

# IRB Policies and Procedures

The mission of MUSC is to provide excellence in patient care, teaching, and research, in an environment that is respectful of others, adaptive to change and accountable for outcomes. Human subjects research is an important element in meeting this mission. MUSC has established policies and procedures for the review of human subject research to ensure the continued support of this mission. MUSC investigators are granted the privilege of using human subjects under assurance to the government that research conducted at MUSC complies with regulations protecting human subjects.

## **Human Subjects Research Guided by Ethical Principles:**

All of the Institution's human subject activities and all activities of the Institutional Review Boards (IRBs) designated under the Assurance, regardless of funding source, will be guided by the ethical principals in: (a) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and (b) other appropriate ethical standards recognized by Federal Departments and Agencies that have adopted the Federal Policy for the Protection of Human Subjects.

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## **Applicability:**

These terms apply for all human subject research, regardless of funding source. The Institution becomes so engaged whenever (a) the Institution's employees or agents intervene or interact with human subjects for purposes of research; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects for purposes of research; or (c) the Institution receives a direct federal award to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator. Federally supported is defined through the FWA and the Terms of Assurance as the U.S. Government providing any funding or other support (including, but not limited to, providing supplies, products, drugs, and identifiable private information collected for research purposes) and/or the conduct of the research involves U.S. Government employees. All human subject research conducted or supported by the DHHS will comply with all Subparts of DHHS regulations at 45 CFR 46 and its Subparts, A, B, C, and D.

## **Definitions 45 CFR 46.102:**

- i. **Research** - A systemic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
- ii. **Human Subject** - A living individual about whom an investigator obtains data through intervention or interaction with the individual, or identifiable private information.
- iii. **Minimal Risk** - 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.

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**Research involving Human Subjects must be reviewed by the MUSC IRB where one or more of the following apply:**

- i. The research is sponsored by this institution, or
- ii. The research is conducted by or under the direction of an individual in connection with his/her institutional responsibilities, or
- iii. The research is conducted by or under the direction of an individual who is receiving remuneration from the institution, or
- iv. The research is conducted by or under the direction of an individual using any property or facility of this institution, or
- v. The research involves the use of this institution's non-public information to identify or contact human research subjects for prospective subjects, or
- vi. The institution's name is used in any way in connection with the study including procurement of sponsorship, announcement or advertisement or other recruitment of subjects.

**Who Can Serve as Principle Investigator and Mentors:**

- i. Full time faculty can serve as principal investigators and mentors.
- ii. Faculty, who do not meet the qualifications stated above, can serve as co-investigators but not as principal investigators. In unique situations, the Provost, may waive this constraint provided a mentor is added to the study.
- iii. MUSC trainees in good academic standing can function as principal investigators with the inclusion of a faculty mentor.
- iv. MUSC employees can function as principal investigators with the inclusion of a faculty mentor.
- v. A principal investigator and the mentor are both responsible for the conduct of the human research. These responsibilities are outlined in the IRB documents signed by the principal investigator and mentor.

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**Employees as research subjects:**

Employees (normal volunteers) may not participate in immediate supervisor's studies if the study poses greater than minimal risk. Exceptions are allowed for those who may derive direct health benefits (e.g. cancer protocol).

### **Students as research subjects:**

Students cannot participate as subjects in their mentor's clinical research if the study poses greater than minimal risk. Exceptions are allowed for those who may derive direct health benefits (e.g. cancer protocol). These will be determined on a case-by-case basis.

- i. Student studies can be performed at the VA provided that:
- ii. The student's mentor is the PI or record at the VA,
- iii. The mentor has VA privileges, and
- iv. The student's name is in the informed consent as a PI.

If the primary mentor does not have VA privileges, another qualified person with VA privileges can be the PI of record at the VA provided that they serve as a secondary mentor to the student. As a secondary mentor, the VA PI will have responsibility over the VA section of the study. The primary mentor will still have ultimate responsibility over the whole study, including the VA and MUSC. The VA R&D Committee determines the PI for VA studies.

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## **JOB DESCRIPTIONS AND RESPONSIBILITIES**

### **Responsibilities of the Institution:**

The institution bears full responsibility for the performance of all research involving human subjects, covered by this Assurance, including complying with federal, state, or local laws as they may relate to such research.

The institution assures the federal government that the university is in compliance with federal regulations on the use of human subjects in research and that no research involving human subjects is conducted without prior review and approval.

The Institution is responsible for ensuring that all institutions and investigators engaged in its U.S. Federally-supported human subject research operate under an appropriate OHRP or other federally-approved Assurance for the protection of human subjects. In some cases, one institution may operate under an Assurance issued to another institution with the approval of the supporting Department or Agency and the institution holding the Assurance.

The Institution will ensure prompt reporting to the Office of Human Research Protections (OHRP) any significant or material finding or action, at least to include the following:

- i. Unanticipated problems involving risks to subjects or others;
- ii. Serious or continuing noncompliance with federal regulations or IRB requirements, and
- iii.
- iv. Suspension or termination of IRB approval.

Research that has been reviewed and approved by the IRB may be subject to further review and disapproval by officials of the institution. Institutional officials may not, however, approve research if it has been disapproved by the IRB.

The institution will provide the IRB with resources and professional and support staff sufficient to effectively carry out their responsibilities under the Assurance.

The Institution provides legal protection for members of the IRB and to principal investigators granted approval to conduct research, provided they have met their obligations in good faith.

The Institution is responsible for investigating incidents or allegations of misconduct pertaining to the use of human subjects in research.

The Institution provides whistle-blowing protection to anyone who reports an activity that violates any regulations or policies on the use of human subjects.

Under the provisions of the Federal Freedom of Information Act, the Institutions is required, upon request, to release to the public documentation on any active or retired research protocol.

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### **Responsibilities of Principal Investigators and Staff:**

Before initiating, modifying, or extending any research project that uses human subjects, Principal Investigators must submit an application to the Institutional Review Board for Human Research (IRB) for review and approval.

In both the design and conduct of their studies, investigators are obligated to consider racial, cultural, and gender diversity among the subject populations and be sensitive to community attitudes.

Investigators will not make the final determination of exemption from applicable federal regulations or provisions of this Assurance.

Any serious or recurring problem unanticipated side effect, or adverse reaction experienced by a subject must be reported to the IRB. Problems related to the conduct of a study or patient participation (including those in the recruitment or consent process) must also be reported.

The violation of an experimental protocol or any use of subjects not approved by the IRB must be reported immediately to the IRB.

Any investigator who uses human subjects without IRB approval or who willfully violates the scope of his or her approval may lose legal protection provided by the

University and may be held liable for any litigation costs and the costs of any medical care provided to subjects who suffer injury under such circumstances.

### **Responsibilities of the IRB:**

It is the responsibility of the IRB to safeguard the rights and welfare of human subjects who participate in research at MUSC. To this end, the Board is obligated and authorized to:

- i. Ensure that subjects are adequately informed of the nature of the study;
- ii. Ensure that subjects' participation is voluntary;
- iii. Ensure that the benefits of a study outweigh its risks;
- iv. Ensure that the risks and benefits of the study are evenly distributed among the possible subject population; and,
- v. Suspend human subjects activity that violates regulations, policies, procedures, or an approved protocol, and report such violation and suspension the Institutional Official.
- vi. The IRB(s) will review, and have the authority to approve, require modification in, or disapprove all research activities, including proposed changes in previously approved human subject research.
- vii. The IRB will conduct initial and continuing review (not less than once per year), approving research, and reporting IRB findings to the investigator and the Institution.
- viii. The IRB will determine which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since the previous IRB review.
- ix. The IRB will ensure that changes in approved research protocols are reported promptly and are not initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject.
- x. Where appropriate the IRB will determine that adequate additional protections are ensured for vulnerable populations as required by Subparts B, C, and D of 45 CFR 46.
- xi. The IRB will forward to the Office of Human Research Protections (OHRP) any significant or material finding or action, at least to include the following:
  - a. Unanticipated problems involving risks to subjects or others;
  - b. Serious or continuing noncompliance with federal regulations or IRB requirements, and
  - c. Suspension or termination of IRB approval.

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### **IRB Membership (for each IRB)**

Membership shall include:

- i. Chair; Vice-chair(s)
- ii. Men and Women from different ethnicities
- iii. Non-scientific members

- iv. Members with experience in patient care from the various colleges and divisions within those colleges
- v. Members to represent the interests of children, pregnant women and persons with disabilities
- vi. Persons not affiliated with MUSC. These members include but are not limited to attorneys, members of the clergy, and educators representing the local community
- vii. Members may satisfy more than one of the above categories

### **IRB Chair:**

Appointed by the Provost for a three-year term and may be reappointed for consecutive terms. The IRB chair must have been a member of the MUSC IRB for at least two years and have participated in research as an investigator. The Provost is responsible for appointing a replacement if the Chair cannot complete the three year term for any reason.

#### Responsibilities:

- i. Preside at meetings of the IRB.
- ii. Call special meetings when necessary.
- iii. Advise investigators.
- iv. Recommend committee members for appointment to IRB.
- v. Make decisions in emergency situations to protect subjects and remain in compliance with regulations.
- vi. Inform IRB and University Officials of developing problems.
- vii. Appoint Vice-chair(s).
- viii. Appoint subcommittees of IRB.
- ix. Relate concerns of IRB staff and members to administration regarding issues in human research review.
- x. Liaison with the University Committees.

### **IRB Vice-Chair:**

Appointed by the Provost at the recommendation of the Chair for a three-year term and may serve consecutive terms. The IRB Vice-Chair must have the same qualifications as IRB members.

#### Responsibilities:

- i. Preside at meetings of the IRB in Chair's absence.
- ii. Assist the Chair with review procedures.
- iii. Chair Subcommittees.
- iv. Other duties in Chair's absence.
- v. Act as Chair's designee as required.

## **IRB Members:**

Appointed by the Provost at the recommendation of the Chair for three-year terms. Members may be appointed to consecutive terms.

Responsibilities:

- i. Attend meetings (or find alternate) and plan to be present for the entire meeting.
- ii. Contact IRB Office if unable to review for a meeting and find their replacement from the alternate reviewer list.
- iii. Review all material provided.
- iv. Contact investigators as necessary.
- v. Present primary reviewed protocols to the Board as requested.
- vi. Do not review or vote on any issue in which there is a conflict, or perceived conflict of interest.
- vii. Participate in subcommittee activities.
- viii. Protect confidentiality of records provided.
- ix. Act as Chair's designee as required.

Any member of the IRB can be removed by the Provost for failure to perform functions and responsibilities.

## **IRB Staff:**

Responsibilities:

- i. Review IRB submissions and keep IRB members aware of current regulations.
- ii. Prepare agenda and attend meetings of the IRB.
- iii. Prepare Minutes.
- iv. Liaison between IRB members and investigators.
- v. Maintain IRB records: IRB discussions, protocols, modifications, correspondence, approvals, continuing reviews, terminations.
- vii. Advise investigators and study coordinators.
- viii. Provide continuing education for IRB members, investigators and study coordinators.
- ix. Attend at least one National meeting for continuing education.
- xi. Prepare reports as required by regulations.
- xii. Keep abreast of changes in regulations and communicate changes to investigators.

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## **Required Training**

The Institutional Official, IRB Chairs and Human Protections Administrator are required to successfully complete the OHRP Assurance Training Module.

IRB Chairs, IRB members, IRB staff involved in the review of human subjects research applications are required to successfully complete the CITI University of Miami on-line tutorial prior to reviewing applications. Additional training includes familiarizing IRB members with regulations and MUSC procedures through an orientation session with an IRB Administrator. Continuing education is presented at the beginning of IRB meetings. IRB members and staff receive the monthly *Human Research Report*, the quarterly *Hastings Center Report* and other applicable publications. Chairs and IRB Administrators attend at least one national meeting annually.

The following must successfully complete the CITI tutorial:

- i. Principal Investigators, Co-investigators, or investigators identified on any human subjects research protocol (which includes faculty, collaborators, **consultants**, post-docs, house staff, fellows, technicians or others who will play a substantial role in the human subjects research, including a major authorship role when work is reported)
- ii. individuals responsible for obtaining informed consent
- iii. research study coordinators and full-time research nurses
- iv. first year graduate students
- v. Deans, Department Chairs, Division Directors and others who sign off on the "Blue Sheet" for grant submissions
- vi. MUSC Departmental Research Compliance Officers and Liaisons, VA Research Compliance Officers
- vii. MUSC Central Administrators who oversee research
- viii. Office staff of the VA R&D office, VA R&D, Biosafety and IACUC Committee members

The University of Rochester Medical Center *Protecting Study Volunteers in Research* course may be substituted for the CITI course with permission of the Provost or the Academic Compliance Officer.

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### **NIH Human Protection Participation Education for Research Teams**

The following individuals are required to successfully complete the NIH tutorial:

- i. Part-time research nurses
- ii. Individuals who directly collect or provide human tissues or fluids or medical/personal data for explicit use in a research Tissue Bank or for human subjects research, but whose participation is less substantial than those described above
- iii. Technicians who handle human tissues or fluids for human subject research, but whose participation is less substantial than those described above
- iv. Managers of human subjects research data bases whose participation is less substantial than those described above

### **Research Coordinator Development Program**

The following individuals involved in screening subjects for eligibility, obtaining informed consent, collecting and recording data, and/or completing forms and submissions to the IRB are required to successfully complete the RCDP, challenge the course by examination or provide documentation of national certification as a clinical research coordinator:

- i. Study coordinators
- ii. Research nurses
- iii. Other individuals that function in such capacities regardless of job title
- iv. Investigators may choose to take the Research Coordinator Development Program or may be required to attend as part of a corrective action plan as determined by the Board.

Investigators can request presentations for their staff, students or department from IRB Chairs and/or IRB Administrators. The IRB periodically holds university wide town meetings to present new information.

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### **The criteria for IRB approval includes:**

Assessment of the risk/benefit ratio and the importance of the knowledge that may reasonably be expected to result,  
Risks to subjects are minimized,  
Equitable selection of subjects,  
Informed consent is sought from each prospective subject or the subject's legally authorized representative,  
Consent will be appropriately documented,  
Appropriate collection of safety data,  
Issues of privacy and confidentiality and  
Attention to special populations.

Reminders contained in the application packet and informed consent document reinforce these items. Procedures, examples and standard sample paragraphs are provided to investigators.

Reviewer checklists are used to ensure consistency.

Checklists include:

Checklist for Expedited Continuing Reviews  
Expedited Review Form  
IRB Reviewer Checklist (Full Board Review)  
Special Subject Populations  
Informed Consent Document  
HIPAA Authorizations/Waiver of Authorizations  
Research Involving Prisoners

Full Board Amendment  
Foreign Language Review Form

**Lists of Specific Documents Distributed to IRB Reviewers:**

Initial Review - Exempt - Primary Reviewer only  
Exempt form

Initial Review - Expedited or Full Board:

Human Research Review Application - all reviewers  
Request for Expedited Review if applicable - primary  
Human Subjects document - all reviewers  
Advertisements if applicable - all reviewers  
Informed Consent(s) or Waiver of Consent or Waiver of Written Consent forms - all reviewers  
Conflict of Interest form if applicable - primary  
Off Campus Study Site form if applicable - primary  
VA Supplement if applicable - primary  
Protocol - primary  
Complete Grant Application if applicable - primary  
Internally Sponsored or Un-sponsored Research form if applicable - primary  
Non-Sponsored Budget Form if applicable - primary  
Investigational New Drug Information Sheet A if applicable - all reviewers  
Marketed Drug Information Sheet B if applicable - all reviewers  
Oncology Group/NCI Drug Sheet C if applicable - all reviewers  
Medical Device Information Sheet D if applicable - all reviewers  
Investigator Drug Brochure if applicable - primary  
HIPAA Authorization/Waiver of Authorization - primary

Continuing Review - Expedited or Full Board:

Continuing Review form - all reviewers  
Current IRB approved Informed Consents - all reviewers  
IRB file that includes the initial application, all amendments, internal and external adverse events, investigator drug brochures if applicable, informed consents, protocol deviation reports and all other applicable forms that pertain to the study - primary

Amendments - Expedited or Full Board:

Request for Amendment form - all reviewers  
Revised documents (informed consents, protocol, advertisements) - all reviewers  
IRB file that includes initial application, all amendments, internal and external adverse events, investigator drug brochures if applicable, informed consents, protocol deviation reports, HIPAA forms and all other applicable forms that pertain to the study - primary  
Request for HIPAA Amendment - primary

Reports of unanticipated problems involving risks to subjects or others or of serious or continuing noncompliance: Full Board

Compliance audit report - all reviewers

Principal Investigator response to audit report - all reviewers

Correspondence - all reviewers

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## **Levels of Review:**

### **Exempt Research:**

**Federal regulations allow for some categories of research to be exempt from Expedited or Full Board review.**

An Exempt Research Review Application must be completed and submitted to the Office of Research Integrity by the investigator. Application is made by the investigator through the on-line form and submission of one hard copy to the IRB office with appropriate signatures. Before exempt research may proceed, written concurrence that the research meets the appropriate criteria must be obtained from the IRB Chair or his/her designee.

IRB Office Procedures for Exempt Research:

- i. Upon receipt of an application, the paper copy is checked for appropriate signatures.
- ii. Study personnel listed on the application are checked against the Compliance Office database to ensure the required Institutional Training has been completed. If not all personnel have completed the training, a letter is sent to the Principal Investigator informing him/her that IRB approval of the study will not be released until the certification has been submitted to the IRB office.
- iii. If the study coordinator has not completed the RCDP, a letter is sent to the Principal Investigator informing him/her that successful completion of the program must occur by the conclusion of the next scheduled course offering, or enrollment into the study will be suspended until the requirement is completed.
- iv. If educational requirements and signatures are complete, then a HR# is assigned to the study.
- v. The study is given to the Chair or his/her designee for review.
- vi. If the Chair has questions or concerns, the Principal Investigator is notified via email by the IRB staff. Principal Investigator responses are given to the Chair for review.
- vii. If responses are satisfactory and if the research fits the Exempt criteria, then the Chair will approve the application; the IRB staff will enter the approval information in the database and release the hard copy to the Principal Investigator.
- viii. If the Chair makes the decision that the research does not fit the Exempt criteria, then the IRB staff will send a cover letter and a copy of the Exempt form to the Principal Investigator informing them of the Chair's decision. The Principal Investigator also has access to the status of the study via the electronic database.

### **Exempt Review Categories - 45 CFR 46.101**

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (a) research on regular and special educational strategies, or (b) research on the effectiveness of or the comparison among instructional techniques, curricula or classroom management methods.
- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), \*survey procedures, interview procedures or observations of public behavior, unless: (a) information is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects and (b) 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 public behavior that is not exempt under paragraph 2(b) of this section, if (a) the human subjects are elected or appointed public officials or candidates for public office; or (b) 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 subjects. \*Existing means already collected and on the shelf; not collected for purposes of the research.
- (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency head and which are designed to study, evaluate, or otherwise examine: (a) public benefit or service programs; (b) procedures for obtaining benefits or services under those programs; (c) possible changes in or alternatives to those programs or procedures; or (d) 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, (a) if wholesome foods without additives are consumed or (b) if a food is consumed that contains a food ingredient at or below the level 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 above exemptions do not apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization. The exemption at (2)\*, for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

To receive approval for exempt research, the Exempt Research Review Application must be completed, and approved by the investigator's Department Chair prior to submitting to the IRB. The IRB Chair or his/her designee must concur with the exemption before the exempt research can proceed.

## **Investigator Responsibilities for Initial Submission for Expedited or Full Board Review:**

No research will be initiated without prospective IRB review and approval. The NIH Format for a written protocol is utilized. Information in the submission conforms to DHHS and where applicable, FDA regulations. Investigators certify to the IRB that any changes in the approved research will not be initiated until the IRB has reviewed and approved these changes.

- i. Investigators submit protocols to the IRB using an IRB application packet that includes:
- ii. Answers to the Use of Human Subjects Section
- iii. Plans for recruitment and enrollment procedures
- iv. Equitable selection of subjects
- v. Provisions to protect privacy of subjects and confidentiality of data
- vi. Additional safeguards to protect rights and welfare of subjects who might be vulnerable
- vii. Payment to subjects
- viii. Informed consent document(s)
- ix. Research protocol
- x. Complete HHS grant application (if applicable)
- xi. Applicable data sheets on status of drugs and devices:
- xii. Form 1571, and 1572 (if applicable)
- xiii. Principal Investigator C.V. (if applicable)
- xiv. Investigator's drug brochure (if applicable)
- xv. Information on conflict of interest
- xvi. The VA may require additional forms

After approval of the research protocol by the IRB, the investigator has the following ongoing responsibilities:

- i. 46.103(b)(5) - Reporting any unanticipated problems involving risks to subjects or others upon discovery to the IRB staff in writing.
- ii. 46.115(b) - Maintaining records relating to the research for at least three years after the conclusion of the study.
- iii. 46.115(a)(7) - Maintaining records of notification to subjects when there were significant new findings that may have effected the subjects' willingness to continue participation.
- iv. Complying with all requirements for informed consent including seeking consent only under conditions that allow the subject or the subject's legally authorized representative sufficient opportunity to consider whether or not to participate and that minimize the opportunity for coercion or undue influence.
- v. Maintaining copies of all pertinent information related to the research activities in this project including copies of informed consent agreements obtained from participants.

- vii. Submitting proposed changes in research for IRB approval, and receiving IRB approval before implementing the changes.
- viii. Submitting timely continuing review reports to the IRB on progress of the project as required by the IRB.
- ix. Notifying the IRB immediately upon termination of a project and/or the departure of the principal investigator from this Institution and the project.
- x. Maintaining data and other research products produced under this research in a central location in a manner that will allow other qualified scientists to verify the accuracy and integrity of reported results of the research.
- xi. Individuals supported in whole or in part by the research and who are in a training status will be given explicit training in the responsible conduct of research.
- xii. Any individual who has a substantive scientific role in the proposed research has been provided a copy of the application and has had an opportunity to comment on it.
- xiii. Criteria for authorship of publications resulting from the proposed research have been discussed and agreed to by the professional staff of the laboratory.
- xiv. Scientists who have a substantive scientific role in the proposed research do not have any financial interests that could affect the objectivity of the research.
- xv. Any material in the grant application/protocol that is a verbatim reproduction of other persons' writings has been identified by quotation marks and properly attributed.
- xvi. If the PI is unable to direct this research personally, as when on sabbatical leave or vacation, they will arrange for a co-investigator to assume direct responsibility in their absence.
- xvii. Study personnel will have completed the mandatory educational compliance training on human research.

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### **Review Process for Expedited and Full Board Protocols (first time submissions or those which have expired and re-activation is requested)**

#### **Expedited**

An investigator may request expedited review by completing the Human Research Review Application and all applicable attachments and checking the appropriate categories for expedited review. Research may not be disapproved by this mechanism; it can only be referred to the Full Board for review. All studies involving FDA regulated products will be reviewed and approved under FDA regulations.

#### **IRB Office Procedures**

- i. Upon receipt of an application, the application is stamped with the date of receipt. The application is checked for appropriate signatures.
- ii. Study personnel listed on the application are checked against the Compliance Office database to ensure the required institutional training has been completed. If not all personnel have completed training, a letter is sent to the PI informing

- him/her that IRB approval of the study will not be released until certification has been submitted to the IRB office.
- iii. If the study coordinator has not completed the RCDP, a letter is sent to the Principal Investigator informing him/her that successful completion of the program must occur by the conclusion of the next scheduled course offering, or enrollment into the study will be suspended until the requirement is completed.
  - iv. If educational requirements and signatures are complete, then a HR# is assigned to the study and the study is assigned to the appropriate IRB as determined by the funding source and specialty content. IRB I and IRB II are divided by departments. IRB III reviews all industry-sponsored protocols from all departments.
  - v. The IRB Administrator reviews the application for regulatory compliance and adherence to established IRB guidelines.
  - vi. The IRB Chair, Vice-Chair or the Chair's designee then reviews the application.
  - vii. Questions or comments by reviewers will be emailed or faxed to the Principal Investigator and study coordinator by the Administrator.
  - viii. The Administrator and Chair will check the investigator's responses.
  - ix. If responses are satisfactory and the study constitutes minimal risk to subjects, then the Chair will approve the study under the Expedited criteria.
  - x. The Administrator will enter approval information into the database; IRB staff will release the approval to the Principal Investigator.
  - xi. Approval of the application is reported to the full Board at a convened meeting.
  - xii. If the application does not fulfill the criteria for expedited review, then the study will be processed for full Board review.

#### **IRB Chair, Vice-Chair or Designee Responsibilities Relative to Initial Review:**

- i. All information required per procedures has been included in the submission,
- ii. Risks to subjects have been minimized by using sound research design, or, whenever appropriate, using procedures already being performed on the subject for diagnostic or treatment purposes,
- iii. Risks, including physical psychological, social and economical, are reasonable relative to anticipated benefits,
- iv. Selection of subjects is equitable,
  - v. When required, documented informed consent must be obtained in compliance with MUSC policies and federal regulations,
- vi. Provisions are adequate to protect the privacy of subjects and maintain confidentiality of the data,
- vii. If the research subjects include a vulnerable group, additional safeguards have been included to protect the rights and welfare of these subjects and all special requirements for the populations have been adequately addressed,
- viii. Determine the frequency of continuing review.

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#### **Expedited Review**

#### Applicability:

- a. Research activities that (1) present no more than minimal risk to human subjects, and (2) 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. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. Minimal risks means that the probability and magnitude of harm or discomfort anticipated are not greater in and of themselves than ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- b. The categories in this list apply regardless of the age of subjects, except as noted.
- c. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects= financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

#### Expedited Categories:

1. (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 increases 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 by noninvasive means. Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat)= (e) uncannulated saliva collected either in an unstimulated fashion or (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra-and subgingival dental plaque and calculus, provided the collection procedure is no more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
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.) Examples: (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
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). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects, 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
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. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b) (2) and (b) (3). This listing refers only to research that is not exempt.
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 new 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.

1 An expedited review procedure consists of a review of research involving human subjects by the IRB chair or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

2 Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).

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### **Full Board Review**

All other research involving human subjects must be reviewed and approved by the Full Board at a convened meeting. All full Board applications are placed on the agenda at a convened meeting where appropriate discussion and voting for approval, modification, or disapproval take place. The Chair or a reviewer may request that an investigator attend the meeting. All studies involving FDA regulated products will be reviewed and approved under FDA regulations. The prisoner representative must be present as a voting member at a convened meeting for all studies that include prisoners (including initial review, continuing review, amendments and review of unanticipated problems involving risks to subjects or others).

### **IRB Office Procedures**

- i. Upon receipt of an application, the application is stamped with the date of receipt. The application is checked for appropriate signatures.
- ii. Study personnel listed on the application are checked against the Compliance Office database to ensure required Institutional Training has been completed. If not all personnel have completed training, a letter is sent to the PI informing them

- that IRB approval of the study will not be released until certification has been submitted to the IRB office.
- iii. If the study coordinator has not completed the RCDP, a letter is sent to the PI informing them that successful completion of the program must occur by conclusion of the next scheduled course offering, or enrollment into the study will be suspended until the requirement is completed.
  - iv. If educational requirements and signatures are complete, then a HR# is assigned to the study.
  - v. The application is assigned to the appropriate IRB and is given to the IRB Administrator who administratively reviews for regulatory compliance and adherence to established guidelines.
  - vi. The application is sent to the Primary Review Group between two and three weeks prior to the convened meeting. Each Primary Review Group includes at least one scientific member and one non-scientific member as well as other reviewers. No reviewer will review a study if he/she has a conflict of interest. The Administrator will assign studies to Primary Review Groups relative to expertise of the members. As determined by the IRB Administrator, appropriate parts of the OHRP and FDA regulations are referenced or attached to the application package for use by the reviewers. The remaining reviewers are sent the Review Application, Human Subject document, and Informed Consent document(s) and any advertisements. The Administrator will request Reviewer critiques by a deadline.
  - vii. The Administrator will enter reviewer comments into the database. A cover letter that gives the Principal Investigator a deadline in which to respond to the Board's concerns and the reviewer comments will be sent to the Principal Investigator and study coordinator by email or fax.
  - viii. The Administrator will review the Principal Investigator response and prepare it for the Board's review.
  - ix. The Administrator will prepare the agenda that is delivered to the reviewing Board members on the Friday before the Tuesday convened meeting.
  - x. Late or additional Principal Investigator responses that come in after the agenda has been sent out will be presented to the Board at the meeting.
  - xi. During the meeting, each study is presented, discussed and voted on individually.
  - xii. The Board can approve, require further modifications, table, or disapprove a study. If minor changes are required, they may be reviewed and approved by the Chair or the Chair's designee. Changes that are substantive in nature must be brought back to the full Board at a convened meeting.
  - xiii. If the study is approved without further changes, the Administrator will prepare the approval for release.
  - xiv. If the study requires further modifications that are minor in nature, the Administrator will notify the Principal Investigator and study coordinator by email or fax. When revisions are received in the IRB office, the Administrator and the Chair will review them; if acceptable, the Chair will sign the approval and the Administrator will prepare the study for release by the IRB staff.
  - xv. If modifications are substantive in nature or if the Board tables or disapproves the study, the Chair will notify the Principal Investigator in writing.

- xvi. Principal Investigator responses to substantive modifications or rewrites due to disapproval are presented to the Full Board for review, discussion and vote at a convened meeting. If approved, then the Administrator will prepare the study for release by the IRB staff.
- xvii. If a Principal Investigator has appealed the Board's decision in writing to the Chair, the Administrator will place the item on the next available agenda for full Board discussion and vote and will notify the Principal Investigator of the date, time and place of the meeting.
- xviii. The Administrator prepares Minutes of the convened meeting, which are approved by the Chair and the Board. Minutes show attendance at meetings and actions taken by the Board including the level of risk and frequency of continuing review. Minutes document the vote on all IRB actions including the number voting for, against, and those abstaining.

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### **Reviewer Responsibilities**

The Board is divided into comparable groups of three to five members each. Each Primary Review Group includes at least one scientific member and one non-scientific member as well as other reviewers. These members act as primary reviewers for a portion of the protocols submitted for the review period (i.e. 30 protocols, each group would review ten.) If a reviewer is unable to attend a meeting, the reviewer is responsible for selecting an appropriate alternate. The reviewers should return their Reviewer Checklist and Comment Sheets by the deadline assigned by the Administrator.

Primary reviewers check each submission for the following and must record their comments on the Reviewer Checklist.

- i. All information required per procedures has been included in the submission,
- ii. Risks to subjects have been minimized by using sound research design, or, whenever appropriate, using procedures already being performed on the subject for diagnostic or treatment purposes,
- iii. Risks, physical, psychological, social and economic, are reasonable relative to anticipated benefits,
- iv. Selection of subjects is equitable,
- v. Informed consent document and process when required, must be obtained in compliance with MUSC policies and federal regulations,
- vi. Provisions are adequate to protect the privacy of subjects and maintain confidentiality of the data,
- vii. If the research subjects include a vulnerable group, additional safeguards have been included to protect the rights and welfare of these subjects and that all special requirements for the populations have been adequately addressed,
- viii. Determine the frequency of continuing review.

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### **Continuing Review:**

Continuing review of on-going research is just as important if not more important than the initial review. It is only after subjects have been enrolled that both the PI and the IRB can make an evidence-based risk/benefit assessment. Federal regulations found at 45 CFR 46.109(e) require the IRB to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once annually. The regulations also give the IRB the authority to have a third party observe the consent process and the process of research.

### **IRB Office Procedures Relative to Continuing Review:**

Approximately two months prior to the expiration date, the IRB Coordinator will send the Principal Investigator an IRB Reminder of Approval Expiration. If continuing reviews are not submitted to the IRB by the deadline, the IRB Coordinator will send a final notice to the Principal Investigator. This notice is copied to the Principal Investigator's Department Chair and the Provost.

Upon receipt of an application, the hard copy is checked for appropriate signatures.

Study personnel listed on the application are checked against the Compliance Office database to ensure the required institutional training has been completed. If not all personnel have completed the training, a letter is sent to the Principal Investigator informing him/her that IRB approval of the study will not be released until the certification has been submitted to the IRB office.

If the study coordinator has not completed the RCDP, a letter is sent to the Principal Investigator informing them that successful completion of the program must occur by the conclusion of the next scheduled course offering, or enrollment into the study will be suspended until the requirement is completed.

The application is assigned to the appropriate IRB and is given to the IRB Coordinator. The Coordinator maintains a continuing review logbook then administratively reviews for regulatory compliance and adherence to established guidelines. This includes administrative review of the application for completeness and accuracy of demographic data reported as well as administrative review of the informed consent. If the application is incomplete, the IRB Coordinator will contact the Principal Investigator and study coordinator via email or fax prior to the IRB meeting. The IRB Coordinator will check the Principal Investigator responses for completeness. If the application is complete, the study is given to the Primary Reviewer.

The IRB Coordinator will prepare continuing review approval forms for the signature of the Primary Reviewer and will enter approval information in the database; IRB staff will release approvals.

If the Principal Investigator does not submit a continuing review form or does not address the IRB's concerns and the IRB approval expires, then the IRB Coordinator sends the Principal Investigator a Letter of Expiration that informs the Principal Investigator to stop enrollment.

**Primary Reviewer Responsibilities Relative to Continuing Review:**

The Primary Reviewer is the Chair, Vice-Chair, or the Chair's designee.

The Primary Reviewer reviews the entire IRB folder that includes the initial application, all amendments, all adverse event reports, data safety monitoring reports, investigator drug brochures, informed consents and all previous continuing review applications.

If the Primary Reviewer has questions or concerns, he/she may contact the Principal Investigator or ask the IRB Coordinator to contact the Principal Investigator. The Primary Reviewer will check the Principal Investigator responses. If responses are satisfactory, then the Primary Reviewer will sign the Continuing Review form.

If the review fits the Expedited Categories under 45 CFR 46.110 for continuing review, the IRB Coordinator will enter the approval information into the database and prepare the approval. The Primary Reviewer will determine the appropriate frequency of continuing review and sign the approval form. The IRB staff will release the approval.

If the study requires Full Board review, the IRB Coordinator will place the continuing review on the agenda for the appropriate convened meeting. Each reviewing IRB member will receive a copy of the Continuing Review Form and the informed consent(s) in the agenda packet that is sent out Friday before the Tuesday meeting. Late applications will be presented to the Board at the convened meeting.

The IRB must determine which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review such as: randomly selected projects; complex projects involving unusual levels or types of risk to subjects; projects conducted by investigators who previously have failed to comply with regulatory requirements; and projects where concern about possible material changes occurring without IRB approval have been raised based upon information provided in continuing review reports or Compliance Audits.

During the convened meeting, each continuing review is presented to the Board by the Primary Reviewer. The Primary Reviewer makes a recommendation to the Board relative to re-approval of the study. The Board will consider the following: no changes, changes due to adverse events, amendments and change due to risk / benefit ratio. Each continuing review is discussed and a determination is made regarding the time frame of re-review for the upcoming year. Examples of studies requiring re-review more frequently than once a year are those with greater risks to subject as evidenced by large numbers of unexpected serious adverse events, or those protocols that are of high risk to subjects.

Expedited Review Category (8): An expedited review procedure may be used for the continuing review of research previously approved by the convened IRB as follows:

- a. Where:
  - the research is permanently closed to the enrollment of new subjects;
  - all subjects have completed all research-related interventions;
  - and 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.

Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedure.

Expedited Review Category (9):

Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (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.

The Chair will notify appropriate agencies, departments and administration officials of non-compliance with annual review resulting in IRB suspension of approval.

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### **Principal Investigator Responsibilities Relative to Continuing Review:**

The Principal Investigator is responsible for developing and maintaining a system for expiration dates of protocols and should not rely on the IRB for reminders of expiration.

The Principal Investigator will submit continuing reviews in a timely manner as requested by the IRB.

The Principal Investigator is responsible for submitting a complete and accurate continuing review report with appropriate informed consent(s) attached.

The Principal Investigator will not enroll subjects if IRB approval expires.

### **Adverse Events (revised 12/15/05):**

#### **Reportable Adverse Events and Unanticipated Problems**

## Internal Adverse Events

**Internal events include Drugs, Biologics, Devices, Loss of Confidentiality, Privacy Issues or Harm to Others:** An unanticipated and related or possibly related, serious or more prevalent event occurring during a research study. Report on-line as soon as possible but no later than 10 working days after the investigator first learns of the event.

**Fatal - Internal:** Report all that occur during the study or 30 days post termination from protocol. Report whether expected or unexpected, related, possibly related or unrelated. Reports must be submitted on-line as soon as possible, but no later than 10 working days after PI learns of the event.

## External Adverse Events

**External events include Drugs, Biologics, Devices, Loss of Confidentiality, Privacy Issues or Harm to Others:** Report on-line as soon as possible but no later than 10 working days after the investigator first learns of the event.

The following conditions must be met for an external adverse event to be reportable to the IRB.

1. The event has been reviewed by the Central Monitoring Entity (CME) for the study (e.g., a Data Safety Monitoring Board (DSMB) or a Data Monitoring Committee (DMC), a coordinating or statistical center, or other sponsor monitoring entity – see definition below).
2. The central monitoring entity has determined that the particular adverse event or series of adverse events represent(s) an unanticipated problem which involves risks to subjects or changes the risk/benefit ratio for the study.
3. The external AE report includes the decision of the central monitoring entity regarding recommendations for action. Examples of such recommendations might include modification of inclusion or exclusion criteria to mitigate the newly identified risks; implementation of additional monitoring procedures of subjects; termination of enrollment of new subjects; modification of informed consent documents to include a description of newly recognized risks; and provision of additional information about newly recognized risks to previously enrolled subjects.

For any report of an external adverse event determined not to be an unanticipated problem, the local investigator maintains a copy of the external adverse event report and documentation of the basis for this determination. Local investigators should document their analysis of all external AEs, and this documentation is subject to review or audit by the IRB or designated compliance arm.

See the following site for:

1. Examples of Adverse Events that Do Not Represent Unanticipated Problems and Do Not Need to be Reported (Appendix B), and

2. Examples of Adverse Events that Represent Unanticipated Problems and Need to be Reported (Appendix C).

<http://www.hhs.gov/ohrp/requests/aerg.html>

**Fatal - External:** Report all that occur during the study or 30 days post termination from protocol only if they meet reportable criteria above.

### **Definitions:**

**Central Monitoring Entity (CME):** The group charged with reviewing the accumulated data to monitor safety, effectiveness, and trial conduct issues as the trial progresses. This group receives and analyzes all adverse events and other reports for the purpose of identifying and communicating important new safety information.

Clinical trials may identify a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) as the central monitoring entity.

MedWatch, the FDA Safety Information and Adverse Event Reporting Program, is not a central monitoring entity.

**Unanticipated Problem:** An unanticipated problem may be identified in various ways, one of which is an adverse event. “Unanticipated problems involving risks to human subjects or others” include those events that (1) are not expected given the nature of the research procedures and the subject population being studied; and (2) suggest that the research places subjects or others at greater risk of harm or discomfort related to the research than was previously known or recognized.

**Unexpected / Unanticipated (adverse event):** Not identified in nature, severity or frequency in the current protocol, informed consent, investigator brochure or with other current risk information.

**Serious:** Results in death, is life threatening, requires inpatient hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, cancer, overdose or causes a congenital anomaly/birth defect.

**More Prevalent:** Adverse events that occur more frequently than anticipated or are more prevalent than expected. Example: nausea noted in consent as occurring in 10% of subjects - if 35% of subjects experience nausea, then report as an adverse event.

**All other (expected adverse events):** Report as aggregate data at time of continuing review.

**Related:** There is a reasonable possibility that the adverse event may have been caused by the drug, device or intervention.

**Possibly Related:** The adverse event may have been caused by the drug, device or

intervention, however there is insufficient information to determine the likelihood of this possibility.

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### **IRB Office Procedures Relative to Adverse Events:**

Adverse event reports are reviewed in the database by the Primary Reviewer.

The informed consent is reviewed relative to the internal or external adverse event.

The IRB Chair or Vice-Chair is notified of situations needing immediate action.

IRB staff will contact the Principal Investigator via email or fax if the Primary Reviewer has questions.

### **Primary Reviewer Responsibilities relative to Adverse Events:**

A Primary Reviewer is the Chair, Vice-Chair or the Chair's designee.

The Primary Reviewer will:

- i. Review the adverse events, protocol, previous adverse events, investigator drug brochure if applicable and informed consent document.
- ii. May contact the Principal Investigator regarding the adverse event.
- iii. Determine if there is increased risk changing the benefit /risk ratio of participation and/or not described in the consent.
- iv. Report the event and make recommendations to the Full Board for action as needed. This action can include:

No action needed

Revision of informed consent

Inform currently enrolled subjects of changes

Stop protocol until more information is available

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### **Amendments:**

Changes made to the informed consent, protocol, or authorization must be submitted for prospective IRB review and approval except where necessary to eliminate apparent immediate hazards to subjects. This is addressed in training programs and educational sessions.

### **PI Responsibility Relative to Amendments:**

The PI will not implement changes until prospective IRB review and approval has occurred.

Investigators submit requests for change on the Request for Amendment form.

The PI indicates whether the change is minimal risk or greater than minimal risk. The PI must clearly mark changes in the documents revised by the amendment and submit an unmarked revised version of the informed consent/authorization if applicable. A master copy of the amended informed consent/authorization document, with an original IRB approval stamp, is sent to the Principal Investigator. If the amended informed consent/authorization document replaces an existing informed consent/authorization document, the existing informed consent/authorization document should be clearly marked "OBSOLETE". The Principal Investigator is also responsible for ensuring any unused copies of the obsolete informed consent/authorization document are discarded.

**Primary Reviewer Responsibilities Relative to Amendments:**

Review the amendment with the informed consent/authorization and protocol. Determine whether the risk is minimal (no increase in risk/benefit ratio); refer to the Full Board if greater than minimal risk. Contact investigator if necessary. Make recommendation of approval, additional changes or disapproval to the full Board.

**IRB Office Procedures Relative to Amendments:**

The Amendment is entered into the database and assigned to the appropriate IRB. The IRB Coordinator administratively reviews the amendment for completeness and accuracy according to federal regulations and notifies the PI via email or fax if there are questions.

Notify Chair if request is urgent or an emergency. When the amendment is complete, it is given to the Primary Reviewer. If the IRB Coordinator questions the level of review that is requested, this is brought to the Primary Reviewer's attention. If the Primary Reviewer approves the amendment by expedited review, then the IRB Coordinator enters the approval information into the database and releases the approval to the PI.

If the amendment requires Full Board review, the IRB Coordinator sends the amendment request with the Primary Reviewers recommendations to the reviewing members with the Agenda on the Friday prior to the convened meeting.

If the amendment is approved at the meeting, the IRB Coordinator enters the approval into the database, prints the approval for the Chair's signature and releases the approval to the PI.

The new version of the informed consent/authorization is date stamped with the amendment approval date. The original informed consent/authorization document is retained for IRB records. A master copy of the amended informed consent/authorization document, with an original IRB approval stamp, is sent to the Principal Investigator.

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**Protocol Deviations:**

A protocol deviation is a deviation committed by the research team that involved the inclusion/exclusion criteria; dose, dosage schedule, or use of device; use of medications not allowed by the protocol; other.

**PI Responsibilities Relative to Protocol Deviations:**

The PI should report protocol deviations committed by the research team to the IRB on the Protocol deviation report form.

**IRB Office Procedures Relative to Protocol Deviations:**

The protocol deviation is given to appropriate IRB staff. The file is pulled and given to the Primary Reviewer with the form. Protocol deviations are reported to the Full Board at a convened meeting.

**Primary Reviewer Responsibilities Relative to Protocol Deviations:**

A Primary Reviewer can be the Chair, Vice-Chair or the Chair's designee. The Primary Reviewer reviews the Protocol Deviation with the protocol; presents the deviation to the Full Board for further recommendation.

**Protocol Violations:**

Protocol violations constitute research not conducted in accordance with IRB requirements.

If a protocol violation occurs or is suspected, the IRB Chair or Vice-Chair will notify the investigator in writing. The investigator will respond within five working days. Upon receipt of the response, the full Board will decide on further action. If no response is received, the IRB will request further action from the Provost and University Officials.

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**Informed Consent Documents:**

The Principal Investigator submits informed consent documents to the IRB for review and approval. Once the informed consent document has been approved, the original copy is stamped with the IRB approval date by the IRB Staff, and retained in IRB records. A Master Copy with an original IRB approval stamp is sent to the Principal Investigator. Copies are to be made only from the Master Copy, which is identified by the original IRB date stamp. No copies are to be made from word processing files or from any other copy without the original stamp. No informed consent, whether written or oral, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or release or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence. 45 CFR 46.116

Investigators follow the MUSC Informed Consent Guide when writing informed consents. The guide includes the following required elements of informed consent 45 CFR 46.116(a)(1) and must be written in lay language:

- i. A statement that the study involves research;
- ii. An explanation of the purpose of the study;
- iii. A description of the procedures to be followed;
- iv. Identification of any procedures that are experimental;
- v. The expected duration of the subject's participation;
- vi. A description of any reasonably foreseeable risks or discomforts to the subject;
- vii. A description of any benefits to the subject or to others which may reasonably be expected from the research;
- viii. A disclosure of alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- ix. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- x. 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;
- xi. 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
- xii. 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.

Additional elements of informed consent may be provided when appropriate under 45 CFR 46 116(1):

- i. 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;
- ii. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- iii. Any additional costs to the subject that may result from participation in the research;
- iv. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- v. 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
- vi. The approximate number of subjects involved in the study.

Informed consent must be obtained from the subject, spouse, court-appointed legal guardian, or from the parent of a minor less than 18 years of age by the person(s) approved by the IRB to obtain consent. Children ages 12-17 must give their assent for participation. One witness to the subject's signature is required. Signatures must be dated. Deviation from this standard must be reviewed and approved by the full IRB at a

convened meeting on a case-by-case basis. Next-of-kin may not give consent unless specifically approved by the IRB.

An investigator may request a waiver of consent, an alteration of consent elements under 45 CFR 46.116(d) or a waiver of written informed consent under 45 CFR 46.117© by filling out the appropriate Request for Waiver form.

Informed consents must be written in a language understandable to subjects. Consents in a foreign language must be submitted to the IRB. The IRB will obtain an interpreter to confirm that the consent written in the foreign language is identical to the English version. The interpreter will sign a statement of confidentiality. If the IRB approves an oral presentation of the informed consent for non-English speaking subjects, both the oral presentation and the short form document should be in a language understandable to the subject; the IRB-approved English language consent document may serve as the summary and the witness should be fluent in both English and the language of the subject.

#### **NIH-Supported Clinical Trials - IRB Review of NIH-Approved Informed Consent Documents:**

The IRB must review and approve the NIH-approved sample informed consent document in conjunction with the NIH-approved protocol. Any deletion or substantive modification information concerning risks or alternative procedures contained in the sample consent must be justified in writing by the investigator, approved the IRB and reflected in the IRB minutes.

#### **Description of Notification of HIV Testing Results:**

PHS policy (applicable to all PHS-supported intramural and extramural, foreign and domestic research and health activities) requires that where HIV testing is conducted or supported by PHS, individuals whose test results are associated with personal identifiers must be informed of their own test results and provided the opportunity to receive appropriate counseling unless the situation calls for an exception under the special circumstances set forth in the Policy. This procedure should be described in the informed consent document.

#### **Right to Appeal:**

Principal Investigators have the right to appeal the IRB's decision in writing to the Chair; the Administrator will place the item on the next available agenda for full Board discussion and vote. The PI will be asked to attend the meeting to provide information and address the Board's concerns.

#### **Suspension or Termination of Research by the IRB:**

The IRB may suspend or terminate approval of research that is not conducted in accordance with the IRB approved protocol, or has been associated with unexpected serious harm to subjects.

The IRB will issue a letter to the investigator with the reason for the IRB's action.

Any termination or suspension will be reported promptly to the Provost and to the appropriate regulatory agencies.

**Description of procedures for implementing other relevant Federal regulations that apply to human subject research:**

FDA regulations are applied to those studies that involve FDA regulated products (drugs, devices or biologics) identified by the review conducted by the IRB Administrators, IRB Chair and IRB members.

**IRB Review in Emergency Situations:** 45 CFR 46.103(b) and 46.116(f)

HHS regulations do not permit human subject research activities to be started, even in an emergency, without prior IRB review and approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject under 45 CFR 46. Such emergency care may not be claimed as research, nor may any data regarding such care be included in any report of a prospectively conceived research activity. When emergency care involves investigational drugs, devices, or biologics, FDA requirements must be satisfied.

**Emergency Use of Investigational Drugs and or Devices:** FDA regulations Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. 21 CFR 56.102(d) Investigators should contact the IRB for further guidance.

**Exception from the Informed Consent Requirement** for an emergency use is found at FDA 21 CFR 50.23(a). Investigators should contact the IRB for further guidance.

**Audits:**

The auditor in the Academic Compliance Office conducts audits of human research studies. These audits are random or can be requested by the IRB. The auditor submits findings to the Principal Investigator, the Compliance Officer and the Provost. The Principal Investigator submits a corrective action plan to the auditor. The audit and the Principal Investigator's corrective action plan are submitted to the IRB Chair. The Chair can stop enrollment in the study if subjects appear to be at risk. The Chair presents the reports to the IRB for review at a convened meeting. The IRB can accept the plan, require further corrective action, or stop the research. Board determinations are reported to the Principal Investigator, the Principal Investigator's Department Chair, the Compliance Officer, the Provost and applicable federal agencies. The auditor conducts QA audits of IRB files. A copy of the audit is submitted to the Human Protection Administrator who submits a response to the Compliance Officer.

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**Issues of Unanticipated Problems Involving Risks to Subjects or Others, Serious or Continuing Noncompliance, Suspension or Termination:**

The IRB is responsible for promptly reporting to the appropriate institutional officials, any supporting Agency or Department heads, and OHRP any unanticipated problems involving risks to subjects or others; any serious or continuing noncompliance with 45 CFR 46 or the requirements or determinations of the IRB; and any suspension or termination of IRB approval.

1. Issues of noncompliance and unanticipated problems involving risks to human research subjects or others initially will be reviewed by the IRB Program Manager and IRB Chair.
2. The IRB Program Manger and the IRB Chair will conduct a preliminary investigation to determine the nature of the noncompliance and/or unanticipated problems and the posed risk to human research participants at the time of the investigation.
3. If the preliminary investigation finds evidence that human research participants are at increased risk because of noncompliance and/or unanticipated problems, the IRB Program Manager and the Chair will decide if the nature of this risk warrants immediate suspension of protocol enrollment/participation or other corrective action.
4. Issues of noncompliance: The IRB Chair and Program Manager will conduct a full investigation of alleged noncompliance including requesting the Office of Compliance to conduct an audit of the protocol. All findings will be reported to the Board at the next scheduled meeting; the investigator involved in the allegation of noncompliance will be invited to attend the Board meeting when appropriate. The Board will decide what action will be taken relative to the noncompliance. The Board's decisions will be reported in a timely manner to the investigator, the MUSC Compliance Officer, and the MUSC Vice President and Provost by the IRB Chair in writing. If the Board determines protocol enrollment or participation should be suspended or terminated due to serious or continuing noncompliance, OHRP, the FDA, if applicable, and the funding agency, if applicable, will be notified within 5 working days.
5. Unanticipated problems involving risks to subjects or others: The IRB Chair and the IRB Program Manager will collect all pertinent data relative to an unanticipated problem involving risks to subjects or others including:
  - a. a full report of the incident from the principal investigator,
  - b. an explanation of immediate corrective actions taken,
  - c. a current risk/benefit assessment of the research given the incident,
  - d. relevant contextual information if the study is a multicenter project, and
  - e. actions relative to notification of all enrolled subjects.
6. All findings will be reported to the Board at the next scheduled meeting; the principal investigator of the study will be invited to attend the Board meeting when appropriate. The Board will decide what actions will be taken based on the nature of the risk to subjects and others including if the occurrence should be reported to OHRP. The Board's decisions will be reported in a timely manner to the investigator and the MUSC Vice President and Provost the IRB Chair in writing. The IRB will notify OHRP of the incident and corrective actions within 5 working days of the Board's decision.

7. Information to be included in incident reports:

**For unanticipated problems involving risks to subjects or others:**

- Name of the institution (e.g., university, hospital, foundation, school, etc) conducting the research;
- Title of the research project and/or grant proposal in which the problem occurred;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the problem; and
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).

**For serious or continuing noncompliance:**

- Name of the institution (e.g., university, hospital, foundation, school, etc) conducting the research;
- Title of the research project and/or grant proposal in which the noncompliance occurred;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the noncompliance; and
- Actions the institution is taking or plans to take to address the noncompliance (e.g., educate the investigator, educate all research staff, suspend the protocol, suspend the investigator, conduct random audits of the investigator or all investigators, etc.).

**For suspension or termination:**

- Name of the institution (e.g., university, hospital, foundation, school, etc) conducting the research;
- Title of the research project and/or grant proposal that was suspended or terminated;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB that was suspended or terminated and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the reason for the suspension or termination; and
- The actions the institution is taking or plans to take to address the suspension or termination (e.g., investigate alleged noncompliance, educate the investigator,

educate all research staff, require monitoring of the investigator or the research project, etc.)

**Time frame for reporting incidents:**

The regulations at 45 CFR 46.103(a) and (b)(5) do not specify a time frame for reporting, except "promptly." For a more serious incident, this may mean reporting to OHRP within days. For a less serious incident, a few weeks may be sufficient. It may be appropriate to send an initial report, and indicate that a follow-up or final report will follow by the earlier of:

- a specific date; or
- when an investigation has been completed or a corrective action plan has been implemented.

**Routine Notification of Institutional Officials:**

Findings and actions taken by all IRBs at each of their meetings are on file and made available in the IRB office for examination by the Provost.

**IRB Authorization Agreement:**

The Human Protections Administrator sends copies of approvals, notices of expiration and letters to PIs that have been written by the Chairs as a result of Board action to the appropriate officials at institutions who have entered into an IRB Authorization Agreement with MUSC.

**Tissue Banks & Repositories:**

Tissue Banks and Repositories are under the oversight of the MUSC IRB per OHRP guidance found @ <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/reposit.htm>

**Retention of Records:**

HHS regulations at 45 CFR 46.115(b) require that IRB records be retained for at least 3 years, and records relating to research which is conducted be retained for at least 3 years after completion of the research. All records must be accessible for inspection and copying by authorized representatives of HHS and FDA at reasonable times and in a reasonable manner. At the end of three years, records are boxed, labeled and sent to central storage for another 7-10 years. A log of stored records is maintained in the IRB office for retrieval if files are needed for audit purposes.

**Health Insurance Portability Accountability Act (HIPAA):**

Research is covered in the HIPAA Privacy Rule at 45 CFR 164.501, 164.508, 164.512(i). The Privacy Rule does not supersede the Common Rule.

**The IRB will review the following aspects of HIPAA:**

Authorizations and Waivers of Authorizations 45 CFR 164.508 / 45 CFR 164.512(i)(1)(i)

**The Privacy Board will review:**

Data Preparatory to Research 45 CFR 164.512 (i)(1)(ii)  
Research on Decedents 45 CFR 164.512(i)(1)(iii)

**Protected Health Information (PHI):**

Individually identifiable health information transmitted or maintained in any form (electronic means, on paper, or through oral communication) that relates to the past, present or future physical or mental health or conditions of an individual. Information will be considered identifiable if the covered entity knows that the identity of the person may still be determined.

Research that involves the use of “de-identified” PHI is exempt from HIPAA requirements if all of the following subject identifiers (individual, employer, relatives, etc) are removed:

1. Names
2. Address – (All geographic subdivisions smaller than a State including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census: (initial 3 digits if geographic unit contains less than 20,000 people, or any other geographical codes).
3. All elements of dates (except for years) related to an individual – including, admission dates, discharge dates, date of death, birth dates, ages >89 and all elements of dates (including year) indicative of such age, EXCEPT that such ages and elements may be aggregated into a single category of >90
4. Telephone Numbers
5. Fax Numbers
6. E-mail Addresses
7. Social Security Numbers
8. Medical Record Numbers
9. Health Plan Beneficiary Numbers
10. Account Numbers
11. Certificate / License Numbers
12. Vehicle Identifiers and Serial Numbers
13. Device Identifiers and Serial Numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) Address Numbers
16. Biometric Identifiers (e.g. finger or voice prints)
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code

**Authorizations:**

Authorizations at MUSC are a stand-alone document separate from the research informed consent. The Principal Investigator submits the authorization to the IRB for review and approval. Once the authorization has been approved, the original copy is stamped with the IRB approval date by the IRB Staff, and retained in IRB records. A Master Copy with an original IRB approval stamp is sent to the Principal Investigator. Copies are to be

made only from the Master Copy, which is identified by the original IRB date stamp. No copies are to be made from word processing files or from any other copy without the original stamp.

Investigators follow the MUSC Authorization Guide when writing authorizations. The guide includes the following required elements of authorization 45 CFR 164.508 and must be written in lay language:

- i. A description of the purpose of use or disclosure of PHI
  - ii. A description of the PHI to be used or disclosed
  - iii. To whom PHI will be disclosed
  - iv. Who will use or disclose PHI
  - v. A statement that treatment, payment or enrolment in any health plan or eligibility for benefits will not be affected if subject refuses to sign authorization
  - vi. A description of how individuals may revoke the authorization and any exceptions to the revocation; revocation must be in writing; subjects should be told that if they revoke, they can no longer participate in research and that researchers may use PHI already obtained to maintain integrity of the data
  - vii. A statement of subject's right to see and copy information described in the authorization
  - viii. A statement of authorization
  - ix. An expiration date
  - x. Subjects are given a signed copy of the authorization
- Authorization must be obtained from the subject or personnel representative. Authorizations in a foreign language must be submitted to the IRB. The IRB will obtain an interpreter to confirm that the authorization written in the foreign language is identical to the English version. The interpreter will sign a statement of confidentiality. MUSC research subjects must be given a copy of MUSC's Privacy Notice as documented in the authorization. VAMC research subjects must be given a copy of the VAMC's Privacy Notice. Prisoners do not have rights to this notice 45 CFR 164.520(3).

**Waiver of Authorization:**

An investigator may request a waiver of authorization under 45 CFR 164.512 (i)(1)(i) by filling out the Request for Waiver of Authorization form. The following criteria must be satisfied for the IRB to approve the waiver:

- i. The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
  - a. An adequate plan to protect the identifiers from improper use and disclosure;
  - b. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; **and**
  - c. Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the

- research project, of for other research for which the use or disclosure of PHI would be permitted by this subpart;
- ii. The research could not practicably be conducted without the waiver or alteration;  
**and**
  - iii. The research could not practicably be conducted without access to and use of the PHI.

**Accounting of Disclosures:**

A release of identifiable health information to anyone or any entity outside MUSC or the VAMC.

45 CFR 164.528

In research approved by the IRB, an Accounting of Disclosures is required of the PI in research with Waivers of Authorizations.

MUSC investigators should contact the MUSC Office of Health Information Services for directions.

VAMC investigators should contact the VAMC for directions.

The IRB will track any disclosures made by the IRB outside the covered entity.

**Minimum Necessary:**

When PHI is used or disclosed, only the information that is needed for the immediate use or disclosure should be made available by the researcher. 45 CFR 164.5

For Research approved by the IRB, the Minimum Necessary standard applies to Waivers of Authorizations, Limited Data Sets and Data Use Agreements.

45 CFR 164.514(e)

A set of data that may be used for research, public health or health care operations without an authorization or waiver of authorization. Tracking of disclosures is not required. PHI that EXCLUDES the following direct identifiers of the individual or of relatives, employers or household members of the individual:

- i. Names
- ii. Postal address information, (other than town or city, State and zip code)
- iii. Telephone and FAX numbers
- iv. Electronic mail addresses
- v. Social Security Numbers
- vi. Medical record numbers
- vii. Health plan beneficiary numbers
- viii. Account numbers
- ix. Certificate / license numbers
- x. Vehicle identifiers and serial numbers, including license plates
- xi. Device identifiers and serial numbers

- xii. Web universal resource locators (URLs)
- xiii. Internet protocol (IP) address
- xiv. Biometric identifiers, including finger and voice prints
- xv. Full face photos, and comparable images

A Limited Data Set can INCLUDE the following:

- i. Dates
- ii. Geographic information (not street address)
- iii. Other unique identifying numbers, characteristics, or codes that are not expressly excluded

**Data Use Agreement (DUA):**

45 CFR 164.514(e)

A covered entity must enter into a data use agreement with the recipient of a limited data set. The DUA and LDS are reviewed and approved by the Office of Research and Sponsored Programs (ORSP).

VAMC Research: Investigators are responsible for contacting the VAMC to obtain a DUA when using a LDS for VAMC research.

*This policy is reviewed annually by the Human Protections Administrator and the IRB Chairs to ensure continuing relevancy to the needs of human subjects, the investigators, and MUSC goals.*

Last Update  
2/10/06