she/he may provide written comments for distribution to the IRB members. Consultants are not voting members, and their attendance is recorded in the Minutes as a Guest - Consultant.

(e) Distribution of Review Materials to IRB Members Approximately two weeks prior to the meeting, copies of forms and documents submitted for IRB review for each item on the agenda scheduled for convened review are distributed to all members. Every member receives copies of the entire submission except for the drug/device brochure, the NIH (or federal) grant application, and standardized instruments with which the IRB is familiar. Only the primary and secondary reviewers, in addition to the IRB Chairperson, receive copies of the drug/device brochure and grant application. The standardized instruments are provided to any member upon request.

(f) Conflicts of Interest IRB members are subject to UMMC's *Conflicts of Interest Policy*. Any member with a conflict of interest must recuse him/herself and leave the room before the discussion and vote on the research protocol takes place, except if the member is providing information at the IRB's request prior to the discussion and vote. The names of those voting members who were recused from voting due to a conflict of interest are recorded in the Minutes. Recused members are not counted towards the quorum requirement; therefore, if

a quorum of the membership is not present for the review of any protocol, action on the protocol is deferred automatically.

(g) Discussion and Vote on Research Protocols on Agenda Attendance at the meeting, voting members present for each review, and the vote on each protocol is recorded by the IRB staff. The IRB Chairperson and assigned reviewer(s) lead the discussion of each new research protocol, continuing review, amendment or adverse event listed on the meeting agenda that require convened review. At the end of the discussion, one of the members present makes a motion to approve, require modifications to secure approval, table review pending receipt of additional information, or disapprove the protocol. A vote on the motion is taken (for, against, abstain) and recorded in the Minutes. All motions are subject to majority vote of the members present for the review.

(h) Requirement for Investigational New Drug (IND) Number When the research activities direct drug (or biologic) administration, investigators are required to provide the IRB with information about the FDA status of the drug (or biologic) being used in the research. If the drug (or biologic) is not marketed or is marketed but is being used for a different indication, the investigator must provide the IND# assigned to the drug (or biologic) by the FDA for the investigation. If the drug (or biologic) has not been assigned an IND#, the IRB may require the investigator to obtain an IND unless the investigational use of the drug (or biologic) meets all of the following conditions: (i) it is not intended to be reported to the FDA in support of a new indication for use or to support any other significant change in the labeling for the drug; (ii) it is not intended to support a significant change in the advertising for the product; (iii) it does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product; (iv) it is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; (v) it is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and (vi) it does not intend to invoke 21 CFR 50.24.

(i) Requirement for an Investigational Device Exemption (IDE) When the research activities involve the use of a non-FDA approved medical device or the off-label use of an FDA-approved device, investigators are required to provide the IRB with information about the FDA status of the medical device being used in the research. The use of any commercially available medical device for research purposes must meet the same hospital safety standards as medical devices being used for patient care. A medical device is defined, in part, as any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized. Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic

aids such as reagents and test kits for in vitro diagnosis of disease and other medical conditions such as pregnancy.

When a medical device is being evaluated for safety and/or efficacy, the device is considered “investigational” and is subject to the requirements of the IDE regulations [21 CFR part 812]. As part of these regulations, the investigational device must be categorized as either “significant risk” (SR) or “nonsignificant risk” (NSR). The sponsor generally makes this determination; however the IRB is responsible for the final determination.

A significant risk device is defined in 21 CFR 812.3(m) as a device that presents a potential for serious risk to the health, safety, or welfare of a subject and: (1) is intended as an implant; (2) is used in supporting or sustaining human life; (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. The risk determination is based on the proposed use of the device in the investigation, and not on the device alone. If the proposed use of the device involves a procedure, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure as well as the device. The sponsor must submit an IDE application to the FDA for clinical investigations of SR devices, and the IDE# assigned to the device for the investigation must be provided to the IRB.

Studies of NSR devices may be submitted directly to the IRB with documentation supporting NSR status. If the IRB concurs that the device is NSR, the investigation may proceed when approved by the IRB. If the IRB disagrees with the sponsor and determines that the device is a SR device, the sponsor must submit an IDE application to the FDA. All clinical investigations of medical devices are scheduled for review at a convened meeting of the IRB. As part of its review, the IRB makes the SR or NSR determination. If the IRB makes a NSR determination and the risk to the research participant is determined to be minimal in accordance with 21 CFR 56.102(i), the IRB may vote to conduct continuing review through the expedited review procedure [21 CF 56.110].

(j) Determining Frequency of Continuing Review When the motion is to approve or require modifications to secure approval, the motion includes the period for which IRB approval is to be granted, i.e., 364 days or less as appropriate to the degree of risk as defined in 45 CFR 46.103(b)(4) and 46.109(e). The duration for which IRB approval is granted is based upon the level of risk to research participants and, if applicable, the analysis of this risk as it relates to the risk of standard care. The IRB performs this risk assessment as part of the review of each protocol at the convened meeting. When the risk is great in relation to the risk associated with alternative procedures, if any, the IRB will consider requiring continuing review be conducted in less than 364 days year, or within 364 days with quarterly or case-by-case reporting. Examples of

protocols that may be considered for review more frequently than annually include:

- phase I studies of a new drug or biologic;
- studies involving Category A significant risk devices;
- studies in which healthy volunteers may undergo anesthesia or medical procedures involving sedation with no direct health benefits;
- studies for which there is little external oversight or data safety monitoring; or
- studies involving gene transfer or xenotransplantation.

(k) Determining Which Studies Need Verification from Sources Other Than the Investigators Investigators are expected to provide all relevant information regarding the conduct of the research to the IRB. This system is based on trust between the investigators and the IRB. For quality assurance purposes, the IRBs rely on random audits performed by the Office of Compliance. In order to ensure that the research is conducted in compliance with all state and federal regulations for the protection of human research participants, the IRBs may require at their discretion verification of information from sources other than the investigators.

Such independent verification may be considered in the following situations:

- complex projects involving unusual levels or types of risk to research participants;
- studies being conducted by persons who have previously failed to comply with all regulations;
- study performance that comes in question as the result of a continuing review;

or

- studies in which substantial segments of the project are conducted off site by collaborators, or in which UMMC's investigators conduct research off site.

Independent verification of information may be requested by the IRBs at convened meetings or by the IRB Chairperson in the course of carrying out reviews through the expedited review procedure. Such verification may include a directed audit by Office of Compliance. As part of this independent verification, the IRBs may also request and evaluate communications between the FDA and the sponsor/IND holder, other third party evaluations and reviews, NIH communications and reviews, back translations of consent forms or other materials for research participants, and letters of review or approval from other collaborating IRBs. Also, the IRBs continue to rely on DSMB reports as a source of external verification.

(I) PI Notifications and Responses to Review

1) Require modifications to secure approval When the IRB votes to require modifications to secure approval, the PI is notified in writing of the action voted on by the IRB and the required modifications to the research proposal. The PI is asked to submit a point-by-point response and revised documents to the IRB within 30 days of the review date. If no response is received, the PI is notified in writing of the outstanding response and given an additional 15 days to respond. Unless there are extenuating circumstances, the protocol is withdrawn from further review at the end of the 45-day period if the PI has not submitted a response. When received, the IRB Chairperson reviews the PI's response, including revised documents, and indicates whether the modifications required by the IRB have been made and whether the protocol can now be approved. The PI is notified in writing of any additional or outstanding revisions that need to be made. When received, the IRB Chairperson reviews the PI's response, including revised documents, and indicates whether the modifications required by the IRB have been made and whether the protocol can now be approved. This cycle continues unless and until all of the modifications required by the IRB have been made and the protocol can be approved. Alternatively, if the modifications have not been made as required, the response is scheduled for review at the next convened meeting of the IRB that reviewed the proposal initially.

(2) Table for more information When the IRB votes to table review pending receipt of additional information, the PI is notified in writing of the action voted on by the IRB and any questions and concerns that need to be addressed as well as modifications required to the research proposal. The PI is asked to submit a point-by-point response and revised documents to the IRB within 30 days of the review date. If no response is received, the PI is notified in writing of the outstanding response and given an additional 15 days to respond. Unless there are extenuating circumstances, the protocol is withdrawn from further review at the end of the 45-day period if the PI has not submitted a response. When received, the PI's response, including revised documents, is scheduled for review at the next convened meeting of the IRB that reviewed the proposal initially.

(3) Disapprove When the IRB disapproves the research, the PI is notified in writing of the basis for the disapproval. Disapproval means that the study as designed is inherently unethical, or has inherent problems that cannot be overcome and the IRB can think of no modifications or additional information that will likely result in an approval. The decision of the IRB to disapprove human research cannot be overruled by any other institutional body or individual(s); however a Principal Investigator (PI) may ask that the decision be reconsidered by submitting a request in writing directly to the Chairperson of the IRB that disapproved the research. The request will be scheduled for review at a convened meeting of the IRB that disapproved the research initially, and the Principal Investigator will be invited to attend the meeting.

B. Review of Proposed Changes During Period of Approval

Investigators are required to submit proposed changes to IRB-approved research activities to the IRBs for approval prior to initiation of the change. The only exception is the rare circumstance in which a change is necessary to eliminate apparent immediate hazards to research participants. The IRBs have developed a form for submission of proposed changes to the IRB for review. The form must be accompanied by all relevant documents revised with proposed changes highlighted.

The IRB Chairperson is responsible for reviewing and determining whether the proposed change (or amendment) is minor, and if minor, may review and approve the change through the expedited review procedure, as described previously. The IRB Chairperson may use a review form to document approval and provide the basis for approving the change through the expedited review procedure. Changes that are not minor are scheduled for review by the assigned IRB at a convened meeting, as described previously.

When the IRB Chairperson is determining whether the proposed change is minor, she/he considers the nature of the change and whether the change alters the risks and benefits considered by the IRB at the time of initial or subsequent continuing review. The IRB Chairperson may request additional information from the PI to make the determination. IRB members are informed of all changes to ongoing research approved through the expedited review procedure by inclusion of the review in the meeting agenda. The meeting agenda listing all new and ongoing research approved through the expedited review procedure is distributed with the meeting materials for the next convened IRB meeting. The investigator is notified of review as described previously. If ancillary committee review(s) is required, activation of the proposed change is subject to approval by the appropriate ancillary committee as described elsewhere in this policy.

C. Notification of Institution

The IO receives copies of all initial (convened, expedited, and exempt) approval letters. Upon request, the IRB Office will provide relevant portions of meeting Minutes to institutional representatives of institutions relying on UMMC's IRBs. The IRB Office uses a human research protections program database to manage the IRB review and oversight process. The database, known as RiSC, Research Information Support and Communication, includes information about the review history of every human research protocol, including all reviews (exempt, expedited and full board) conducted by the IRB and action taken. In addition, the database includes the content of all correspondence from the IRB to the PI. Portions of the database are viewable by the Office of Research and Office of

Compliance, departments that provide services to investigators and need to verify IRB approval. Portions of the database are also viewable by PIs and research staff. The extent of access is determined by the IRB office based on the need for and the purpose of the information.

X. IRB APPROVAL OF HUMAN RESEARCH

In order to approve research involving human participants, the IRB must determine that all of the following requirements are satisfied, as outlined in 45 CFR 46.111(a)(1-7) and (b):

1. Risks to participants are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk, and (ii) whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
 2. Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result.
 3. Selection of participants is equitable.
 4. Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with, and to the extent required by 46.116.
 5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 46.117.
 6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.
 7. When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.
- (b) When some or all of the research participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these participants.

A. Assessing Sound Study Design

The IRBs consider the following points when assessing sound study design:

1. Has the rationale and basis for the study hypothesis been provided in the background information?
2. Is the scientific design adequate to answer the research questions posed?
3. Is the sample size (number of participants) adequate?
4. Is the method proposed for selecting and assigning participants to treatment groups unbiased?
5. Are the study endpoints and methods of data analysis appropriate for the study?

B. Assessing Risks and Anticipated Benefits, if Any, to Participants

The IRBs consider the following points when assessing risks and anticipated benefits, if any, to participants:

- What are the anticipated risks to individual participants?
- What are the potential benefits, if any, to individual participants?
- Are there any groups of people who might be more susceptible to the risks presented by the study and who therefore ought to be excluded from the research? Are the procedures for identifying such individuals adequate?
- Are there adequate plans to exclude participants who are vulnerable to injury during the period of withdrawal of active and effective therapy, if that is part of the research design?

In evaluating risks and benefits, the IRB considers only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies participants would receive even if not participating in the research). The IRB does not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility [45 CFR 46.111(2)].

C. Assessing Equitable Selection of Participants

The IRBs consider the following points when assessing equitable selection of participants:

- Does the nature of the research require or justify using the proposed study population?
- Will the solicitation of participants avoid placing a disproportionate share of the risks and discomfort as well as inconvenience of the research on any single group of individuals?
- Are women of childbearing potential eligible for participation or, if not eligible, has their exclusion been justified?
- Has the selection process overprotected potential participants who are considered vulnerable so that they are denied opportunities to participate in research?
- Are any payments to participants reasonable, based upon the complexities and inconveniences of the study and the particular study population? In making this assessment the IRB takes into account the purposes of the research and the setting in which the research will be conducted and is particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons [45 CFR 46.111(3)].

D. Assessing Methods for Obtaining Informed Consent of Participants or Representatives

The IRBs consider the following points when assessing the methods for obtaining informed consent:

- Who will make first contact with potential participants? If the investigator wants to recruit potential participants while they are in-patients or at UMMC for an office visit, are participants first approached by their physician or health care provider involved in their care?
- Who will be explaining the research to potential participants? Should the principal investigator or a physician co-investigator be required to obtain consent? Should someone in addition to, or other than, the investigator be present (for example, a participant advocate)?
- Does the investigator serve a dual role that may pose a conflict of interest?
- Will the consent process take place under conditions most likely to provide potential participants an opportunity to make a decision about participation without undue pressure?

- Is the language and presentation of the information to be conveyed appropriate to the study population, taking into consideration the reading level, use of complex sentence structure and use of technical terms, as well as the need for translation into languages other than English?
- Do the consent documents describe the study design (including plans for randomization, use of placebos, and the probability that the participant will receive a given treatment), conditions for breaking the code (if the study is masked), and any specimen banking and future use?
- Do the consent documents describe the risks and benefits of each of the proposed interventions and alternative courses of action available to the participants?
- Do the consent documents clearly describe the extent to which participation in the study precludes other therapeutic interventions?

(1) General Requirements for Informed Consent

The following information shall be provided to each participant in accordance with 45 CFR 46.116(a)(1-8) and (b)(1-6), as quoted below:

(a) Basic elements of informed consent.

Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

- (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- (2) A description of any reasonably foreseeable risks or discomforts to the subject;
- (3) A description of any benefits to the subject or to others which may reasonably be expected from the research;
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent.

When appropriate, the following information must be provided to each participant:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

No informed consent, whether oral or written, may include any exculpatory language through which the participant or the representative is made to waive or appear to waive any of the participant's legal rights, or release or appear to release the investigator, the sponsor, the institution or its agents from liability for negligence. While all of the additional elements of informed consent are included in the standard template for consent documents and are required for most studies, others are required for interventional studies depending upon the nature of the intervention. Where the risks of the intervention are not well known, there may be unknown risks to the participant or a developing fetus, and this should be

stated. Where participants are receiving a therapeutic intervention and their participation may be terminated or they may withdraw from participation, the consent form should include the procedure for stopping the study medication and additional procedures or visits the participant will be asked to undergo. This may include procedures such as returning for a final study visit, returning unused study medications, and being referred back to their primary care physician for ongoing care for their medical condition.

(2) Alteration or Waiver of Informed Consent

Under the Common Rule (45 CFR 46.116(d)(1-4)) IRBs have the authority to alter or waive the requirement for informed consent of research participants; however the FDA (21 CFR 50.24) only provides an exception from informed consent requirements for emergency research. For research not subject to FDA regulations, an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that the regulatory requirements in 45 CFR 46.116(c) and (d) quoted below are satisfied:

(c)(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: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration.

Or the IRB finds and documents that:

(d)(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

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

(3) Informed Consent Requirements in Emergency Research

(a) Research subject to FDA regulations (IND or IDE research)

When the research involves the planned enrollment of participants who are in a life-threatening situation, who are in need of emergency therapy, and for whom legally effective informed consent cannot be obtained because of their medical condition and the unavailability of a legally authorized representative, the IRB may approve an exception from informed consent if the IRB finds and documents that the requirements detailed in 21 CFR 50.24 are met.

(b) Research not subject to FDA regulations

When the research involves the planned enrollment of participants who are in a life-threatening situation, who are in need of emergency therapy, and for whom legally effective informed consent cannot be obtained because of their medical condition and the unavailability of a legally authorized representative, the IRB may approve a waiver of informed consent if the IRB finds and documents and reports to OHRP that the requirements detailed in the OPRR Report *Informed Consent Requirements in Emergency Research* dated October 31, 1996 are met.

E. Assessing Documentation of Informed Consent

An individual's willingness to join a study must be documented by a written consent form, or, in certain types of studies as the IRBs deem appropriate, by oral consent, noted in the participant's medical record (or research study record where no medical record exists). In rare cases, the IRBs may waive documentation of informed consent when such documentation might constitute a potential risk to the research participant's privacy, or alter or waive the requirement as described below.

In certain circumstances, the regulations allow the IRB to waive the requirement of written informed consent. For research subject to FDA regulations, the IRB may waive written informed consent only for research that meets (2) below. An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all research participants, if it finds either:

(1) That the only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether the participant wants documentation linking the participant to the research, and the participant's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required

outside the research context. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide participants with a written statement regarding the research.

The IRBs consider the following points when assessing documentation of informed consent:

- Does the consent form include the required elements of informed consent and additional elements, if applicable?
- Does the consent form include the requirement for the signature of the participant or his/her legally authorized representative?
- Does the research involve minimal risk and would written consent be required for these procedures if they were not part of a research study? In most cases a written consent form must be used to obtain informed consent of the participant or the participant's legally authorized representative. The consent form must include the elements of informed consent required by 45 CFR 46.116 and must be signed and dated by the participant or his/her legally authorized representative, and the PI.

Examples of situations where the IRB may waive the requirement for written documentation of informed consent include studies limited to focus groups, or mail or telephone surveys or interviews. When the IRB waives the requirement for written documentation of informed consent, the findings will be documented in the IRB database and in the IRB study file.

F. Assessing Data and Safety Monitoring Plan

The IRBs require investigators proposing interventional research with human participants to address plans for monitoring the data to ensure the safety of the research participants. The plan may be described by the sponsor in the corporate or cooperative group protocol, or by the investigator in an investigator-initiated protocol. The Data and Safety Monitoring Plan (DSMP) must be presented in sufficient detail for the IRB to determine whether it is appropriate for the research.

Data and safety monitoring is the process for reviewing accumulated outcome data for groups of participants to determine if the research should be altered or stopped. Ongoing review of the aggregate data ensures that the study can continue without undue risk to participants.

Safety monitoring also includes the continual assessment of risks and benefits through the review of individual adverse events and other safety parameters as

they occur during the study to determine whether individual participants can safely continue to participate.

Data monitoring is the process for ensuring the scientific integrity of the research data including its accuracy, completeness and its collection in compliance with the protocol.

A Data and Safety Monitoring Plan is unique to the study and should be commensurate with the potential risks and with the size and complexity of the study. Appropriate DSMPs may fall anywhere along a continuum from monitoring by the principal investigator or group of investigators to the establishment of an independent Data and Safety Monitoring Board (DSMB). Regardless of the type of DSMP, the individuals participating in the monitoring plan must be objective.

In general, a DSMB is the most appropriate way to monitor data and safety for studies that involve:

- Large number of participants;
- Multiple sites;
- High risk therapies/procedures;
- High rates of morbidity or mortality related to the underlying disease process being studied; and/or
- Blinded studies.

The IRBs consider the following points when assessing the plan for monitoring the data:

- How will the study be monitored? Will there be an independent data and safety monitoring board?
- How will decisions about stopping the study be made, by whom, and on what basis?

G. Assessing Privacy and Confidentiality Protections

During the course of a study, the highest standards should be maintained with regard to the privacy and confidentiality of information, including interviews, photographs, and other records concerning the participant. Although more investigators and staff may be involved in the conduct of a study than might occur in the usual course of treatment of a patient, confidentiality standards should not be relaxed. The IRBs consider the following points when assessing privacy and confidentiality protections:

- If the investigator wants to review existing records to select participants for further study, are participants recruited through their physician or health care provider involved in their care?
- Will the investigator(s) be collecting sensitive information about individuals (e.g., related to sexual practices, substance abuse, or illegal behavior)? If so, have they made adequate provisions for protecting the confidentiality of the data through coding, destruction of identifying information, limiting access to the data, or other methods that may be appropriate to the study?
- If the information obtained about participants might interest law enforcement or other government agencies to the extent that they might demand personally identifiable information, should a certificate of confidentiality be sought from a federal or state agency to try and protect the research data and the identity of the participants from subpoena or other legal process?
- Are there adequate plans to protect participants from the risks of breach of confidentiality and invasion of privacy? If the protocol involves an epidemiologic study, will participants or their relatives be protected from learning inappropriate information?

The IRBs do not serve as the Privacy Officer for the institution. The IRBs' responsibilities as they pertain to HIPAA include:

- Development and implementation of research policies to comply with HIPAA and the Privacy Rule;
- Review of authorization language, which is required to be merged with the research consent form; and
- Approval of waivers of authorization for research-related activities.

The IRBs serve as a resource to the Privacy Officer for any HIPAA research questions or concerns.

H. Vulnerable Populations

When the research involves the inclusion of vulnerable populations (e.g., pregnant women, human fetuses and neonates, prisoners, children, cognitively impaired persons), the IRBs are responsible for considering additional protections [45 CFR 46 Subpart B, C, D]. The inclusion of a vulnerable population in the research must be justified and adequate safeguards must be in place to minimize risks unique to the particular vulnerable population.

1. Pregnant Women or Fetuses

Pregnant women or fetuses may be involved in research if all of the regulatory conditions in 45 CFR 46.204 are met, as quoted below:

(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or if there is no such prospect of direct benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

(c) Any risk is the least possible for achieving the objectives of the research;

(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A;

(e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

(f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(g) For children as defined in 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;

(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

(i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

(j) Individuals engaged in the research will have no part in determining the viability of a neonate.

2. Neonates

Neonates may be involved in research if all of the regulatory conditions in 45 CFR 46.205 are met, as quoted below:

(a) Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

(1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;

(2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and

(3) Individuals engaged in the research will have no part in determining the viability of a neonate.

(b) Neonates of uncertain viability may not be involved in research unless:

(1) The IRB determines that:

(i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

(ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

(2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained except that consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(c) Nonviable neonates may not be involved in research unless all of the following additional conditions are met:

(1) Vital functions of the neonates will not be artificially maintained;

(2) The research will not terminate the heartbeat or respiration of the neonate;

- (3) There will be no added risk to the neonate resulting from the research;
- (4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- (5) The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 subpart A, except that the waiver and alteration provisions of 46.116(c) and (d) do not apply.

However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice. Consent of the father need not be obtained if the pregnancy resulted from rape or incest. Consent cannot be obtained from a legally authorized representative.

(d) Viable neonates may be included in research only to the extent permitted by 45 CFR 46 Subpart D - Additional Protections for Children Involved as Subjects in Research.

3. Prisoners

Research involving prisoners can only be approved by an IRB that satisfies the following regulatory requirements in 45 CFR 46.304, as quoted in part below:

(a) The majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.

(b) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

“Prisoner” is defined by HHS regulations at 45 CFR 46.303(c) as “any individual involuntarily confined or detained in a penal institution. Guidance provided by OHRP extends the definition to individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. Investigators are required to describe the study population in the IRB submission and to indicate, when applicable, that prisoners will be recruited and enrolled in the research.

If during the course of the research, an individual participant becomes a “prisoner” as defined above, the investigator is required to notify the IRB

promptly. At that point the investigator must discontinue all research activities with the participant unless the investigator asserts in writing and the IRB Chairperson agrees in writing that it is in the best interests of the participant to continue to participate in the research while the research is being re-reviewed by the IRB in accordance with the additional protections for research involving prisoners.

In making this determination the IRB Chairperson will consider

- (1) whether the research involves an intervention or procedure that holds out a prospect of direct benefit that is important to the health or well-being of the individual and is available only in the context of the research; and
- (2) whether the research can be performed safely while the individual is a prisoner.

Until such time as the IRBs include a prisoner representative, research involving prisoners will not be accepted for review.

4. Children

According to Mississippi State Law, minors are persons under the age of eighteen. The general rule is that a person may consent for his or her own medical care at the age of eighteen, and, pursuant to Miss. Code Ann. 41-41-17, may consent to participate in research. Certain statutes and case law provide minors with majority status in some circumstances, for example: emancipated minor; mature minor; or minor seeking care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion.

The IRBs may approve research that involves children as research participants if regulatory requirements at 45 CFR 46.404, 405, 406 are met, as quoted in part below:

- (a) The research does not involve greater than minimal risk;
- (b) The research involves greater than minimal risk but presents the prospect of direct benefit to the individual subjects; or
- (c) The research involves greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition.

If the IRB finds that the research is not approvable as indicated above, but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, the research can be submitted for

review by the Secretary of HHS in accordance with 45 CFR 46.407. When investigators plan to enroll minors in research, they must address the level of risk to participants and, if greater than minimal risk, the prospect for direct benefit to individual participants, if any, and the importance of the information to be gained about the participant's condition in the protocol submission to the IRB. The IRBs have a form for review of research involving children as research participants, to assist IRB members in their review.

5. Cognitively-Impaired Persons

A person is generally legally competent to give informed consent to participate in research when she/he understands the difference between treatment and research, understands the risks and benefits of a specific research protocol and its procedures, appreciates the consequences of acting (or not acting), and is able to make a choice. In research involving a person with impaired decision-making capacity who cannot give informed consent, federal regulations require that consent be obtained from the person's legally authorized representative, as determined by state or local law.

In such cases, the first step is for a qualified professional to assess the individual's competency. General competency measures – such as the Clinical Dementia Rating (CDR) or the Activities of Daily Living scale – may be helpful, but generally should not be the sole measure of competency. Similarly, the Mini Mental Status Exam (MMSE) may be a helpful starting point, but is not appropriate as a sole measure. A formal psychiatric and/or medical assessment may be warranted, and importantly, should consider what level of understanding is needed for the specific research. The investigator should describe in detail how competency will be assessed, who will perform the assessments, and what that professional's relationship is to the individual and the research team in the protocol submission to the IRB.

In order to strengthen the integrity of the enrollment process, in any research involving more than a questionnaire or cognitive test – such as a study of a new medication – consideration should be given to using an independent professional (who is not part of the research team) to assess a potential participant's competency.

The IRBs consider the following points, where applicable, when assessing research involving vulnerable populations:

- Is the inclusion of the vulnerable population necessary, e.g., the research pertains specifically to the vulnerable population;
- Has the research been preceded by adequate preclinical and clinical studies;

- Is the risk to the participant, and, if applicable, the fetus, minimal or greater than minimal risk;
- Is there the potential for direct benefit to individual participants;
- Is the information or knowledge to be gained important;
- Are the procedures for determining competency to consent appropriate;
- Should decision-making capacity be assessed by an independent physician;
- Should the consent process be monitored;
- Is permission of both parents required;
- Is assent required; and
- Should a research participant advocate be involved in the consent process, initially and throughout the course of the study.

I. Ancillary Committee Review

In addition to obtaining approval of the IRBs, when applicable, the following ancillary review committees must review and approve the research activity prior to initiation of the research and enrollment of participants. The ancillary committees are responsible for communicating issues and/or concerns to the investigators and the IRBs, and when approved, for providing written notification of approval to the IRBs.

1. Radiation Safety Committee UMMC's Radiation Safety Committee must review and approve human research that meets the following criteria:

- Research activities involving exposure to ionizing radiation for research purposes;
- Research activities involving exposure to nonionizing radiation for research purposes; or
- Research activities that involve the use of radiopharmaceuticals.

2. Institutional Biosafety Committee (IBC) The IBC must review and approve human research that involves the use of recombinant DNA and/or microbiological agents that pose a potential risk to humans.

J. Corporate Sponsored Research

When the research is corporate sponsored, the clinical trial agreement must be executed between the sponsor and UMMC's Grants and Contracts office before the research may begin.

K. Notification to PI of IRB Approval

When the research protocol is approved, the PI is notified in writing of the date of IRB approval and expiration as well as the following responsibilities:

- Requirement to submit in writing any and all changes to the research project to the IRB for review and approval prior to initiation of the changes(s), except where necessary to eliminate apparent immediate hazards to the participant. Changes made to eliminate apparent immediate hazards to participants must be reported to the IRB within 24 hours.
- Requirement to submit in writing any and all adverse event(s) that occur during the course of the study that are both serious and unexpected within 14 days of notification of the event, with the exception of unexpected death of a UMMC study participant, which must be reported within 24 hours of discovery;
- Requirement to submit in writing any and all unanticipated problems involving risks to participants or others;
- Requirement to use only IRB approved copies of the consent document(s), questionnaire(s), letter(s), advertisement(s), and/or other materials; and
- Responsibility to inform all physicians listed on the project of changes and unanticipated problems.

XI. MONITORING AND OVERSIGHT

A. Ensuring Continuing Review Prior to Expiration of Approval

Ninety, sixty, and thirty days prior to expiration of IRB approval, the PI is notified in writing that continuing review of the research protocol is coming due. Notices include available meeting dates and submission deadlines. Ninety and sixty day notices are sent via email, while thirty day notices are sent via email and campus mail. The required continuing review form is available on the IRB web page. Once the completed form and required documents are received, the protocol is reviewed either at a convened meeting of the reviewing IRB, or through the expedited review procedure as described previously.

If and when IRB approval expires, the PI is notified that all research activities must stop. Research activities include, but are not limited to, recruitment and enrollment of participants, collection of specimens, research on previously collected specimens, review of medical records or other health information, data analysis, and performance of research tests/procedures, treatment or follow-up on previously enrolled participants. In addition, copies of notifications of expiration of IRB approval are forwarded to the appropriate department chairperson and the Office of Compliance. If treatment and/or follow-up of participants is necessary for the safety and welfare of participants, the PI must inform the IRB in writing immediately and request permission to continue previously enrolled participants on study. The IRB Chairperson is responsible for considering these requests on a case-by-case basis and providing written documentation of permission, when granted.

B. Ensuring Prompt Reporting to the IRB of Proposed Changes in Research Activities and Ensuring that Changes are not Initiated Without IRB Review and Approval, Except Where Necessary to Eliminate Apparent Immediate Hazards

Federal regulations 45 CFR 46.103(4) require IRBs to have written procedures to ensure prompt reporting to the IRB of proposed changes in a research activity, and for ensuring 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 hazards to the participant. Investigators are required to promptly report to the IRB proposed changes in research for approval prior to initiation of the proposed change.

The procedures used by the IRB to ensure compliance with this requirement include the following:

- Inclusion of statement in the approval letter reminding investigators of requirement to submit any changes to the protocol and/or consent form to the IRB for approval prior to initiation of the change;
- Inclusion of statement in the Investigator's Responsibilities appended to each approval letter.
- Inclusion in the required education program for research personnel of requirement to obtain IRB approval of changes to the protocol and/or consent form prior to initiation of changes;

- Inclusion of statement in the approval letter requiring investigators to use latest version of IRB-approved and validated consent form(s) when enrolling participants;
- Inclusion in the required education program for research personnel of the requirement to use the latest version of IRB-approved and validated consent form(s) when enrolling participants;
- Reminder of requirement in other educational venues, e.g., research coordinator orientation, lectures, random roundtable discussions, focus groups, and departmental Q/A sessions held by the chairpersons and/or IRB Director; and
- Random assessments of investigator's protocol-specific records and files by the Office of Compliance.

Proposed changes during the period of IRB approval are reviewed by the IRB as described previously in this policy.

C. Ensuring Reporting of Unanticipated Problems Involving Risks to Participants or Others

Federal regulations 45 CFR 46.103(b)(5) require IRBs to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any unanticipated problems involving risks to subjects or others. Investigators are required to promptly report to the IRB unanticipated problems involving risks to participants or others. An unanticipated problem involving risks to participants or others is defined as any unexpected, untoward event that involves any aspect of the research and places the participant or anyone else at risk of serious harm. The following are examples of unanticipated events that need to be reported to the IRB if they involve risks to participants or others. Examples of unanticipated events:

- Serious unanticipated and related adverse events;
- Events resulting in unplanned changes to the protocol;
- Events resulting in one time planned changes;
- One time inclusion/exclusion changes;
- Interim results;
- Safety monitoring reports;
- Participant complaints;
- Laboratory errors;
- Medication errors;
- Disclosure of confidential information;
- Lost or stolen confidential information;
- Disqualification of investigators; or

- Suspension of investigator.

The IRBs have developed specific guidelines and forms for investigators to use when reporting adverse events and protocol deviations, exceptions and violations. All other unanticipated problems involving risks to participants or others should be reported in writing by letter or email to the IRB.

Consistent with the adverse event reporting guidelines, unanticipated problems involving risks to participants or others must be reported to the IRB within ten (10) business days of discovery of the problem or event. The only exception to the time frame for reporting is unexpected deaths that may be related to the research. Unexpected deaths that may be related to the research must be reported immediately, within 48 hours of discovery of the event. The IRB Chairperson is responsible for reviewing and determining whether the participant(s) participating in the research or others were placed at risk of serious harm and whether the problem or event is unanticipated. If the reported problem is unanticipated and involves risks to participants or others, the report is referred to the applicable IRB for review at a convened meeting.

The applicable IRB is responsible for the review of the unanticipated problem and by majority vote may take one or more of the following actions:

- Accept the report and approve the proposed changes, if any, with no further action required;
- Require additional information;
- Require modifications to the protocol and/or consent form;
- Require that participants currently on protocol be notified of the event;
- Require that participants whose participation has ended be notified of the event;
- Require that participants currently on protocol be re-consented;
- Modify the continuing review schedule;
- Suspend the research;
- Terminate the research;
- Request an audit by the Office of Compliance; or
- Other actions deemed appropriate by the IRB.

The IRB staff is responsible for recording the findings and actions of the IRB in the Minutes. The Principal Investigator and Institutional Official are notified in writing of the actions of the IRB as described previously. Copies of the notification may be sent to the following, as applicable:

- Department Chairperson;
- Institutional Representatives and IRB Chairperson(s) of institutions relying on UMMC's IRBs for review;
- Sponsor
- Grants and Contracts (sponsored research);
- Food and Drug Administration (FDA-regulated research); and

- Office for Human Research Protections (OHRP).

D. Noncompliance with Human Research Protection Regulations or IRB Requirements and Determinations

Investigators are required to report to the IRB any noncompliance with human research protection regulations, or the requirements and determinations of the IRB. Noncompliance related to the conduct of a particular protocol is considered a protocol violation. A protocol violation is defined as any deviation from the IRB-approved protocol that is not approved by the IRB prior to its initiation or implementation. The protocol includes the protocol and information related to the conduct of the research approved by the IRB.

When the investigators or others in the course of carrying out their responsibilities discover noncompliance with the regulations or requirements or determinations of the IRB, the Principal Investigator is to be informed and is responsible for reporting the noncompliance and any corrective action taken to the applicable IRB, as described below.

1. Minor Noncompliance (Minor Violation)

Minor violations are violations that do not impact participant safety, compromise the integrity of the study data and/or affect the participant's willingness to participate in the research. When the noncompliance is considered minor, the noncompliance (or violation) is to be reported with the continuing review. Minor violations are reviewed at the time of continuing review either at a convened meeting or, as appropriate to the research activities, through the expedited review procedure. If the IRB or IRB Chairperson finds the violation to be serious, the review and reporting requirements for serious and continuing noncompliance are followed, as described below.

2. Serious or Continuing Noncompliance (Major Violation)

Federal regulations 45 CFR 46.103(b)(5) require IRBs to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB. Serious or continuing noncompliance is considered a major violation. A major violation is a violation that may impact participant safety, affect the integrity of the study data and/or affect the participant's willingness to participate in the study. When the noncompliance is considered major, the noncompliance and any corrective action taken is to be reported promptly to the IRB within 14 days of discovery of the noncompliance.

The IRB is responsible for the review of the serious or continuing noncompliance and by majority vote may take one or more of the following actions:

- Accept the report and approve the proposed changes, if any, with no further action required;
- Require additional information;
- Require modifications to the protocol and/or consent form;
- Require that participants currently on protocol be notified of the noncompliance;
- Require that participants whose participation has ended be notified of the noncompliance;
- Require that participants currently on protocol be re-consented;
- Modify the continuing review schedule;
- Require remedial education;
- Require oversight by a senior investigator;
- Restrict, suspend, or terminate research privileges;
- Suspend the research;
- Terminate the research;
- Require periodic audits by the Office of Compliance; or
- Other actions deemed appropriate by the IRB.

The IRB staff is responsible for preparing a description of the noncompliance, reporting it on the meeting Agenda, and recording the findings and actions of the IRB in the Minutes. The description of the noncompliance and report of the findings and actions of the IRB are communicated in writing to the Principal Investigator (PI), as well as the Institutional Official(s), and IRBs relying on UMMC's IRBs for review and oversight of the protocol, as applicable. The Chairperson of the IRB is responsible for preparing a report to the Institutional Official within 30 days of the IRB meeting. Copies of the report are sent to the following, as applicable:

- Principal Investigator;
- Dean of the School of Medicine, School of Dentistry, School of Nursing, School of Health Related Professions, as applicable;
- Department Chairperson;
- Institutional Representatives and IRB Chairperson(s) of institutions relying on UMMC's IRBs for review;
- Sponsor
- Grants and Contracts (sponsored research);
- Food and Drug Administration (FDA-regulated research);
- Office for Human Research Protections (OHRP).

3. Possible or Suspected Noncompliance

When, in the course of carrying out its duties or by other means, the IRB becomes aware of possible serious or continuing noncompliance with the regulations governing research involving human participants or the requirements of the IRB, the possible serious or continuing noncompliance is investigated by the Director of IRB and/or the Director of the Office of Compliance, or his/her designee, at the direction of the Chairperson of the applicable IRB. The Director of the IRB and/or the Director of the Office of Compliance will prepare and forward a report to the applicable IRB for review and reporting as described previously. Depending upon the scope of the noncompliance, the IRB may elect to form a subcommittee of the membership to review the report and make recommendations to the IRB. In such cases, the subcommittee must include at least one nonscientist member and one member who is not otherwise affiliated with UMMC. The recommendations of the subcommittee are discussed and voted on by the IRB at a convened meeting.

E. Suspension or Termination of Research

The IRB may suspend or terminate a research protocol involving human participants for reasons including, but not limited to:

- unanticipated problems involving risks to participants or others; or
- serious or continuing noncompliance with the research.

When the IRB votes to suspend or terminate a research protocol the IRB considers whether the suspension or termination requires that participants be withdrawn from the study and/or places participants at risk of harm. When participants must be withdrawn from an interventional study, the IRB considers and determines necessary termination procedures for the safety and welfare of those participants, e.g., drug taper, final visit, lab tests, other follow-up, and arrangements for continued care by the participant's physician or through appropriate referrals. If the IRB determines that the suspension or termination will place participants at risk of harm, the IRB must determine what participants should be told and the manner in which they will be notified, e.g., in writing or by telephone. Depending upon the reasons for the suspension or termination and the design of the protocol, the IRB may require that the following participants be notified of the suspension or termination:

- all participants who have been or are enrolled;
- participants currently on protocol; or
- participants who participated in a certain aspect of the protocol.

Whenever the IRB suspends or terminates a research protocol involving human research participants, the following individuals, as appropriate, are notified by the

Chairperson of the applicable IRB of the suspension or termination within 10 working days of the suspension or termination:

- Study participants;
- Principal investigators, co-investigators and study staff;
- Department Chairperson;
- Departments involved in the conduct of the research;
- Director, Office of Integrity and Compliance;
- Office of Research
- Institutional Official(s);
- Institutional Representatives and IRB Chairperson(s) of institutions relying on UMMC's IRBs;
- Sponsor
- Grants and Contracts (sponsored research);
- Food and Drug Administration (FDA);
- Office for Human Research Protections (OHRP).

Expiration of IRB approval is not considered termination of research and is not subject to the reporting requirements outlined above.

XII. RECORDKEEPING AND RETENTION REQUIREMENTS

A. The University of Mississippi Medical Center's IRBs

The IRBs maintain records of their activities for at least 6 years after completion of the research in accordance with 45 CFR 46.115(b). The records are available for inspection and copying by the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), other federal or state government agencies, institution or hospital departments, as needed, or hospital accrediting agencies in the course of carrying out their respective duties.

1. IRB Membership The IRB Office maintains a list of IRB members that includes the following information:

- Name;
- Earned degrees;
- Representative capacity (physician scientist; other scientist; nonscientist);
- Indications of experience, such as board certifications, licenses; and
- Affiliation, if any, to UMMC.

The membership roster for each IRB and OHRP IRB registration is updated as required, and, as needed, when there are changes in the membership. The updated OHRP IRB registration is submitted to OHRP as required.

2. IRB Minutes The IRB Office maintains Minutes of IRB meetings that include the following information:

- Voting members (or alternates) present;
- Guests, including consultants, present; and

For each new or continuing protocol, and amendment to a continuing protocol reviewed at the meeting:

- Action taken by the IRB;
- Votes for, against, or abstentions;
- Members attending but not present for the discussion and vote;
- Recusals of voting members;
- Period of IRB approval, i.e., one year or less;
- Findings and determinations of the IRB;
- Summary of the discussion of controverted issues and their resolution; and
- Basis for requiring changes or disapproving the research.

3. Research Proposals Reviewed The IRB Office maintains files for every research proposal reviewed by the IRBs that include:

- All of the documents submitted with the research proposal for review, initially and subsequently, including, but not limited to, the application form, protocol summary, detailed protocol, recruitment materials (letters, flyers, advertisements, etc.), consent form(s), drug/device brochures, NIH (or federal) grant, NIH cooperative group protocol, NIH cooperative group sample consent form, ancillary committee/department review, scientific evaluations, if any;
- Checklists and review documentation (if any);
- IRB-approved recruitment materials;
- IRB-approved consent form;
- Progress reports, interim analyses, safety reports, DSMB reports;
- Reports of injuries to participants;
- Reports of unanticipated problems involving risk to participants or others;
- Reports of protocol violations;
- Proposed changes to the protocol and revised documents (amendments);
- Copies of all correspondence between the IRB and investigator;
- Continuing review submissions for review including, but not limited to application form, protocol summary, detailed protocol, recruitment materials, NIH progress reports; and
- Statements of significant new findings provided to participants.

4. Written IRB Procedures The IRB Office maintains the IRB policies and procedures, including IRB guidance documents, and significant communications to the research community. The written policies and procedures include, but are not limited to procedures for:

- Conducting initial and continuing review of research;
- Reporting its findings and actions to the investigator and the institution;
- Determining which projects require review more often than annually;
- Determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review;
- Ensuring prompt reporting to the IRB of proposed changes in the research activity;
- Ensuring that such changes in approved research, during the period for which IRB approval has already been given, are not initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to participants;
- Ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any unanticipated problems involving risks to participants or others;
- Ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB;
- Ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any suspension or termination of IRB approval.

B. Investigators

Investigators are required to maintain records of their research involving human participants. In general, investigators should keep a file for each study in which copies of documents are placed, including all submissions to the IRB, and all correspondence to and from the IRB and the Office of Compliance. Investigators should also keep a file for each participant enrolled or screened for a study in which documents are placed, including the signed and dated consent form and copies of case report forms.

Good records are essential for verifying the quality of study data produced and demonstrating investigator compliance with good clinical practice guidelines and applicable regulatory requirements. Depending upon the nature of the study, a case report form (CRF) provided by the sponsor or data collection/work sheets should be used to capture all data required by protocol for each participant. All primary data should be promptly recorded in clear, adequate, original and permanent form and source documents should be retained to corroborate entries on the CRF or data collection sheets. The scientific documentation and material products of all research carried out at the institution are the property of the institution. Department chairpersons have been delegated the responsibility for the scientific non-commercial management of the property under the Patent and Intellectual Policies and Procedures of the University of Mississippi Medical

Centers. They, in turn, may delegate on-site responsibility to the principal investigator for the particular project.

Research records should be retained for at least five (5) years from the time the study has been completed, or longer if required by the sponsor. All such permanent records must remain in the laboratory or department upon departure of the investigator from the institution. Consideration of alternative arrangements for copies to be kept at the institution, instead of original records, must be done with the department chairperson or his/her designee.

1. Investigational Drugs The investigator is expected to conduct a clinical investigation according to the plan agreed upon by the sponsor and approved by the IRB. The investigator must keep certain records of the investigation as detailed in the federal regulations 21 CFR 312.62(a)(b)(c), as quoted below:

(a) *Disposition of drug.* An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 312.59.

(b) *Case histories.* An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

(c) *Record retention.* An investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

2. Investigational Devices The investigator is expected to conduct a clinical investigation according to the plan agreed upon by the sponsor and approved by the IRB. The investigation must be conducted under his/her supervision and he/she may not supply an investigational device for use by any investigator not authorized under the approved plan. In addition, the investigator must keep certain records of the investigation as detailed in the federal regulations 21 CFR 812.140(a)(d), as quoted below:

(a) *Investigator records.* A participating investigator shall maintain the following accurate, complete and current records relating to the investigator's participation in an investigation:

(1) All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.

(2) Records of receipt, use or disposition of a device that relate to:

- (i) The type and quantity of the device, the dates of its receipt and the batch number or code mark.
- (ii) The names of all persons who received, used, or disposed of each device.
- (iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

(3) Records of each subject's case history and exposure to the device. Such records shall include:

- (i) Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
- (ii) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering and during the course of the investigation, including results of all diagnostic tests.
- (iii) A record of the exposure of each subject to the investigational device, including the date and time of each use and other therapy.

(4) The protocol, with documents showing the dates of and reasons for each deviation from protocol.

(5) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

(b) *Retention Period.* An investigator or sponsor shall maintain the records required by this subpart during the investigation and for a period of 6 years after one of the following two dates, whichever is later: the date on which the investigation is terminated or completed; or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

XIII. EMERGENCY USE

A. Emergency Use of an Investigational Drug or Biologic

The IRBs allow the emergency use of an investigational drug or biologic if the FDA requirements for emergency use are met. Whenever possible, an IRB Chairperson should be notified of the intent to use the investigational drug or biologic to ensure that the FDA requirements for emergency use are met.

Emergency use of an investigational drug or biologic is defined as the use of an investigational drug or biological product with a human in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain approval from the IRB. The emergency use provision in the FDA regulations is an exemption from prior review and approval by the IRB and may not be used unless each of the following conditions exist:

- the patient is in a life-threatening or severely debilitating situation;
- there is no standard acceptable treatment available; and
- there is not sufficient time to obtain approval from the IRB.

Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical study analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the participant must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Even in an emergency situation, the investigator is required to obtain informed consent from the participant or the participant's legally authorized representative unless both the investigator and an independent physician certify in writing all of the following:

- the participant is confronted by a life-threatening (or severely debilitating) situation necessitating the use of the investigational drug;
- informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the participant;

- time is not sufficient to obtain consent from the participant's legally authorized representative; and
- no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the participant.

Although the IRB does not have to prospectively review the emergency use of an investigational drug in a life-threatening situation, whenever possible, investigators are required to contact the IRB Office and document that an emergency exists. Investigators are required to submit a report on the emergency use to the IRB within 5 working days. The report is reviewed by the Chairperson of the IRB to ensure that the emergency use met FDA regulations. The investigator is informed that prospective review by the IRB is required if s/he anticipates the need to use the investigational drug in additional participants.

B. Emergency Use of an Unapproved Device

The IRBs allow for the emergency use of an unapproved device if the FDA requirements for emergency use are met. Whenever possible, the IRB Chairperson should be notified of the intent to use an unapproved device. *Emergency use of an unapproved device* is defined as the use of an unapproved device for a purpose or condition for which the device requires, but does not have, an approved application for pre-market approval (FDA approval for marketing) with a human participant in a life-threatening situation where the unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE.

Using its enforcement discretion, the FDA has not objected if a physician chooses to use an unapproved device in such an emergency, provided that the physician later justifies to the FDA that an emergency actually existed. Each of the following conditions must exist to justify emergency use:

- the patient is in a life-threatening condition that needs immediate treatment;
- no generally acceptable alternative for treating the patient is available; and
- because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

Even in an emergency situation, the investigator is required to obtain informed consent from the participant or the participant's legally authorized representative unless both the investigator and an independent physician certify in writing all of the following:

- the participant is confronted by a life-threatening situation necessitating the use of the investigational device;
- informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the participant;
- time is not sufficient to obtain consent from the participant's legally authorized representative; and
- no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the participant.

Although the IRB does not have to prospectively review the emergency use of an unapproved device in a life-threatening situation, whenever possible, investigators are required to contact the IRB and document that an emergency exists. Investigators are required to submit a report on the emergency use to the IRB within 5 working days. The report is reviewed by the Chairperson of the IRB to ensure that the emergency use met FDA regulations. The investigator is informed that prospective review by the IRB is required if s/he anticipates the need to use the investigational device in additional participants.

Changes and Modifications of Policies and Procedures These policies and procedures are supplemented by guidance documents and instructional material prepared by the IRB and made available to investigators on the IRB website. From time to time, as may be necessary or appropriate to ensure fulfillment of institutional responsibilities under existing Assurances, to improve operational efficiency, or to address other concerns that may arise, these *Policies and Procedures* may be revised. All revisions will be documented as an addendum until such time as a revised version of this document is prepared.

Adopted October 1, 2005
University of Mississippi Medical Center



**The University of Mississippi Medical Center
Institutional Review Board**

Policies and Procedures - Addendum 1

Assent from Minors Participating in a Research Study

Addendum Number: 1	Effective Date: 1/1/08
Version Number & Date: V1. 12/1/07	
Superseded Version Number & Date (if applicable):	

BACKGROUND

Consent:

The most comprehensive definition of informed consent is to be found in the Nuremburg Code (1947):

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the subject matter involved as to enable him to make an understanding and enlightened decision.

Informed consent is the process by which a competent research volunteer voluntarily agrees to participate in research study, after having been informed of, and having comprehended all aspects of the study that are relevant to the decision to participate. The Informed consent process is an exchange of information, which involves the giving of information, the discussion and clarification of the information and obtaining the research volunteer's consent. The consent form is **only one part** of the ongoing dialogue between researchers and participants. Obtaining the consent and/or assent of each participant is a process that lasts throughout the study. It is morally and professionally unacceptable to perform any research related procedure on someone without first obtaining informed consent from the volunteer.

Assent:

Minors (volunteers under 18 years of age) cannot give legal consent and are instead asked for 'assent' to participate in research. Permission of the minor's parent(s) or legally authorized representative is also required.

Pursuant to 45CFR46.408, adequate provisions must be made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. When determining whether children are capable of providing assent, the IRB must take into account the ages, maturity and psychological state of the children involved.

PURPOSE

This document describes the procedure for obtaining parental permission and assent from a minor when proposing to enroll minors into a research study.

DEFINITIONS

Children - persons who have not attained the legal age of consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted [45CFR46.402(a)]. In the state of Mississippi, "minors" include any persons under the age of 18 UNLESS the child has been emancipated by court order, marriage, or is on active military duty. (The term 'minor' is interchangeable with "child".)

Assent - a child's affirmative agreement to participate in research. Mere failure to object is not assent.

Child Assent Document – an age appropriate form (2nd – 3rd grade reading level) with a simple explanation of why the study is being done, why the minor is being invited to be in the study, what the minor will be asked to do if he/she agrees to be in the study, common risks, expected benefit(s), and a clear statement that participation is voluntary. This document will be used to help obtain assent from children between the ages of 9 through 13 years.

Adolescent Assent Document – an age appropriate form, written at most on an eighth grade reading level, with an explanation of the study purpose, procedures, risks and benefits, and a clear statement that participation is voluntary. This document will be used to help obtain assent from children between the ages of 14 through 18 years.

Permission – the agreement of the child’s parent(s) or legally authorized representative to the child’s participation in the research.

Permission Document – a form written on an eighth grade reading level (similar to a consent document but using “your child” throughout) that contains all essential elements of consent, <http://irb.umc.edu/newdoc/informed%20consent%20checklist.htm>. This form will be used to help obtain permission from a minor’s parent(s) or legally authorized representative for a minor’s study participation.

Investigators – all persons listed on the FDA1572 or protocol.

PROCEDURE

1. The Permission Document

1a. General Guidelines

Parents should be approached first regarding the child’s participation in the research study, and parental permission should be granted prior to seeking assent from a child who is between 9 through 18 years of age. For children less than 9 years of age, only parental permission is required, but the child should be involved in the consent process and discussion as early as possible.

The parental permission document should be easy to read and understand, written at no more than an **eighth grade reading level**, and give the parent or legally authorized representative a clear understanding of the experience the child can expect to have if the child participates in the research.

The document should be single sided, printed with a minimum of 1 inch margins (the lower right corner of each page must have sufficient blank space (1.5 x 1.5 inches) for the IRB stamp), using the same font type and size (13 or larger) throughout, double space between the paragraphs, and bold or underline the section headers. The document should be written in the second person, using the present or future tense. **The term “your child” should be used throughout the document.** Do not begin sentences with “You understand that”, “It has been explained to you that”, or similar **assumptive phrases**. To avoid confusion, use “study doctor” throughout the document, instead of “doctor”, “researcher” or “physician”, and “participant” instead of “patient” or “subject”.

Each page of the parental permission document must be numbered and contain a header or footer with the study title and the name and title of the Principal Investigator, permission document version number and date, and, for studies

with multiple documents, a short description of the document. **The IRB stamp will be added to the lower right corner of each page once the document has been approved.**

1b. Components

The following information must appear in each permission document:

- A statement that the study involves research
- An explanation of the purposes of the research and the expected duration of participation
- A description of the procedures to be followed
- Identification of any experimental procedures or treatments
- A description of any reasonably foreseeable risks or discomforts to the volunteer
- A description of any benefits to the volunteer or to others which may reasonably be expected from the research
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the volunteer
- A statement describing the extent, if any, to which confidentiality of records identifying the volunteer will be maintained and that notes the possibility that study records may be reviewed and identifies the entities that may inspect the records
- For research involving more than minimal risks, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research volunteer's rights, and whom to contact in the event of a research-related injury to the volunteer.
- A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the volunteer is otherwise entitled, and that the volunteer may discontinue participation at any time without penalty or loss of benefits to which the volunteer is otherwise entitled.

1c. Signatures

The parental permission document shall contain the following signature lines documenting permission from the minor's parent(s) or legally authorized representative for the child's participation in the research study.

Printed Name of Minor Participant

Printed Name of Parent or Legally Authorized
Representative of Minor Participant

Relationship to Minor

Signature of Parent or Legally Authorized Representative

Date

Printed Name of Person Obtaining Permission

Signature of Person Obtaining Informed Permission

Date

I acknowledge that the participant identified above has been entered into this study, with properly obtained informed permission.

Signature of Principal Investigator

Date

2. The Assent Document

2a. General Guidelines

Adequate provision must be made for soliciting the assent of those children capable of providing a meaningful agreement. The process must be appropriate to the study as well as the age, maturity and psychological state of the child.

Parental permission for the minor's participation in the study should be obtained before approaching the minor. Unless the IRB waives the assent requirement (see section 3, Waiver), once assent is requested from a child, the child's decision must be respected. If the child declines participation the child cannot be enrolled into the study.

Children under 9 years of age

Children 8 years of age or younger should be told about the study and included in the discussion as early as possible, to the level of their ability to understand.

Children 9 - 18 years of age

An assent document is recommended for all children ages 9 to 18 years. The assent document should be single sided document, printed with a minimum of 1 inch margins, (the lower right corner of each page must have sufficient blank space (1.5 x 1.5 inches) for the IRB stamp), using the same font type and size (13 or larger) throughout, double space between the paragraphs, and bold or underline the section headers. When writing the assent document please follow the template located on the IRB web page, <http://irb.umc.edu/newdoc/Sample%20Child%20Assent.htm>.

The document should be written in the second person, using the present or future tense. **The term 'you' should be used throughout the document.** Do not begin sentences with "You understand that", "It has been explained to you that", or similar **assumptive phrases**. To avoid confusion, use "study doctor" throughout the document, instead of "doctor", "researcher" or "physician", and "participant" instead of "patient" or "subject".

Each page of the assent document must be numbered and contain a header or footer with the study title and the name and title of the Principal Investigator, assent version number and date, and, for studies with multiple assent documents, a short description of the document. **The IRB stamp will be added to the lower right corner of each page once the document has been approved.**

2b. Components

Information must be presented in language and format that is understandable to the child. The child should have an understanding of the research procedures and it should be clear that participation is voluntary. Once the child provides affirmative agreement, the assent document must be signed by the child before participation may begin.

Minimal risk studies

One type of assent document may be used for all minor participants (9 through 17 years of age), however, it must be written in language that will be easily understood by the youngest participants.

Greater than minimal risk studies

Two different types of assent documents will be used based upon the age of participants.

- **For minors 9 through 13 years of age**, a child assent document will be used. The document should be **written on a 2nd- 3rd grade level**, be age

appropriate and contain at a minimum the following elements in simplified language:

- Study purpose
- Procedures
- Common risks
- Expected benefit(s)
- Statement that participation is voluntary

- **For minors 14 through 17 years of age**, an adolescent assent document will be used. The document should be written at most on an **eighth grade** level. The document can follow the same format as the parental permission document described above, but the term ‘you’ should be used throughout the document.

2c. Signatures

The assent document shall contain the following signature lines documenting the minor participant’s affirmative agreement to participate in the study.

Printed Name of Minor Participant

Signature of Minor Participant

Date

Printed Name of Person Obtaining Assent

Signature of Person Obtaining Assent

Date

I acknowledge that the participant identified above has been entered into this study, with properly obtained informed assent.

Signature of Principal Investigator

Date

3. Waiver

3a - Protocol Specific Waiver

Investigators may request waiver of assent for participants (all or specified age group) in the initial IRB application for a specific protocol under the following circumstances.

- If children are not likely to be capable of assenting (e.g. due to illness, intellectual development, or complexity of study)
- If most of the child participants are expected to be capable of assenting, but some may not, a protocol specific waiver should not be requested. Please see Child Specific Waiver below.
- If the research offers the prospect of direct benefit not available outside of the research.

3b - Child Specific Waiver

If, in the investigator's professional judgment, a child is not capable of providing assent due to illness or intellectual development, the investigator must clearly document in the participant's research chart why assent was not obtained and notify the IRB with the next continuing review. *****This must be determined prior to approaching the child about the study and not in lieu of the child declining to participate.**

Note: The child should still be informed about the study and involved to the extent of his/her capabilities, but assent should not be requested.

4. Documentation

The process of obtaining informed permission and assent must be documented in the participant's research chart and medical record, if applicable. If assent is not obtained, complete and clear documentation of this decision and justification for the decision must be kept in the research files and provided to the IRB.

A copy of the signed permission and assent documents must be filed in the study file and in the participant's medical record, if applicable, and a copy of each must be given to the parent/participant.