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| Policy Name: Description, Principles and Authority for MUSC HRPP | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 17 | Section: HRPP 1.1 |
| Replaces Policy: Effective 01/27/2012 | | |

I. OVERVIEW

The Medical University of South Carolina (MUSC) is South Carolina’s only comprehensive academic health science center. Our purpose is to preserve and optimize human life in South Carolina and beyond. MUSC provides an interprofessional environment for learning, discovery, and healing through (1) education of health care professionals and biomedical scientists, (2) research in the health sciences, and (3) provision of comprehensive health care.

MUSC operations abide by the Federal Policy for the Protection of Human Subjects (the Common Rule) and the principles outlined in 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, the Declaration of Helsinki, the Nuremberg Code, and the VA Handbook 1200.05. The ethical conduct of research on human subjects is an essential component of our research mission, and the rights and welfare of all persons participating in research are vigorously protected.

All human research studies operate under the auspices of a campus-wide Human Research Protection Program (HRPP) with oversight and management from the Office of the President of MUSC through the Vice President of Research and the Assistant Provost for Research Compliance and Regulatory Affairs as the responsible organizational officials for its operation. Individual elements of HRPP operation include the following

- a) education and training of all personnel involved in human subject research (researchers and research staff, IRB members and IRB staff);
- b) submission and review of human subject research protocols by independent review committees (Institutional Review Boards) with required expertise and community representatives;
- c) human subject outreach, communication and education;
- d) financial management and review;
- e) risk management;
- f) research integrity;
- g) conflict of interest disclosure and management;

- h) clinical services and investigational drug pharmacy;
- i) community outreach and engagement;
- j) monitoring of all approved human subject research; and
- k) quality improvement programs.

We have a number of programs in place to educate and reach out to the community on human subjects research and mechanisms are in place to allow human subjects to voice complaints, issues, concerns and suggestions providing ongoing connectivity and mechanisms for quality improvement (see HRPP Program Guide Section 7.7 - Subject Complaints, Issues, Concerns and Suggestions Policy and Procedures and Section 10.3 - Quality Improvement Initiatives, MUSC Community Engaged Research).

These individual elements blend to form a system that is robust, interactive and constantly improving with the ability to adapt and address any issue in a prompt and transparent process.

MUSC is committed to providing the best possible program for protection of human research subjects under the auspices of our institutional wide HRPP to ensure the allocation of necessary resources, continued oversight and compliance, and to nurture these programs for the benefit of human subject participants and society.

II. TYPES OF HUMAN SUBJECTS RESEARCH CONDUCTED AT MUSC

MUSC has over 2000 active research projects involving human subjects in the biomedical, behavioral sciences, social sciences and medical economics as well as Phase 1 through Phase IV medication trials. These studies are conducted by approximately 500 active Principal Investigators (MD, PhD, PharmD, DDS and/or RN) and 1000 study coordinators and research staff.

The categories of study participants include adults with normal decision-making capacity, adults with impaired decision making capacity, pregnant subjects, children, prisoners, employees and students. No categories of human subjects are specifically excluded. We have a limited number of transnational studies. Special oversight mechanisms are in place for the review and monitoring of studies with vulnerable populations.

III. REGULATORY GUIDELINES AND ASSURANCES

The MUSC human subjects research program operates under a Federal Wide Assurance (FWA #00001888) from the Office for Human Research Protections (OHRP).

MUSC becomes engaged in human research whenever (a) the Institution's employees or agents intervene or interact with human subjects; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects; or (c) the Institution receives a direct federal award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

MUSC is the University Affiliate IRB for the Ralph H. Johnson Veterans Affairs Medical Center (VAMC). The VA operates under FWA #00001591. The specific guidelines and governance articulating the operational agreement are described in the Memorandum of Understanding between MUSC and Ralph H. Johnson VAMC concerning the Utilization of MUSC's Institutional Review Boards.

All research involving human subjects at MUSC must comply with all Federal Regulations and requirements that address the protection of human subjects, including Regulations and requirements that address the protection of human subjects, including 21 Code of Federal Regulations (CFR) Parts 45, 50, 56 and all related policy and procedural documents (45 CFR) in accordance with the regulations and expectations of the Department of Health and Human Services and other organizations such as the Food and Drug Administration, the Veterans Administration (38 CFR, VA Handbook 1200.05) and the State of South Carolina as applicable. These regulations and requirements, along with approval of our Institutional Review Board, must be met before any research involving human subjects is initiated and adherence must be sustained throughout the conduct of research. The regulations specific for the Veterans Administration (38 CFR 16 and VHA Handbook 1200.05) guide all studies conducted at the Ralph H. Johnson VA Medical Center in Charleston for which MUSC serves as the University Affiliate for the IRB.

All individuals involved with human subjects research at MUSC are required to complete training prior to initiating any such research. MUSC is registered for training through the Miami Collaborative Institutional Training Initiative or CITI (<http://www.musc.edu/citi>). All individuals involved in human research must complete the initial 17 basic modules focused on biomedical or social/behavioral research when commencing such research. All individuals involved in human research must also complete the MIAMI CITI COURSE REFRESHER MODULE 101 every three years providing a mechanism of continuing education. Additional training requirements are in place for VA investigators through the federal regulations described in the VA Handbook 1200.05.

IRB approval is required before commencing any human subjects research protocol and several mechanisms (see below) are in place to assure that this policy is followed.

Education and outreach

- HRPP Program Guide Section 5.1 Principal Investigator Responsibilities - The section entitled "Supervision of Staff and Protection of Subjects" states that "No research will be initiated without prospective IRB review and approval".
- Human Subject Regulations Decision Charts are provided to assist investigators in determining whether an activity is research that must be reviewed and approved by the IRB.
- The IRB management and staff routinely present to research groups and research support teams on campus providing information on IRB operations and the requirement for IRB approval for human subject research.
- All investigators and staff involved in human subject research must complete specific training modules before commencing research.
- Core Clinical Research Training – A two week course for investigative teams that covers human research policies and procedures including the requirement for IRB approval before commencing any human subjects research protocol.
- Mentoring - Students and trainees involved in human subject research are assigned mentors familiar with IRB operations.
- Faculty Research Orientation - Provides information to new faculty on policies and procedures for human subjects research.
- South Carolina Clinical and Translational Research Center - Staff with experience in human subject research policies and procedures provide support and guidance for research teams.
- There are regular lunch and learn sessions focused on various aspects of human subjects research. Human Subject Regulations Decision Charts are provided to assist investigators in determining whether an activity is research that must be reviewed and approved by the IRB.

Operational

- The Principal Investigator, the Department Chair and the Mentor if applicable must all electronically sign the human research protocol submitted to the IRB before it is reviewed.
- The Clinical and Translational Research Center requires IRB approval on all human subjects research protocols prior to beginning research.
- For industry-sponsored human subjects research, the Office of Research and Sponsored Programs and the Office of Research Integrity review the IRB-approved informed consent and the contract to validate consistency prior to release of funds for expenditure.
- IRB approval is required for expenditure of research funds awarded in support of human subjects research.
- Investigative Drug Services requires IRB approval prior to releasing the study drug.

- Human subjects research involving cancer requires approval by Hollings Cancer Center Protocol Review Committee prior to release of IRB approval.
- Human subjects research involving the MUSC Simulation Center requires ancillary review by the center director.
- For human subjects research involving non-routine radiation, approval by the Office of Radiation Safety approval is required prior to release of IRB approval.
- For human subjects research involving biohazardous material, approval by the Institutional Biosafety Committee is required prior to release of IRB approval.
- The Research and Development Committee of the Ralph H. Johnson VA Medical Center, which reviews all human subjects research at the VA, requires IRB approval prior to commencing research.
- The University provides whistle-blowing protection to anyone who reports an activity that violates any regulations or policies related to human subjects research.

IV. AUTHORITY AND ORGANIZATIONAL STRUCTURE

The HRPP program involves all aspects of our operations at MUSC including research teams and their staff, the Office of Research Integrity, Institutional Review Boards, Office of Sponsored Research, Office of Grants and Contracts, Clinical Services, University General Counsel, the Office of Compliance and many other aspects of our organization. The overall organizational structure for these offices is indicated in the organizational charts provided as MUSC Organizational Charts (HRPP Program Guide Section 1.2).

Vice President for Research Kathleen Brady, M.D., Ph.D. is recorded as the Institutional Official (IO) on the FWA and she has appointed the Associate Provost for Research Compliance and Regulatory Affairs (Patrick Flume, M.D.) and the Director of the Office of Research Integrity (Aimee McRae-Clark, Pharm.D.) as the responsible organizational officials for the operation of the MUSC HRPP. Drs. Flume and McRae-Clark have signatory authority for the IO. These three individuals form the leadership core for the University and have regular meetings facilitating communication. The active involvement of senior administration ensures that adequate resources are provided to operate an effective HRPP. The description of the Individual elements of the HRPP and their interaction is described in the following text.

Vice President of Research (VPR) and Assistant Provost for Research Compliance and Regulatory Affairs - Serve as the Responsible Institutional Officials for administration and oversight of the HRPP. The Assistant Provost for Research Compliance and Regulatory Affairs serves as the coordinating individual for the HRPP and meets regularly with Directors of each component of the HRPP.

Office of Research Integrity (ORI)- Responsible for review of all human research protocols for the Medical University of South Carolina and the Ralph H. Johnson VA Medical Center. This office serves as the administrative unit for the Institutional Review Board, the Institutional Biosafety Committee, the Institutional Animal Care and Use Committee and the Research Integrity Officer for scientific misconduct. The Office of Research Integrity developed a course “Core Clinical Research Training” that is now offered through our Clinical and Translational Research Center for all research teams and coordinators involved in human research. The Director of this office reports to the Assistant Provost for Research Compliance and Regulatory Affairs. The ORI Director meets twice monthly with the Assistant Provost for Research Compliance and Regulatory Affairs.

Office of Research and Sponsored Programs (ORSP) – Responsible and the Institutional Signatory Authority for submission of sponsored research proposals. The Director of this office reports to the Assistant Provost for Research Compliance and Regulatory Affairs. The ORSP Director meets weekly with the Assistant Provost for Research and Regulatory Affairs.

Office of Grants and Contracting – Responsible for monitoring and reporting financial information related to the University’s externally sponsored grants and contracts. The Director of this office reports to the Vice President of Finance and Administration. The Director meets monthly with the Assistant Provost for Research and Regulatory Compliance.

University Compliance Office – Provides a proactive program to ensure full compliance with all applicable policies, procedures, laws and regulations while promoting ethical behavior in accordance with MUSC’s core values as expressed in the MUSC Mission Statement and Code of Conduct. The Director of this office reports to the Office of the Provost.

Investigative Drug Services – Supports clinical investigations conducted by scientists affiliated with MUSC by 1) randomization and blinding of study drug, 2) controlling drug inventory including performance of routine audits, 3) preparation and dispensing of oral and parenteral admixture study drugs, 4) in-service training for patients and staff.

South Carolina Clinical and Translational Research Institute (SCTR) – Facilitates cross-disciplinary research in translational research including support for development and management of human subjects research. SCTR, which serves as the home of our Clinical and Translational Sciences Award from NIH, includes the Nexus Research Center, a specialized, JCAHO-accredited patient unit facilitating investigator-initiated, peer-reviewed, clinical research projects within the institution. Kathleen Brady, MD, Ph.D. is Principal Investigator of the MUSC CTSA award and is Vice President for Research.

Office of Risk Management – Responsible for the prevention of harm, protection of assets and the financial resources of MUSC by affirming and assuring compliance with applicable statutory and regulatory codes. The Director of this office reports to the Vice President for Finance and Administration. The Director meets regularly with the Assistant Provost for Research Compliance and Regulatory Affairs.

Office of the General Council – General Counsel reports to the President. This position also serves on the Research Conflict of Interest Review Committee and meets regularly with the Vice President for Research.

Community Outreach - Establishing research partnerships between medical and communal societies that advance the health of its citizens is fundamental for the University. In its promotion of community-engaged research, MUSC sustains programs and activities that facilitate cross-disciplinary research that can provide answers to complex health concerns and disparities by coordinating expertise and resources throughout the community. Our community based partnerships are currently led through the Pearls initiative and S.C. Clinical and Translational (SCTR) Institute Community Engagement Program. The combined efforts and activities of these programs, projects and educational avenues have strengthened the capacity and resources for existing and potential academic-community partnerships, stimulating new research discoveries through community based participatory research, and facilitating the translation and adoption of new research findings into community settings.

Conflict of Interest - The organization has in place a series of policies and oversight mechanisms regarding code of conduct, ethical behavior and conflict of interest. These policies and oversight mechanisms provide the process for annual disclosure, review and management of faculty, staff and institutional conflicts of interest related to research, professional relationships and clinical operations. Current operations provide additional checkpoints for disclosure of real or potential conflicts of interest to the appropriate review committee. Such mechanisms include the checklist that accompanies any submission of a proposal for extramural funding and any research protocol submitted to the IRB for review. As a state institution, the South Carolina State Ethics Law also provides policy and guidelines for many aspects of our operation. A Research Conflict of Interest Committee reviews all conflict of interest disclosures related to research.

Research Subject Ethics and Advocacy - A number of resources are available for ethical issues related to patient advocacy are accessed through the Institute for Human Values at MUSC under the direction of Dr. Robert Sade (MUSC Institute on Human Values in Health Care), the MUSC Ethics Committee chaired by Dr. Walter Limehouse and the Research Subject Advocate program (HRPP Program Guide Section 7.6 – Research Subject Advocacy Policy and

Procedures). These areas of subject advocacy are also covered in the “Core Clinical Research Training” offered through SCTR.

Ralph H. Johnson VAMC - MUSC has a longstanding, close working partnership with the Ralph H. Johnson VAMC, which is adjacent to campus, with many of our physicians serving as VA staff. MUSC and the VAMC also share a ~100,000 sq ft research building and an increasing partnership on healthcare delivery. The VAMC research program is led by the Director who is the Institutional Official for the VAMC FWA

V. HUMAN SUBJECTS RESEARCH REVIEW AND MONITORING

The Institutional Review Boards (IRBs) provide the primary review of all human research protocols and are organized under the Office of Research Integrity. This office reports to the Assistant Provost for Research Compliance and Regulatory Affairs. The Office of Research Integrity includes the Institutional Animal Care and Use Committee, the Institutional Biosafety Committee and the Research Integrity Committee and the Dual Use Committee. Additional internal review mechanisms are provided through Department Chairs, various mentoring groups, the Hollings Cancer Center Clinical Trials Office and our South Carolina Clinical and Translational Research Institute.

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

The IRB(s) review, and have the authority to approve, require modification in, or disapprove all research activities, including proposed changes in previously approved human subject research. The decisions of the IRB in all matters

relating to the protection of humans involved in research shall not be influenced by any outside entity, including institutional officials. Research that has been reviewed and approved by the IRB may be subject to further review and disapproved by officials of the institution. Institutional officials may not, however, approve research if it has been disapproved by the IRB.

In reviewing research protocols involving transnational study sites, the MUSC IRB must obtain sufficient knowledge of the local research context and comply with all applicable required standards. All policies and procedures that are applied to research conducted domestically are applied to research conducted in other countries, as appropriate.

There are currently three IRBs, each under the direction of a Chair and Vice-Chair, that focus on different areas of research and consist of faculty with appropriate expertise, community representatives and staff support as detailed in our governance document (see HRPP Program Guide Section 2). The IRB serves to safeguard the rights and welfare of human subjects who participate in research at MUSC including special protection for vulnerable participants. Procedures are in place to review the quality of human subjects research protocols (see HRPP Program Guide Section 1.4 – Scientific/Scholarly Review of Protocols Policy and Procedures), and these procedures include the review by the Department Chair or their designee, external peer review and various internal review mechanisms offered through individual units such as the Hollings Cancer Center and SCTR.

The three Institutional Review Boards focus on different areas of research within their scope of work. All three IRBs may review studies involving investigational drugs and devices, questionnaires and surveys or behavioral modification. Each of the IRBs may have expedited studies that include retrospective chart reviews, blood draws, prospective collection of biological samples by non-invasive procedures, and research involving materials collected for non-research purposes.

IRB-I - IRB-1 reviews protocols from Cell Biology and Anatomy, Cell and Molecular Pharmacology & Experimental Therapeutics, Clinical Services, College of Health Professions, College of Nursing, College of Pharmacy, Harper Student Life Center, Dermatology, Medical Lab Sciences, Otolaryngology, Pathology and Laboratory Medicine, Pediatrics, Pharmaceutical Sciences, Pharmacy Practice, Physical Therapy, Psychiatry and Behavioral Sciences, Radiology and Urology. Psychiatry protocols may involve cognitively impaired subjects, subjects with addictions to alcohol, illegal drugs and/or nicotine, schizophrenic, and depressed subjects. The second largest volume of work for IRB-I involves pediatric studies related to cancer, cardiology or neonatology. IRB-I also has active protocols involving the prisoner population. Such protocols receive review by the prisoner representative on the IRB membership roster and follow the certification procedures outlined in the federal regulations.

IRB-II - IRB-II reviews protocols from Anesthesiology, Biochemistry and Molecular Biology, the Center For Health Care Research, College of Graduate Studies, Experimental Oncology, Family Medicine, General Dentistry, Medicine, Microbiology and Immunology, Molecular and Structural Biology, Neuroscience, Obstetrics and Gynecology, Ophthalmology, Oral & Maxillofacial Surgery, Orthopedic Surgery, Pediatric Dentistry/Orthodontics, Physical Medicine & Rehabilitation, Prosthodontics, Radiation Oncology, Stomatology, and Surgery. Human subject research protocols include investigational drug cancer trials, digestive disease studies and transplant surgery. Protocols may include vulnerable populations (i.e. pregnant subjects, cognitively impaired from stroke or dementia)

IRB-III - IRB III reviews all corporate sponsored studies. Protocols may include vulnerable populations (i.e. children, pregnant women, cognitively impaired).

The MUSC FWA includes the use of the National Cancer Institute Central IRB #1 (IRB00000781) for adult protocols, the National Cancer Institute Central IRB #2 (IRB00004296) for pediatric protocols and Western Institutional Review Board (IRB00000533) for selected multi-site clinical trials as needed or defined for specific studies. Ralph H. Johnson VA studies may use the central VA IRB.

The seven components of HRPP Program Guide section 2 detail operational elements crucial for an effective review and management of human subjects research. Records and documentation of all activities indicate the implementation of the policies and procedures and ensure effective operation of review and management process. HRPP Program Guide Section 1.3 – Definitions of Terms, defines all terminology used throughout the MUSC HRPP, ensuring consistency of application throughout the various components of the plan.

The Principal Investigator (PI) is the ultimate protector of the human subjects who participate in his/her research and is expected to abide by the highest ethical standards (see HRPP Program Guide Section 5.1 – Principal Investigator Responsibilities – Supervision of Staff and Protection of Subjects). The Principal Investigator is responsible for developing a protocol that incorporates the principals of the Belmont Report. He or she is expected to conduct the research in accordance with the approved protocol and to oversee all aspects of the research, including supervision of the research support staff, students, post-doctoral fellows, residents, and other staff involved in the project. The Principal Investigator is responsible for ensuring that all subjects give true informed consent and for establishing and maintaining an open line of communication with his or her research subjects. The Principal Investigator is expected to comply with the institutional policies and administrative requirements for conducting research and is accountable for compliance with institutional policies and administrative requirements.

Appropriate mechanisms are in place for the IRBs and any individual to inform appropriate institutional officials of any unanticipated problems involving risks to

subjects or others and/or serious or continuing noncompliance with federal regulations or IRB requirements. Mechanisms are in place to act upon such information and to suspend or terminate research studies upon review of the problems or noncompliance. Findings and actions taken by all IRBs at each of their meetings are on file and made available at the IRB office for examination by University Compliance and any delegated representatives of the Institutional and Organizational Officials.

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 provides whistle-blowing protection to anyone who reports an activity that violates any regulations or policies on the use of human subjects. The University Compliance Officer and/or designated representative conducts a regular review of the HRPP and this may be conducted together with the MUSC Office of Internal Auditing with results reported to the senior leadership and the MUSC Board of Trustees. The Institution is responsible for investigating incidents or allegations of misconduct pertaining to the use of human subjects in research.

Outreach, education and post review monitoring form the foundation of initiatives to maximize compliance with policies and procedures. These activities include the items listed above related to education and outreach regarding IRB approval as well as the following items

- Continuing education on human research protocol regulations is provided through special training sessions, visiting scholars and HRPP program directors.
- Updates on regulations and compliance awareness are communicated to investigators and research staff by the Vice President for Research and the Director of the Office of Research Integrity by a list serve email platform and regularly held research town hall meetings.
- Distribution of Human Research Participant Brochure in English and Spanish.
- Regular communication with departmental business managers on compliance monitoring.
- Mechanism for reporting compliance issues via a Compliance hotline (Confidential Hotline Posters). The University provides whistle-blowing protection to anyone who reports an activity that violates any regulations or policies on the use of human subjects.
- Post-review random audits conducted by the University Compliance Office.

- Posting and distribution of Guidelines for Ethical Conduct of Research (MUSC Guidelines for the Ethical Conduct of Research).

VI. PROGRAM REVIEW AND QUALITY IMPROVEMENT

MUSC is accredited by the Southern Association of Colleges and Schools Commission on Colleges. The most recent reaffirmation of accreditation was in 2007; it is due for its decennial review in 2017.

MUSC has been proactive in providing the operational structure required for an effective HRPP and its oversight. Leadership places high priority on compliance and regulatory monitoring to ensure that all aspects of research integrity are valued and that the proper mechanisms are in place for education, training and continuing review. The Ralph H. Johnson VAMC was among the first in the country to appoint a monitor for post-approval review of all human subjects research. This culture of operational compliance and education is a core, integrated philosophy for the university. Monitoring by the Office of Compliance includes validation of required training, annual review of each individual research protocol, internal audits and mechanisms to follow implementation of any required corrective action. The process of post-approval review of human subjects protocols was established at MUSC in 2002 under the Office of University Compliance and is continuously monitoring for quality improvement.

The ongoing improvement and quality of our HRPP is initiated through multiple mechanisms including post-review monitoring, education, quarterly visits and/networking with external advisors and consultants, ongoing monitoring by the Office of Compliance, ongoing review of best practices, regularly scheduled reviews of the IRB operations and weekly discussions among the multiple offices involved in our HRPP (see HRPP Program Guide Section 10.1 – Human Research Audit Policy and Procedures and Section 10.3 – Quality Improvement Initiatives). Visiting academicians and consultants meet with staff and consult with the institutional and organizational officials responsible for our HRPP.

We consider the ongoing review of educational and training requirements for all individuals involved in human research to be another important vehicle for quality improvement and have training requirements in place for individuals just beginning in research and for continuing education through the CITI. In addition, the Office of Research Integrity developed a course “Core Clinical Research Training” that is now offered through South Carolina Translational Research Institute for all research teams and coordinators involved in human research. In addition, many centers and institutes on campus have training and mentoring opportunities in place to assist in education and awareness. Finally, we have active community-based outreach and education programs to increase awareness in the community for human subjects’ research, including a Human Research Participant Brochure ([English](#) and [Spanish](#) Versions). Our community based partnership initiatives are currently led through the Pearls initiative

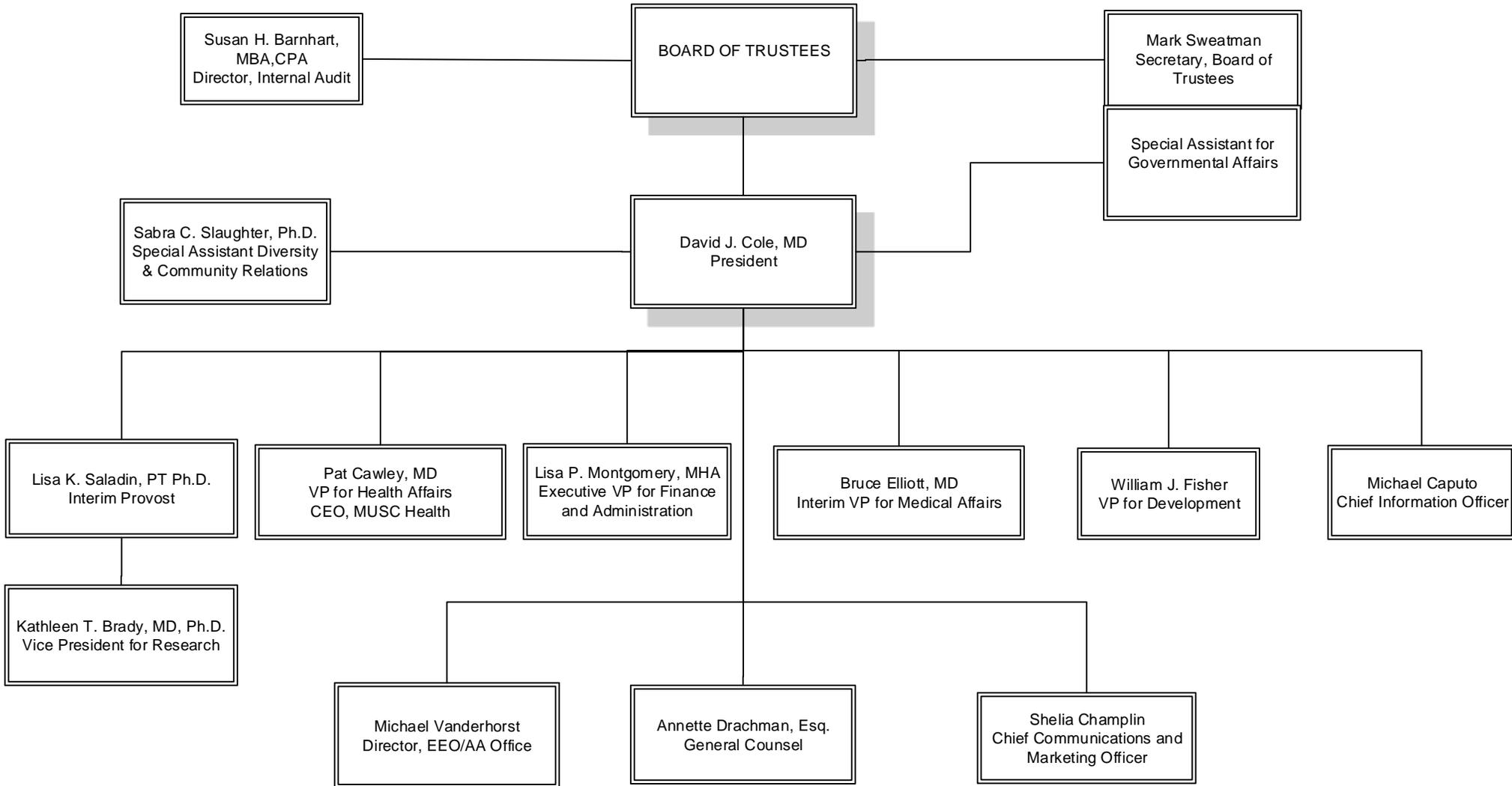
and S.C. Clinical and Translational (SCTR) Institute Community Engagement Program,

VII. MUSC HUMAN RESEARCH PROTECTION PROGRAM GUIDE

Many of the core aspects of our HRPP are captured in our MUSC Human Research Protection Program Guide that are published on the MUSC web site (<http://academicdepartments.musc.edu/research/ori/irb/policies.html>) and freely available to guide both investigators and human research participants. The Guide provides an organizational scheme that serves as an important educational tool for all aspects of our HRPP.

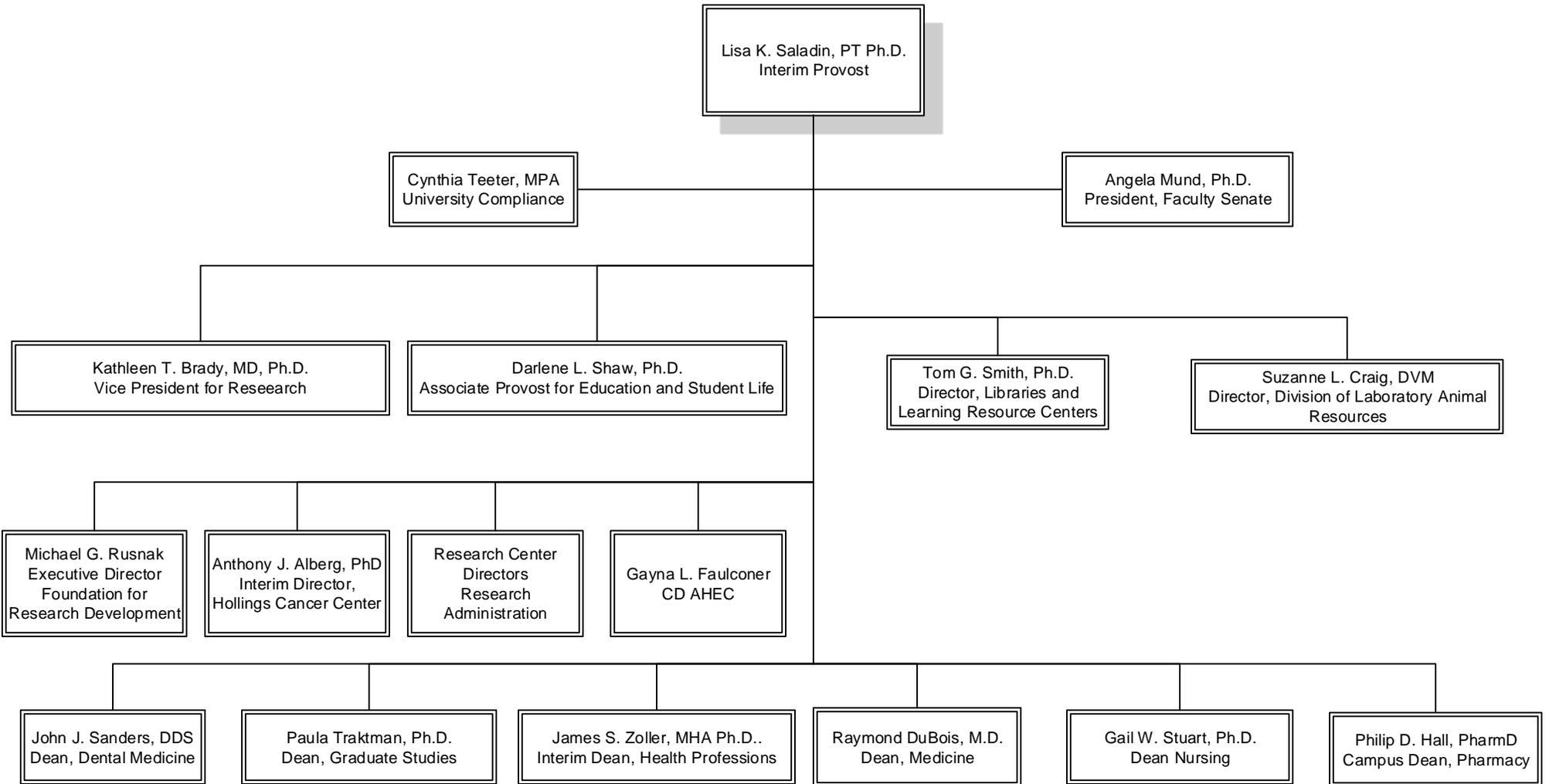
MUSC ORGANIZATIONAL CHARTS

CENTRAL ADMINISTRATION



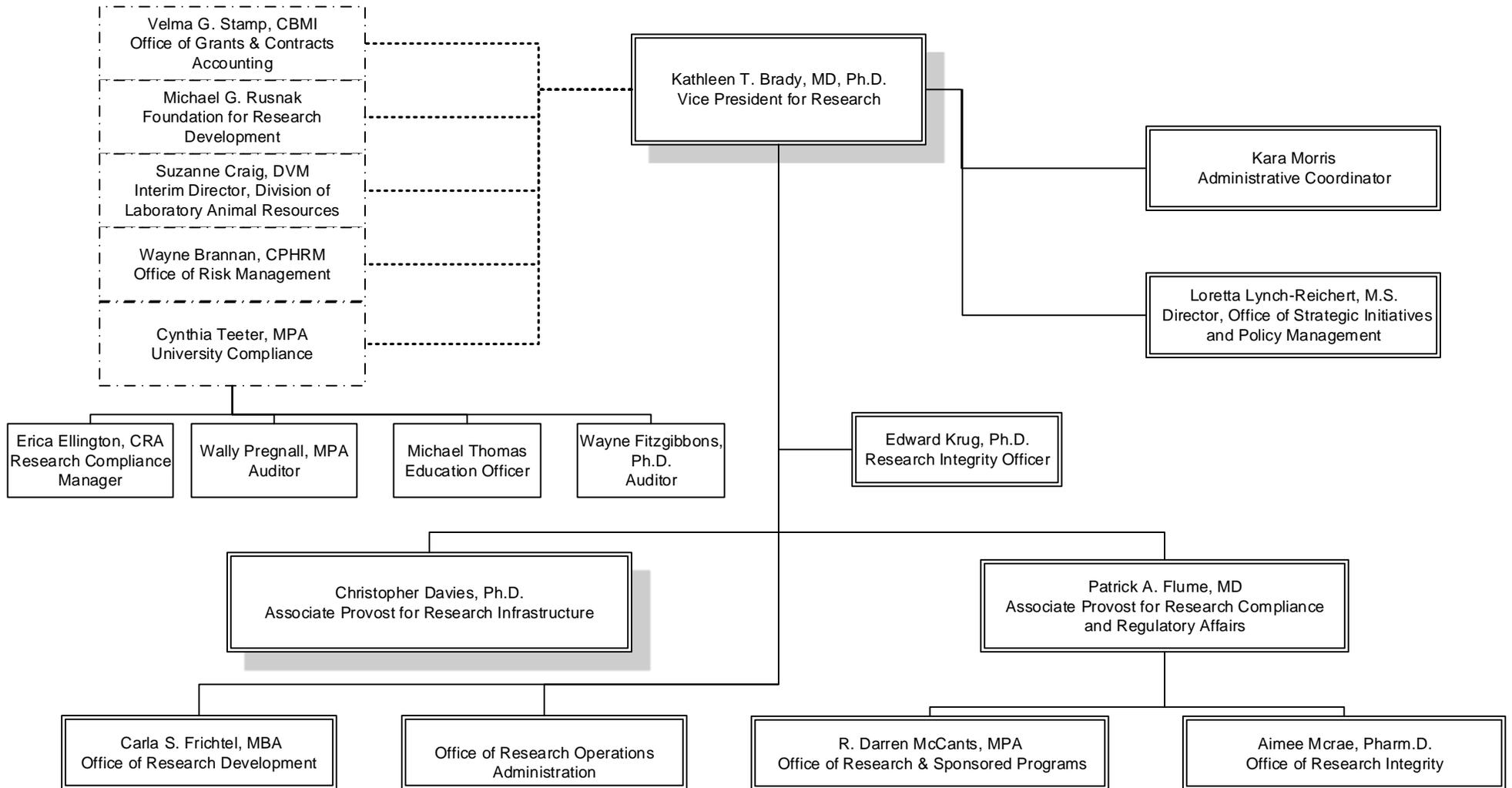
MUSC ORGANIZATIONAL CHARTS

PROVOST



MUSC ORGANIZATIONAL CHARTS

VICE PRESIDENT FOR RESEARCH



Dotted lines represent offices that have separate direct reporting lines but have extensive involvement and engagement with the Office of the Vice President for Research.

MUSC ORGANIZATIONAL CHARTS

OFFICE OF RESEARCH INTEGRITY

Standing Committees

Institutional
Animal Care and Use

Institutional
Biosafety

Research
Integrity

-----Institutional Review Boards-----

Rupak Mukherjee, Ph.D.
Chair
Kelley Argraves, Ph.D.
Vice-Chair

Carolyn Westwater, Ph.D.
Chair

Richard M. Silver, MD
Chair

Mark Hamner, MD
Chair, IRB I
Susan Newman, RN, PH.D.
Vice-Chair, IRB I

Susan C. Sonne, PharmD
Chair, IRB II
Steven Swift, MD
Vice-Chair, IRB II

David Lewin, MD
Chair, IRB III
Andrew D. Hardie, MD
Vice-Chair, IRB III

Aimee L. Mcrae-Clark, Pharm.D.
Director

Donna Heartley
Business Manager

Cyndi Rosenblatt, CIPA
IACUC
Program Manager

Yashmin Karten, Ph.D.
IBC
Program Manager

Stacey Goretzka, CIP
IRB
Program Manager

Sarah Oakes
IACUC Administrator

Katherine Bright
Grants Administrator II

Summer Young, JD, MPH, CIP
Grants Administrator II

Paul Kelly, CIP
Grants Administrator II

Jackie Shedrow, CIP
Grants Administrator II

Susan Franklin
IACUC Coordinator

Kristin Zaks
Grants Coordinator II

Kay Roberts
Grants Coordinator II

Cheryl Green
Grants Coordinator II

Grants Coordinator II

Amy Haynes
Grants Coordinator II



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| Policy Name: Definitions of Terms | | |
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I. POLICY

A. Introduction

In order to ensure that terminology and definitions are consistent throughout the Human Research Protection Program, this document will serve as the source for terms and definitions. Subsequent references to terms and definitions will refer to this document.

B. Application

The definitions in this policy apply to all other policies established for the Protection of Human Subjects in Research.

C. DEFINITIONS

1. **ABUSE-LIABLE** – Pharmacological substances that have the potential for creating abusive dependency. Abuse able substances can include both illicit drugs (e.g., heroine) and licit drugs (e.g. methamphetamines).
2. **AD HOC** – For or concerned with one specific purpose or case; often improvised or impromptu.
3. **ADJUVANT THERAPY** – Therapy provided to enhance the effect of a primary therapy; auxiliary therapy.
4. **ADVERSE EFFECT** – An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention (e.g., headache following spinal tap or intestinal bleeding associated with aspirin therapy).
5. **ADVERSE EVENT** – Expected or unexpected harmful events as a result of the use of an investigational or approved drug, biologic or device, or of an investigational procedure, observed in the approved project or in other research studies similar to that of the approved project.
6. **AGENT** – Person authorized to act on behalf of MUSC. This includes an individual performing MUSC designated activities or exercising MUSC-delegated authority or responsibility.

7. **ALLEGATION OF NON-COMPLIANCE** – An assertion of non-compliance that has yet to be proved or supported by evidence.
8. **ANONYMIZED SAMPLES (UNLINKED)** – Samples that may have been acquired from identified human sources, but for which all identifiers or codes have been removed and destroyed such that the ability to identify particular individuals, via clinical or demographic information, would be extremely difficult for the investigator, the repository or a third party.
9. **APPROVAL PERIOD** – Research involving human subjects may be approved for a maximum period of one year from the date of approval or for a shorter period of time, as determined by the IRB.
10. **ASSENT** – Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research.
11. **ASSURANCE** – A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved.
12. **AUTHORIZATION** – Express written permission that an individual permits the release and use of their individually identifiable health information for a particular purpose. Authorizations are not required to use an individual's health information to treat them, obtain payment or for a provider's health care operations. However, under HIPAA, research is not considered health care operations, and therefore, requires an authorization or waiver of authorization with limited exception. The provider (or investigator) is responsible for obtaining an authorization from an individual.
13. **AUTHORIZED INSTITUTIONAL OFFICIAL** – An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research.
14. **AUTONOMY** – Personal capacity to consider alternatives, make choice, and act without undue influence or interference of others.
15. **AUTOPSY** Examination by dissection of the body of an individual to determine cause of death.

16. **BELMONT REPORT** - A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.
17. **BENEFICENCE** - An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.
18. **BENEFIT** - A valued or desired outcome; an advantage.
19. **BIOLOGIC** - Any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries.
20. **BLIND STUDY DESIGNS** - See: Masked Study Designs; Double-Masked Design; and Single-Masked Design.
21. **BOTANICAL DRUG PRODUCTS** consist of vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof, that are intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans.
22. **CADAVER** - The body of a deceased person.
23. **CASE-CONTROL STUDY** - A study comparing persons with a given condition or disease (the cases) and persons without the condition or disease (the controls) with respect to antecedent factors. (See also: Retrospective Studies.).
24. **CAT SCAN** - Computerized Axial Tomography, an X-ray technique for producing images of internal bodily structures through the assistance of a computer.
25. **CDC** - Centers for Disease Control and Prevention; an agency within the Public Health Service, Department of Health and Human Services.
26. **CHILDREN** - Persons who have not attained the legal age for consent to treatment or procedures involved in the research or clinical investigations, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.402(a) and 21 CFR 50.3(c)]. "Children" as defined by the state of South Carolina are individuals less than 18 years of age.
27. **CLASS I, II, III DEVICES** - Classification by the Food and Drug Administration to 510(k) medical devices based on the level of risk

and, therefore, the level of FDA oversight needed to ensure the device is safe and effective as labeled (FDA Information Sheets, Medical Devices, 1998 Update).

28. **CLINICAL INVESTIGATION** – See definition for Research (as defined by FDA regulations).
29. **CLINICAL TRIAL** - A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions.
30. **CODE OF FEDERAL REGULATIONS (CFR)** – A codification of federal agency regulations which has the force and effect of law.
31. **COGNITIVELY IMPAIRED** - Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished (Institutional Review Board Guidebook, 1993). Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.
32. **COHORT** - A group of subjects initially identified as having one or more characteristics in common who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences.
33. **COMMON RULE** – See: Federal Policy (The)
34. **COMPENSATION** - Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research. (Compare: Remuneration.)
35. **COMPETENCE** - Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice (Institutional Review Board Guidebook, 1993). (See also: Incompetence, Incapacity).
36. **COMMUNITY BASED PARTICIPATORY RESEARCH (CBPR)** - a type of community-engaged research that is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each

brings. This type of research begins with a research topic of importance to the community and has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities. (W.K. Kellogg Foundation)

37. **COMMUNITY ENGAGED RESEARCH** - Community-engaged research is a framework or approach for conducting research, not a methodology in and of itself. It is characterized by the principles that guide the research and the relationships between the communities and academic researcher's community engaged research requires partnership development, cooperation and negotiation, and commitment to addressing local health issues.
38. **CONFIDENTIALITY** - Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure (IRB Guidebook, 1993). Further information: Joan E. Sieber "[Privacy and Confidentiality: As Related to Human Research in Social and Behavioral Science \(Research Involving Human Participants V2\)](#)" Online Ethics Center for Engineering 5/25/2007 12:04:01 PM National Academy of Engineering.
39. **CONFLICT OF INTEREST IN SCIENCE** refers to situations in which financial or other personal considerations (i.e. service on Board of Directors, Consulting, intellectual property related to protocol under consideration, protocol submitted by members of immediate family) may compromise, or have the appearance of compromising, an investigator's professional judgment in designing, conducting or reporting research (MUSC Conflict of Interest, Financial Disclosure).
40. **CONSENT** - See: Informed Consent.
41. **CONTINUING NONCOMPLIANCE** – a pattern of recurring or on-going instances of actions or omissions which indicates an underlying deficiency in knowledge of the regulations and/or IRB requirements and/or willingness to comply with them. In VA Research, continuing non-compliance is a persistent failure to adhere to the laws, regulations, or policies governing human research. In all cases, the determination that non-compliance is continuing rests with the IRB.
42. **CONTRACT** - An agreement; as used here, an agreement that a specific research activity will be performed at the request, and under the direction, of the agency providing the funds. Research

performed under contract is more closely controlled by the agency than research performed under a grant. (Compare: Grant.)

43. **CONTROL (SUBJECTS) or CONTROLS SUBJECT(S)** - used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of study. Control conditions may be concurrent (occurring more or less simultaneously with the condition under study) or historical (preceding the condition under study). When the present condition of subjects is compared with their own condition on a prior regimen or treatment, the study is considered historically controlled.
44. **CONTRAINDICATED** - Disadvantageous, perhaps dangerous; a treatment that should not be used in certain individuals or conditions due to risks (e.g., a drug may be contraindicated for pregnant women and persons with high blood pressure).
45. **CORRECTIVE ACTIONS** – Suggestions for corrections or improvements to be made to assure regulatory agency inspection readiness and alignment with regulations and standards and a listing of current good practices.
46. **CORRELATION COEFFICIENT** - A statistical index of the degree of relationship between two variables. Values of correlation coefficients range from -1.00 through zero to +1.00. A correlation coefficient of 0.00 indicates no relationship between the variables. Correlations approaching -1.00 or +1.00 indicate strong relationships between the variables. However, causal inferences about the relationship between two variables can never be made on the basis of correlation coefficients, no matter how strong a relationship is indicated.
47. **CROSS-OVER DESIGN** - A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy. For example, half of the subjects might be randomly assigned first to the control group and then to the experimental intervention, while the other half would have the sequence reversed.
48. **CUSTOM DEVICE** – A device that: [21CFR § 812.3(b)]
 - a) Necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician;
 - b) Is not generally available to, or generally used by, other physicians;

- c) Is not generally available in finished form for purchase or for dispensing upon prescription;
 - d) Is not offered for commercial distribution through labeling or advertising; and
 - e) Is intended for use by an individual patient named in the order of a physician, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician in the course of professional practice.
49. **DATA AND SAFETY MONITORING BOARD** - A committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.
50. **DEAD FETUS** - An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached) [45 CFR 46.203(f)]. Generally, some organs, tissues, and cells (referred to collectively as fetal tissue) remain alive for varying periods of time after the total organism is dead.
51. **DEBRIEFING** - Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting information.)
52. **DECLARATION OF HELSINKI** - A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It was revised in 1975 and 1989.
53. **DE-IDENTIFIED** – Health information is de-identified if there is no reasonable basis to believe that the data can be used to identify an individual, or if the provider has no reasonable basis to believe it can be used to identify the individual. The Privacy rule requires one of the two following approaches to de-identify data:
- a) If a person with appropriate knowledge and experience applying generally accepted statistical and scientific principles and methods for rendering information not individually identifiable makes a determination that the risk is very small that the information could be used, either by itself

or in combination with other available information, by anticipated recipients to identify a subject of the information.

- b) If all 18 identifiers have been removed, including name, all geographic subdivisions smaller than a State including street address, city, county, precinct, zip codes and equivalent geocodes, (except for the initial 3 digits of a zip code if more than 20,000 people reside in the area), all dates including birthdays (other than the year) and ages over 89, phone numbers, fax numbers, email addresses, social security numbers, medical record numbers, health plan beneficiary numbers, account numbers, certificate/license numbers, vehicle identifiers and serial numbers (including license plate number), device identifiers and serial numbers, URLs, IP addresses, biometric identifiers, full face photographic images and any comparable images, any other unique identifiers, characteristic or code.

NOTE: Other demographic information, such as gender, race, ethnicity, and marital status are not included in the list of identifiers that must be removed.

54. **DEPENDENT VARIABLES** - The outcomes that are measured in an experiment. Dependent variables are expected to change as a result of an experimental manipulation of the independent variable(s).
55. **DESCRIPTIVE STUDY** - Any study that is not truly experimental (e.g., quasi-experimental studies, correlation studies, record reviews, case histories, and observational studies).
56. **DEVICE (MEDICAL)** - See: Medical Device.
57. **DHEW** A federal agency: U.S. Department of Health, Education and Welfare; reorganized in 1980 as the Department of Health and Human Services (DHHS) and the Department of Education.
58. **DHHS** – U.S. Department of Health and Human Services
59. **DIAGNOSTIC (PROCEDURE)** - Tests used to identify a disorder or disease in a living person.
60. **DISSENT** – An individual's negative expressions, verbal and/or non-verbal that they object to participation in the research or research activities.
61. **DOUBLE-BLIND OR DOUBLE-MASKED DESIGN** - A study design in which neither the investigators nor the subjects know the treatment group assignments of individual subjects.

62. **DRUG** - Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions.
63. **ELECTRONIC MEDIA** – The mode of electronic transmission, includes the Internet (wide-open), Extranet (using Internet technology to link a business with information only accessible to collaborating parties), leased lines, dial-up lines, private networks, and transmissions that are physically moved from one location to another using magnetic tape, disk, or compact disk media.
64. **EMANCIPATED MINOR** - A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (See also: Mature Minor.)
65. **EMBRYO** - Early stages of a developing organism, broadly used to refer to stages immediately following fertilization of an egg through implantation and very early pregnancy (i.e., from conception to the eighth week of pregnancy). (See also: Fetus.)
66. **EMERGENCY USE**
- a) The use of an investigation device in a patient : 1) there is an “exemption” from prospective IRB prior review and approval of the IND one time treatment use because there is insufficient time for the IRB to convene and review the request, and 2) the patient is in a life-threatening or severely debilitating position (21 CFR 56.102(d)). Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the “subjects” must be in a life-threatening situation requiring intervention before review at a convened IRB meeting is feasible (FDA Information Sheet, 1998).
 - b) The use of an investigational device in a patient:
 - (1) Who is in a life-threatening situation and,
 - (2) Necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician;
 - (3) Is not generally available to, or generally used by, other physicians;
 - (4) Is not generally available in finished form for purchase or for dispensing upon prescription;

- (5) Is not offered for commercial distribution through labeling or advertising; and
 - (6) Is intended for use by an individual patient named in the order of a physician, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician in the course of professional practice.
67. **ENCRYPTION** – The process of converting information, particularly information such as social security number and name that identifies individuals, into a code.
68. **ENGAGED IN RESEARCH** – being involved in one or more of the following activities: 1) Receiving an HHS award for research, 2) Intervening with participants for research purposes (invasive or noninvasive), 3) Manipulating the environment, 4) Interacting with participants for research purposes, and/or 5) Obtaining identifiable private information or identifiable biological specimens for any source for research purposes (OHRP Engagement of Institutions in Research at : <http://www.hhs.gov/ohrp/policy/engage08.html>)
69. **EPIDEMIOLOGY** - A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or given population.
70. **EQUITABLE** - Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.
71. **ETHICS ADVISORY BOARD** - An interdisciplinary group that advises the Secretary, HHS, on general policy matters and on research proposals (or classes of proposals) that pose ethical problems.
72. **ETHNOGRAPHIC RESEARCH** - Ethnography is the study of people and their culture. Ethnographic research, also called fieldwork, involves observation of and interaction with the persons or group being studied in the group's own environment, often for long periods of time. (See also: Fieldwork.)
73. **EXCULPATORY LANGUAGE** - language through which the subject waives or appears to waive the subject's legal rights or releases or appears to release the investigator, sponsor, the institution, or its agents from liability for negligence (45 CFR 46.116).

(See <http://www.hhs.gov/ohrp/policy/exculp.html> for examples of exculpatory and acceptable language)

74. **EXPANDED AVAILABILITY** - Policy and procedure that permits individuals who have serious or life-threatening diseases for which there are no alternative therapies to have access to investigational drugs and devices that may be beneficial to them. Examples of expanded availability mechanisms include Treatment INDs, Parallel Track, and open study protocols.
75. **EXPEDITED REVIEW** - Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.
76. **EXPERIMENTAL** - Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness. (See also: Research.)
77. **EXPERIMENTAL STUDY** - A true experimental study is one in which subjects are randomly assigned to groups that experience carefully controlled interventions manipulated by the experimenter according to a strict logic allowing causal inference about the effects of the interventions under investigation. (See also: Quasi-Experimental Study).
78. **EXPERIMENTAL SUBJECT** – For research sponsored or funded by the U.S. Department of Defense (DoD), this is a living individual about whom an investigator is conducting research and obtaining data through intervention or interaction with the individual or identifiable private information. Limitations on the use of humans as experimental subjects are outlined in [DOD Directive 3216.02](#).
79. **FALSE NEGATIVE** - When a test wrongly shows an effect or condition to be absent (e.g., that a woman is not pregnant when, in fact, she is).
80. **FALSE POSITIVE** - When a test wrongly shows an effect or condition to be present (e.g. that is woman is pregnant when, in fact, she is not).
81. **FDA** – U.S. Food and Drug Administration. An agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.

82. **FEDERAL GUIDANCE** – Information published by federal agencies on the topic that represents the agency's current thinking or view but does not have the effect or force of law.
83. **FEDERAL POLICY (THE)** The federal policy that provides regulations for the involvement of human subjects in research. The Policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that takes appropriate administrative action to make the Policy applicable to such research. Currently, sixteen federal agencies have adopted the Federal Policy. (Also known as the "Common Rule.")
84. **FEDERALWIDE ASSURANCE (FWA)** – A document filed with the Office for Human Research Protections (OHRP) of the Department of Health and Human Services expressing an institution's commitment to comply with the department's regulations for the protection of human subjects.
85. **FETAL MATERIAL** - The placenta, amniotic fluid, fetal membranes, and umbilical cord.
86. **FETUS** - The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant [45 CFR 46.203(c)]. The term "fetus" generally refers to later phases of development; the term "embryo" is usually used for earlier phases of development. (See also: Embryo.)
87. **FIELDWORK** - Behavioral, social, or anthropological research involving the study of persons or groups in their own environment and without manipulation for research purposes (distinguished from laboratory or controlled settings). (See also: Ethnographic Research.)
88. **FINANCIAL INTEREST RELATED TO THE RESEARCH** – A financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.
89. **510(k) DEVICE** - A medical device that is considered substantially equivalent to a device that was or is being legally marketed. A sponsor planning to market such a device must submit notification to the FDA 90 days in advance of placing the device on the market. If the FDA concurs with the sponsor, the device may then be marketed. 510(k) is the section of the Food, Drug and Cosmetic Act that describes premarket notification; hence the designation "510(k) device." (FDA Information Sheets, Medical Devices, 1998 Update).

90. **510(k) SUBMISSION** – The purpose of a 510(k) submission is to demonstrate that a device is “substantially equivalent” to a predicate device (one that has been cleared by the FDA or marketed before 1976). The 510(k) submitter compares and contrasts the subject and predicate devices, explaining why any differences between them should be acceptable.
91. **FTE** – Full-time equivalent appointment.
92. **FULL BOARD REVIEW** - Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.
93. **GENERAL CONTROLS** - Certain FDA statutory provisions designed to control the safety of marketed drugs and devices. The general controls include provisions on adulteration, misbranding, banned devices, good manufacturing practices, notification and record keeping, and other sections of the Medical Device Amendments to the Food, Drug and Cosmetic Act [21 U.S. Code §360(c) (Food, Drug and Cosmetic Act §513)].
94. **GENERALIZABLE KNOWLEDGE** – Conclusions derived from a systematic investigation of a group of subjects (sample) that can be applied to populations beyond the one from which the sample is derived.
95. **GENE THERAPY** - The treatment of genetic disease accomplished by altering the genetic structure of either somatic (nonreproductive) or germline (reproductive) cells.
96. **GENETIC RESEARCH** – Research (not diagnostic testing) which involves either the analysis of human chromosomes or DNA from an individual an/or family members for the purpose of deriving information concerning the individual or family about the presence, absence or mutation of genes, DNA markers or inherited characteristics or other studies with the intent of collecting and evaluating information about heritable diseases and/or characteristics within a family.
97. **GENETIC SCREENING** - Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders.
98. **GENOTYPE** - The genetic constitution of an individual.

99. **GRANT** - Financial support provided for research study designed and proposed by the Principal Investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant. (Compare: Contract.)
100. **GREATER THAN MINIMAL RISK** – The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
101. **GUARDIAN** - An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care [45 CFR 46.402(e) and 21 CFR 50.3(s)].
102. **HELSINKI DECLARATION** - See: Declaration of Helsinki.
103. **HIPAA** – The Health Insurance Portability and Accountability Act of 1996. Also referred to as the Privacy Rule.
104. **HISTORICAL CONTROLS** - Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. The study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment.
105. **HUMAN IN VITRO FERTILIZATION** - Any fertilization involving human sperm and ova that occurs outside the human body.
106. **HUMAN SUBJECT** –
- a) **(as defined by DHHS and VA regulations)** – A living individual about whom an investigator conducting research obtains: (1) data through *intervention* or *interaction* with the individual or (2) identifiable *private information*. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be

ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. (The Common Rule [38 CFR 16.102(f)] which is identical to [45 CFR 46.102(f)(1)(2)]

b) **(as defined by FDA regulations)** – An individual who becomes a participant in research regulated by the Food and Drug Administration (FDA), either as a recipient of a test article or as a control. A subject may be either a healthy human or a patient. In the case of research involving medical devices, a human subject includes an individual on whose specimen a medical device is used. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

107. **HUMAN SUBJECTS RESEARCH** – Any activity that is either (a) “research” as defined by DHHS regulations that involves “human subjects” as defined by DHHS regulations or (b) “research” as defined by FDA regulations that involves “human subjects” as defined by FDA regulations.
108. **IDE** – See Investigation Device Exemption.
109. **IMMEDIATE FAMILY** – Refers to a person’s spouse and dependent children.
110. **INCAPACITY** - Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence. (See also: Incompetence.)
111. **INCOMPETENCE** - Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (See also: Incapacity.)
112. **IND** – See Investigational New Drug.
113. **IDENTIFIABLE INFORMATION** – information where the identity of the subject is or may be readily be ascertained by the investigator or associated with the information.
114. **IDENTIFIED SAMPLES** – Biological samples obtained by an investigator or a 3rd party which have identifiers attached or a link permitting determination of the individual subject source through the use of a code.
115. **IDENTIFIERS** – Information that can be used to link a sample or scientific result with a specific person or group of people.

Examples include name, social security number, hospital number or other unique identifier. It should also be noted that using current information technology, a combination of descriptive data may be sufficient to allow identification of the donor and thereby collectively may be considered identifiers (e.g. zip code, birth date or profession may be sufficient to identify a specific individual.)

116. **INDEPENDENT VARIABLES** - The conditions of an experiment that are systematically manipulated by the investigator.

117. **INFORMED CONSENT** -

a) A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence [Federal Regulations [45 CFR 46.116(a) and 21 CFR 50.20 and 50.25]].

b) An active participatory process which involves three key features: a) disclosing to potential subjects information needed to make an informed decision, b) facilitating the understanding of what has been disclosed, and 3) promoting the "voluntariness" of the decision about whether or not to participate in the research (OHRP Informed Consent Frequently Asked Questions, <http://answers.hhs.gov/ohrp/categories/1566>

c) The investigator must seek consent only under conditions that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence [45 CFR 46.116].

118. **INSTITUTION** –

a) Any public or private entity or agency (including federal, state, and local agencies).

b) A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.

119. **INSTITUTIONAL AUTHORIZATION AGREEMENT (IAA)** An IAA sets forth the terms and conditions under which one institution/facility may rely on the other for IRB review. Together with the FWA, this agreement allows many off campus community sites to rely on MUSC to act as the IRB of record in situations where the community site is engaged in research but does not have its own IRB.
120. **INSTITUTIONAL OFFICIAL (IO)** – The individual with the legal authority to represent the institution.
121. **INSTITUTIONAL REVIEW BOARD** - A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.
122. **INSTITUTIONALIZED** - Confined, either voluntarily or involuntarily (e.g., a hospital, prison, or nursing home).
123. **INSTITUTIONALIZED COGNITIVELY IMPAIRED** - Persons who are confined, either voluntarily or involuntarily, in a facility for the care of the mentally or otherwise disabled (e.g., a psychiatric hospital, home, or school for the retarded).
124. **INTERACTION** includes communication or interpersonal contact between investigator and subject.
125. **INTERVENTION** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
126. **INTERVENTIONAL CLINICAL RESEARCH** means any prospective biomedical or behavioral research study involving human subjects that is designed to answer specific questions about the safety, efficacy, and effectiveness of biomedical or behavioral interventions (NIH, PHS 398, Human Subjects Research Supplement, 2006).
127. **INVESTIGATIONAL DEVICE EXEMPTION** - (IDE) - An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission to FDA. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE **before** the study is initiated. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

128. **INVESTIGATIONAL DRUG OR DEVICE** –
- a) A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.
 - b) A new drug or biologic drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms **investigational drug** and **investigational new drug** are deemed to be synonymous. [21 CFR 312.3(b)]
 - c) An **investigational device** is a medical device that is the object of an investigation [21CFR § 812.3(g)], i.e., the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.
129. **INVESTIGATIONAL PROCEDURES** – Any procedure tested for safety and effectiveness, not yet considered standard procedure for the particular use being researched.
130. **INVESTIGATOR** - In clinical trials, an individual who actually conducts an investigation [21 CFR 312.3]. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the investigator. (See also: Principal Investigator.)
131. **IN VITRO** - Literally, "in glass" or "test tube;" used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo.
132. **IN VIVO** - Literally, "in the living body;" processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).
133. **IRB** - See: Institutional Review Board.
134. **JUSTICE** - An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.
135. **KEY PERSONNEL** – All individuals responsible for the design or conduct of the study. Everyone who has contact with human subjects, with confidential data about human subjects, or data that was obtained from human subjects, for research purposes is included.

136. **LACTATION** - The period of time during which a woman is providing her breast milk to an infant or child.
137. **LEGALLY AUTHORIZED REPRESENTATIVE** or **LEGAL REPRESENTATIVE** –
- a) A person authorized either by statute or by court appointment to make decisions on behalf of another person. In human subjects research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research [21 CFR 50.3(l)].
 - b) An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures involved in the research [45 CFR 46.102(c)]. The legal representative must have documentation of this legal status.
138. **LEGAL GUARDIAN** - an individual who is authorized under applicable South Carolina law to consent on behalf of the child to general medical care [45 CFR 46.402 (e)]. A legal guardian may consent for a “ward” to participate in research in lieu of a child’s adoptive or biological parents.
139. **LIFE-THREATENING** - Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted, and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subject-patient must be in a life threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
140. **LOD SCORE** - An expression of the probability that a gene and a marker are linked.
141. **LONGITUDINAL STUDY** - A study designed to follow subjects forward through time.
142. **MASKED STUDY DESIGNS** - Study designs comparing two or more interventions in which either the investigators, the subjects, or some combination thereof do not know the treatment group assignments of individual subjects. Sometimes called "blind" study designs. (See also: Double-Blind or Double-Masked Design; Single-Blind or Single-Masked Design.)
143. **MATURE MINOR** - Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain

purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (See also: Emancipated Minor.)

144. **MEDICAL DEVICE** – An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
 - a) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
 - b) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
 - c) intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

145. **MEDICAL DEVICE AMENDMENTS (MDA)** - Amendments to the Federal Food, Drug and Cosmetic Act passed in 1976 to regulate the distribution of medical devices and diagnostic products.

146. **MEDICAL DEVICE CLASS** - See **CLASS I, II, III DEVICES**

147. **MENTALLY DISABLED** - See: Cognitively Impaired.

148. **METABOLISM (OF A DRUG)** - The manner in which a drug is acted upon (taken up, converted to other substances, and excreted) by various organs of the body.

149. **MINIMAL RISK** - A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed 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. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination. [45 CFR 46.102(i)][21 CFR 56102(i)] The definition of minimal risk for research involving prisoners means the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [See 45 CFR 46.303(d) and Guidebook Chapter 6, Section E, "Prisoners."]

150. **MINOR MODIFICATIONS** – Modifications to a research protocol which have minimal risk to study participants such as wording changes and correction of typographical errors. In order for minor modifications to be reviewed using the expedited process, modifications involving new procedures must involve no more than minimal risk and fall into one of the expedited categories (1)-(7) detailed in HRPP Program Guide Section 2.5 Expedited Review of Research Policy and Procedures.
151. **MINORS** – see Children.
152. **MONITORING** - The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections.
153. **MUSC** – Medical University of South Carolina
154. **MUSC Facilities** – Facilities owned and operated by MUSC.
155. **MUSC Institutional Official** – Individual authorized to act for MUSC and, on its behalf, obligates MUSC to the Terms of the Federalwide Assurance with the Department of Health and Human Services and OHRP.
156. **NATIONAL COMMISSION** - National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. An interdisciplinary advisory body, established by Congressional legislation in 1974, which was in existence until 1978, and which issued a series of reports and recommendations on ethical issues in research and medicine, many of which are now embodied in federal regulations.
157. **NDA** - See: New Drug Application.
158. **NEONATE** – A newborn baby less than 30 days old.
159. **NEW DRUG APPLICATION** - Request for FDA approval to market a new drug.
160. **NIAAA** - National Institute on Alcohol Abuse and Alcoholism; an institute in NIH.
161. **NIDA** - National Institute on Drug Abuse; an institute in NIH.
162. **NIH** – See National Institutes of Health.
163. **NATIONAL INSTITUTES OF HEALTH** - A federal agency within the Public Health Service, DHHS, comprising 21 institutes and

centers. It is responsible for carrying out and supporting biomedical and behavioral research.

164. **NIMH** - National Institute of Mental Health; an institute in NIH.
165. **NONAFFILIATED MEMBER** - Member of an Institutional Review Board who has no ties to the parent institution, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker).
166. **NONCOMPLIANCE** with federal and/or state regulations or IRB requirements for human subject protections is evidenced by intentional or unintentional behavior demonstrating lack of adherence to these regulations/requirements.
167. **NON-SCIENTIFIC MEMBER** – Member whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline.
168. **NONSIGNIFICANT RISK DEVICE** - An investigational medical device that does not present significant risk to the patient and does not meet the definition of a significant risk study (FDA Information Sheets, Medical Devices, Updated 1998)... (See also: Significant Risk Device.)
169. **NON-SIGNIFICANT RISK (NSR) DEVICE STUDY** - A study of a device that does not meet the definition for a significant risk study.
170. **NONTHERAPEUTIC RESEARCH** - Research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future.
171. **NONVIALE FETUS** - An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy [45 CFR 46.203 (d) and (e)]. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams [Federal Register 40 (August 8, 1975): 33552], a specific determination as to viability must be made by a physician in each instance. (See also: Viable Infant.)
172. **NONVIALE NEONATE** – A neonate after delivery that, although living is not viable [45 CFR 46.202].

173. **NORMAL VOLUNTEERS** - Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease.
174. **NULL HYPOTHESIS** - The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the investigator to reject the null hypothesis.
175. **NUREMBERG CODE** - A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects.
176. **OFFICE FOR PROTECTION FROM RESEARCH RISKS (OPRR)** - The office within the National Institutes of Health, an agency of the Public Health Service, Department of Health and Human Services, responsible for implementing DHHS regulations (45 CFR Part 46) governing research involving human subjects. Reorganized to OHRP.
177. **OHRP** – *Office for Human Research Protections* of the Department of Health and Human Services.
178. **OPEN DESIGN** - An experimental design in which both the investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.
179. **OPRR** - See: Office for Protection from Research Risks.
180. **PARENT** – A child's biological or adoptive parent.
181. **PARTICIPANT** – A living individual about whom a research investigator (whether a professional or a student) obtains data through intervention or interaction with the individual or from individually identifiable information. An individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A participant may be either a healthy human or a patient.

182. **PARTICIPATE** – Take part in the described activity in any capacity, including but not limited to serving as the Principal Investigator, co-investigator, research collaborator or provider of direct patient care. The term is not intended to apply to individuals who provide primarily technical support or who are purely advisory, with no direct access to the data (e.g., control over its collection or analysis) or, in the case of clinical research, to the trial participants, unless they are in a position to influence the study's results or have privileged information as to the outcome.
183. **PATERNALISM** - Making decisions for others against or apart from their wishes with the intent of doing them good.
184. **PERMISSION** - The agreement of parent(s) or guardian to the participation of their child or ward in research [45 CFR 46.402(c)].
185. **PHARMACOLOGY** - The scientific discipline that studies the action of drugs on living systems (animals or human beings).
186. **PHASE 1, 2, 3, 4 DRUG TRIALS**- Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3), to postmarketing studies (Phase 4).
- a) **PHASE 1 DRUG TRIAL** - Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.
- b) **PHASE 2 DRUG TRIAL** - Phase 2 trials include controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the

disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well-controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.

- c) **PHASE 3 DRUG TRIAL** - Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand patient-subjects.
- d) **PHASE 4 DRUG TRIAL**- Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain postmarketing (Phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time [21 CFR 312.85].

- 187. **PHENOTYPE** - The physical manifestation of a gene function.
- 188. **PHS PUBLIC HEALTH SERVICE**. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.
- 189. **PLACEBO** - A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than actual power of a drug.
- 190. **POSTAMENDMENTS DEVICES** - Medical devices marketed after enactment of the 1976 Medical Device Amendments.

191. **PREAMENDMENTS DEVICES** - Medical devices marketed before enactment of the 1976 Medical Device Amendments.
192. **PRECLINICAL INVESTIGATIONS** - Laboratory and animal studies designed to test the mechanisms, safety, and efficacy of an intervention prior to its applications to humans.
193. **PREDICATE DEVICES** - Currently legally marketed devices to which new devices may be found substantially equivalent under the 510(k) process.
194. **PREGNANCY** - The period of time from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (i.e., has been delivered). Implantation is confirmed through a presumptive sign of pregnancy such as missed menses or a positive pregnancy test [45 CFR 46.203(b)]. This "confirmation" may be in error, but, for research purposes, investigators would presume that a living fetus was present until evidence to the contrary was clear. Although fertilization occurs a week or more before implantation, the current inability to detect the fertilization event or the presence of a newly fertilized egg makes a definition of pregnancy based on implantation necessary.
195. **PREMARKET APPROVAL** - Process of scientific and regulatory review by the FDA to ensure the safety and effectiveness of Class III devices.
196. **PRESIDENT'S COMMISSION** - President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. An interdisciplinary advisory group, established by congressional legislation in 1978, which was in existence until 1983, and which issued reports on ethical problems in health care and in research involving human subjects.
197. **PRINCIPAL INVESTIGATOR** - The scientist or scholar with primary responsibility for the design and conduct of a research project. (See also: Investigator.)
198. **PRISONER** –
 - a) An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution [45 CFR 46.303(c)].

- b) “Prisoner” is defined by HHS regulations at 45 CFR 46.303(c) as “any individual involuntarily confined or detained in a penal institution. Guidance provided by OHRP extends the definition to individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.
199. **PRIVACY** – Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others (IRB Guidebook, 1993).
200. **PRIVATE INFORMATION** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [45 CFR 46.102(f)(1)(2)]
201. **PROBAND** - The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.
202. **PROPHYLACTIC** - Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder.
203. **PROSPECTIVE STUDIES** - Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.
204. **PROTECTED HEALTH INFORMATION (PHI)** – Individually identifiable health information transmitted by electronic media, maintained in any electronic media, or transmitted or maintained in any other form or medium.
205. **PROTOCOL** - The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be

employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

206. **PROTOCOL AMENDMENT** – Any change, clarification, advertisement, (including minor consent form changes) made to the approved protocol.
207. **PROTOCOL DEVIATION** – Any variance from the protocol involving a subject or subjects that is not approved by the IRB prior to its initiation or implementation, and occurs when a member of the study team departs from the IRB-approved protocol in any way **without the investigator first obtaining IRB approval.**
208. **PURITY** - The relative absence of extraneous matter in a drug or vaccine that may or may not be harmful to the recipient or deleterious to the product.
209. **QUASI-EXPERIMENTAL STUDY** - A study that is similar to a true experimental study except that it lacks random assignments of subjects to treatment groups. (See also: Experimental Study.)
210. **RADIOACTIVE DRUG** - Any substance defined as a drug in Section 201(b)(1) of the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons [21 CFR 310.3(n)]. Included are any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products," as defined in 21 CFR 600.3(ee). Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.
211. **RADIOLOGY DEVICE** - A radiology device that is used as a diagnostic device, or is used as a therapeutic device, or has two or more types of uses (e.g., used both as a diagnostic device *and* a therapeutic device. See [21CFR § 892.1000 - 892.6500] for specific listings of device types for each category.
212. **RADIOPAQUE CONTRAST AGENTS** - Materials that stop or attenuate radiation that is passed through the body, creating an outline on film of the organ(s) being examined. Contrast agents, sometimes called "dyes," do not contain radioisotopes. When such agents are used, exposure to radiation results only from the X-ray equipment used in the examination. The chemical structure of radiopaque contrast agents can produce a variety of adverse

reactions, some of which may be severe and possibly life-threatening in certain individuals.

213. **RADIOPHARMACEUTICALS** - Drugs (compounds or materials) that may be labeled or tagged with a radioisotope. These materials are largely physiological or subpharmacological in action, and, in many cases, function much like materials found in the body. The principal risk associated with these materials is the consequent radiation exposure to the body or to specific organ systems when they are injected into the body.
214. **RANDOM, RANDOM ASSIGNMENT, RANDOMIZATION, RANDOMIZED** - Assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention.
215. **RECOMBINANT DNA TECHNOLOGY** - "The ability to chop up DNA, the stuff of which genes are made, and move the pieces, [which] permits the direct examination of the human genome," and the identification of the genetic components of a wide variety of disorders [Holtzman (1989), p. 1]. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.
216. **RECUSAL** – The temporary absence of the IRB member during deliberation and vote on the project with respect to which the member has a conflict.
217. **REM (ROENTGEN EQUIVALENT IN MAN)** - the unit of measurement for a dose of an ionizing radiation that produces the same biological effect as a unit of absorbed dose (1 rad) of ordinary X-rays. One millirem is equal to 1/1000 of a rem.
218. **REMISSION** - A period in which the signs and symptoms of a disease are diminished or in abeyance. The term "remission" is used when one cannot say with confidence that the disease has been cured.
219. **REMUNERATION** - Payment for participation in research. (NOTE: It is wise to confine use of the term "compensation" to payment or

provision of care for research-related injuries.) (Compare: Compensation.)

220. **REPOSITORY** – A common site for storage of collection of human biologic specimens available for study. This may be one geographic location or may be a virtual aggregation of biologic specimens from many locations. Repositories are also referred to as tissue banks, collection, resources, inventories, or by other terms. Repository activities involve three components: (i) the **collectors** of tissue samples; (ii) the **repository** storage and data management center; and (iii) the **recipient**.

221. **RESEARCH**

a) **(as defined by DHHS regulations)** – A systematic investigation, including research development, testing and evaluation designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)].

b) **(as defined by FDA regulations)** (*synonymous with the term **Clinical Investigation***)

(1) Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of Part 58 of 21 CFR 58 (“Good Laboratory Practice for Nonclinical Laboratory Studies”). The terms **research**, **clinical research**, **clinical study**, **study**, and **clinical investigation** are deemed to be synonymous. [21 CFR 50.3(c) and 21 CFR 56.102(c)]

(2) Any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. An experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. [21CFE 312.3(b)]

(3) **Investigation** means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

222. **RESEARCH CERTIFICATES OF CONFIDENTIALITY** – Situations where the Investigator requires protection of research of a sensitive

nature and the Principal Investigator has applied to the Department of Health and Human Services to protect this information. This allows a researcher to protect the privacy of research subjects by withholding from most persons not connected with the research team the names and other identifying information relating to research subjects. The protection will be granted only when the research is of a sensitive nature where the protection is judged necessary to achieve the research objectives. Examples include research relating to sexual attitudes, preferences, or practices, the use of alcohol, drugs, or other addictive products, pertaining to illegal conduct or to an individual's psychological well being or mental health, genetic information, information that, if released, could be damaging to an individual's financial standing, employability, or reputation, and information that would normally be recorded in a patient's medical record that, if released, could lead to social stigmatization or discrimination. Researchers may receive a Certificate of Confidentiality regardless of funding source. Researchers who receive a certificate may not be compelled by Federal, State or local legal processes or subpoenas to disclose information that they possess as a consequence of the research.

223. **RESEARCH MISCONDUCT** – Intentional, reckless or negligent failure to abide by applicable law, regulations, or IRB procedures; plagiarism; fabrication or intentional falsification of data, research procedures or data analysis; or other deliberate misrepresentation in proposing, conducting, reporting, or reviewing research. It does not include honest error or honest differences in interpretations or judgments of data. In cases of allegations involving activities submitted to or supported by a federal agency, the definition for misconduct specified in the agency's regulations will apply.
224. **RESPECT FOR PERSONS** - An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.
225. **RETROSPECTIVE STUDIES** - Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research.
226. **REVIEW (OF RESEARCH)** - The concurrent oversight of research on a periodic basis by an IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis.

227. **RISK** - The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (See also: Minimal Risk.)
228. **SAMHSA SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION** - includes the Center for Substance Abuse Prevention, the Center for Substance Abuse Treatment and the Center on Mental Health Services. Previously the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). (See also: ADAMHA.)
229. **SAMPLE** – In context of this policy, a sample refers to any human biological material. This includes, but is not limited to, molecular material such as DNA, cells tissue (blood, bone, muscle, etc), organs (liver, bladder, heart, etc) gametes, embryos, fetal tissue, waster (hair, nail clippings, urine, feces, saliva, sputum, etc) and other materials of human origin.
230. **SCIENTIFIC REVIEW GROUP** - A group of highly regarded experts in a given field, convened by NIH to advise NIH on the scientific merit of applications for research grants and contracts. Scientific review groups are also required to review the ethical aspects of proposed involvement of human subjects. Various kinds of scientific review groups exist, and are known by different names in different institutes of the NIH (e.g., Study Sections, Initial Review Groups, Contract Review Committees, or Technical Evaluation Committees).
231. **SECRETARY** - A U.S. Cabinet Officer. In the context of DHHS-conducted or -supported research, usually refers to the Secretary of Health and Human Services.
232. **SENSITIVE INFORMATION** - includes, but is not limited to, information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information relating to illegal conduct; information that if released, might be damaging to an individual's financial standing, employability, or reputation in the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples (NIH, Frequently Asked Questions on Certificates of Confidentiality, March, 2002).
233. **SERIOUS NONCOMPLIANCE** – knowingly disregarding or violating federal regulations or institutional policies and procedures

applicable to human subjects research, which, in the judgment of the IRB, could place subjects at risk of significant harm. For VA research, serious non-compliance is a failure to adhere to the laws, regulations, or policies governing research involving human subjects that may reasonably be regarded as: 1) involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others and/or 2) substantively compromising the effectiveness of a VA facility's HRPP. In all cases, the determination that non-compliance is serious rests with the IRB.

234. **SERIOUS UNANTICIPATED PROBLEM (SAE)** – Any event that results in death, a life-threatening situation, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity or a congenital anomaly/birth defect or requires medical intervention to prevent one of the outcomes listed above. SAEs require prompt reporting to the Sponsor, the FDA and the IRB.
235. **SEVERELY DEBILITATING** - diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke (FDA Information Sheet, 1998).
236. **SIGNIFICANT COMPLAINTS, ISSUES OR CONCERNS** - problems that relate to subjects' safety, rights, and/or welfare.
237. **SIGNIFICANT FINANCIAL CONFLICT OF INTEREST** is aligned with the guidelines of the Public Health Service and exists when any member of a research team or his/her immediate family receives or is likely to receive direct, personal remuneration of at least \$10,000 from or holds a 5% or greater ownership in a company involved in research, training, patient care and/or administrative activities related to the sponsored project.
238. **SIGNIFICANT RISK DEVICE** or **SIGNIFICANT RISK INVESTIGATIONAL DEVICE** - An investigational medical device that a potential for serious risk to the health, safety, or welfare of a subject and a) is intended as an implant, or b) used in supporting or sustaining life, or c) is of substantial importance in diagnosing, curing, mitigating, or curing disease, or otherwise prevents impairment of human health, or d) otherwise prevents a potential for serious risk to the health, safety, or welfare of a subject [21 CFR 812.3(m)].

239. **SIGNIFICANT RISK (SR) DEVICE STUDY** – A study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and
- a) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a participant;
 - b) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a participant;
 - c) Is for a use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety or welfare of a participant; or
 - d) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
240. **SINGLE-BLIND OR SINGLE-MASKED DESIGN** - Typically, a study design in which the investigator, but not the subject, knows the identity of the treatment assignment. Occasionally the subject, but not the investigator, knows the assignment.
241. **SITE VISIT** - A visit by agency officials, representatives, or consultants to the location of a research activity to assess the adequacy of IRB protection of human subjects or the capability of personnel to conduct the research.
242. **SOCIAL EXPERIMENTATION** - Systematic manipulation of, or experimentation in, social or economic systems; used in planning public policy.
243. **SPONSOR (OF A DRUG TRIAL)** - A person or entity that initiates a clinical investigation of a drug - usually the drug manufacturer or research institution that developed the drug. The sponsor does not actually conduct the investigation, but rather distributes the new drug to investigators and physicians for clinical trials. The drug is administered to subjects under the immediate direction of an investigator who is not also a sponsor. A clinical investigator may, however, serve as a sponsor-investigator. The sponsor assumes responsibility for investigating the new drug, including responsibility for compliance with applicable laws and regulations. The sponsor, for example, is responsible for obtaining FDA approval to conduct a trial and for reporting the results of the trial to the FDA. [21 CFR 312.3(b)]
244. **SPONSOR-IMPOSED HOLD** – A sponsor-initiated action to place all or some specific research activities on hold. This decision may be made from interim data analysis, inadequate drug stocks,

response to a DSMB report; or a preplanned stopping point. This may also occur as a result of new information potentially altering participants' risk/benefit ratio.

245. **SPONSOR-INVESTIGATOR** - an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part [21 CFR 312 Subpart D] include both those applicable to an investigator and a sponsor. [21 CFR 312.3(b)].
246. **SPONSORED RESEARCH** – Research that is commercially funded by a business enterprise (e.g., pharmaceutical company or device manufacturer); government sponsored research and/or private sponsored research.
247. **STATISTICAL SIGNIFICANCE** - A determination of the probability of obtaining the particular distribution of the data on the assumption that the null hypothesis is true. Or, more simply put, the probability of coming to a false positive conclusion. [See McLarty (1987), p. 2.] If the probability is less than or equal to a predetermined value (e.g., 0.05 or 0.01), then the null hypothesis is rejected at that significance level (0.05 or 0.01).
248. **STERILITY**
- a) The absence of viable contaminating microorganisms; aseptic state.
 - b) The inability to procreate; the inability to conceive or induce conception.
249. **STUDY SECTION** - See: Scientific Review Group.
250. **STUDY STAFF** – Research nurses and study coordinators that are involved in the research process, including but not limited to, patient recruitment, patient care, data collection and records completion.
251. **SUBJECTS (HUMAN)** - See: Human Subjects.
252. **SUBSTANTIVE CHANGES** - Non-minor changes that significantly alter the study design, study population and/or risks.
253. **SURVEYS** - Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

254. **SUSPENSION OF IRB APPROVAL** – The IRB Board may direct a Principal Investigator and his/her colleagues to cease enrollment and/or to cease all or part of study procedures in the interest of subject safety. This may, upon direction of the board, become a full study termination. With corrective action on the part of the Principal Investigator the full board may withdraw study suspension, returning the study to full active status. Under emergency circumstances, this decision may be made by the Chair, Vice-Chair or ORI Director.
255. **SYSTEMATIC INVESTIGATION** – A planned and orderly process through which a hypothesis or research questions is formulated, data are collected and analyzed, and results are interpreted in terms of the hypothesis or research question.
256. **TECHNOLOGY** – Any compound, drug, device, diagnostic, medical or surgical procedure intended for use in health care delivery.
257. **TERMINATION OF IRB APPROVAL** – The IRB may direct a Principal Investigator and his/her colleagues to cease enrollment and all other study procedures in the interest of subject safety. The IRB will notify the Principal Investigator that all currently enrolled subjects must be notified of study termination and given recommendations of clinical treatment, as appropriate. Under emergency circumstances, this decision may be made by the Chair, Vice-Chair or ORI Director.
258. **TEST ARTICLE** – A drug or device that is being tested for safety and effectiveness, not yet approved by the FDA for general use, or not yet approved for the particular use being researched.
259. **THERAPEUTIC INTENT** - The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition as well as assessing the safety and pharmacology of a drug.
260. **THERAPY** - Treatment intended and expected to alleviate a disease or disorder.
261. **UNANTICIPATED PROBLEM** – Any unplanned occurrence that may affect the risks and/or potential benefits involved in the research study. Unplanned occurrences are usually related to study

design or methods. Such occurrences can be favorable or unfavorable to participants and may or may not influence the study objectives or results (e.g., loss of confidentiality).

262. **UNEXPECTED UNANTICIPATED PROBLEM (UAE)** – Any problem that was unanticipated or not previously observed (e.g., not included in the consent form or investigator brochure). This includes adverse events that occur more frequently or with greater severity than anticipated. Events that are unexpected and serious require prompt reporting to the Sponsor, the FDA and the IRB.
263. **UNAPPROVED DEVICE** - A device that is used for a purpose or condition for which the device requires, but does not have an approved application for pre-market approval under section 515 FD&C Act & [21 United States Code (USC) chapter 9, subchapter IV, § 360(e)]. An unapproved device may be used in human subjects only if approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under the FDCA [21USC ch9, subch. IV § 360(j)(g) and [21CFR part 812.] Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices.
264. **UNIFORM ANATOMICAL GIFT ACT** - Legislation adopted by all 50 States and the District of Columbia that indicates procedures for donation of all or part of a decedent's body for such activities as medical education, scientific research, and organ transplantation.
265. **VACCINE** - A biologic product generally made from an infectious agent or its components - a virus, bacterium, or other microorganism that is killed (inactive) or live-attenuated (active, although weakened). Vaccines may also be biochemically synthesized or made through recombinant DNA techniques.
266. **VARIABLE (NOUN)** - An element or factor that the research is designed to study, either as an experimental intervention or a possible outcome (or factor affecting the outcome) of that intervention.
267. **VIABLE INFANT** - When referring to a delivered or expelled fetus, the term "viable infant" means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy [45 CFR 46.203(d)]. This judgment is made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of viability. Such guidelines were published in 1975, and specify an estimated gestational age of 20 weeks or more and a body weight of 500

grams or more as indices of fetal viability [Federal Register 40 (August 8, 1975): 33552]. These indices depend on the state of present technology and may be revised periodically. (See also: Nonviable Fetus.)

268. **VOLUNTARY** - Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity.
269. **VULNERABLE SUBJECTS/PARTICIPATION** – Individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be subject to undue influence or coercion. Vulnerable subjects include, for example, children, prisoners, individuals with emotional or cognitive disorders/impairments and economically or educationally disadvantaged persons.
270. **WAIVER OF HIPAA AUTHORIZATION** – Documented HIPAA permitted waiver of authorization when an IRB reviews the request according to the required criteria.
271. **WAIVER OR ALTERATION OF REQUIRED ELEMENTS OF CONSENT** - An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent. HHS CFR 45.46.116(d)
272. **WAIVER OF WRITTEN DOCUMENTATION OF INFORMED CONSENT** - An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds:
 - a) that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research. : HHS CFR 45.46.117(c)(1)
 - b) that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (e.g. telephone survey). In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement

regarding the research. If requesting a waiver of documentation of informed consent, provide the script or information sheet that will be used. HHS CFR 45.46.117(c)(2)

- 273. **WARD OF THE STATE** – Person who, because of age or infirmity or by statute put under the protection of the state which supports the person and makes decisions for them. Commonly used with minor children, abused elderly person, and prisoners.
- 274. **WITNESS** - an individual 18+ years of age who observes the subject signing the informed consent document. When authorized by the IRB, a short form written consent document stating the elements of informed consent can be presented orally. When this method is used, the witness signature verifies s/he was present to the oral presentation.



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| Policy Name: Scientific/Scholarly Review of Protocols Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 2 | Section: HRPP 1.4 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

A. Introduction

Each department chairman or center director is ultimately responsible for the review and scientific integrity of any proposal that will be sent to the IRB. In the case of most centers, such as the Hollings Cancer Center, Clinical and Translational Research Center (CTRC), and the Alcohol Research Center, there are standing committees of scientists, physicians, statisticians, and other health professionals that review protocols for scientific integrity prior to review by the director or chairman's office. The evaluation of the available non-clinical and clinical information on an investigational product is adequate to support the proposed clinical trial.

B. Large Clinical Research Departments

Some large clinical research departments, such as Medicine and Psychiatry, have a vice-chair designated to review scientific integrity and merits of research protocols. Vice-chairman for research review research documents personally or delegate them to individuals with greater scientific expertise in the area of the proposed research topic.

C. Routing

There is a system of electronic routing tracts within departments and centers that ensures that proposals are reviewed and signed off by a consistent and appropriate group of faculty and staff responsible for oversight. Within departments and centers, fellows and junior faculty are usually assigned a senior faculty mentor to guide scientific literature review, research methodology design, statistical analytical procedures, discussion of best clinical practices and the bioethics of human scientific research. Other resources for scientific review available to investigators include the statistical clinical trials group in the Biometry & Epidemiology Division of the Department of Medicine, the Master in Clinical Science Research faculty, and the recently developed Research Navigation Services in the SC Clinical and Translational Research Center. All of these divisions are available for consultation on design, methodology, statistics, and ethical issues.

D. VAMC

If the Ralph H. Johnson VA Medical Center's Research and Development Committee conducts scientific review, the review is communicated to the Medical University of South Carolina's IRB.

0. The Research and Development Committee may delegate scientific review to the affiliate IRB.
1. The Research and Development Committee may delegate scientific review to a different process at the VA or affiliate, and the review is communicated to the affiliate IRB.

E. Guidance on Additional Requirements of Federal Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage](http://research.musc.edu/ori/irb/resources.html) (<<http://research.musc.edu/ori/irb/resources.html>>).

F. IRB Responsibilities for Minimizing Risk

1. The IRB is responsible for determining that risks to subjects are minimized by:
 - a) Using procedures which are consistent with sound research and design and which do not unnecessarily expose subjects to risks,
 - b) Using procedures, whenever appropriate, already being performed on subjects for diagnostic or treatment purposes,
 - c) The IRB Chair, in consultation with the IRB Administrator, assigns studies to Primary Review Groups relative to expertise of the members, and
 - d) If vulnerable populations are involved, the IRB Chair, in consultation with the IRB Administrator, assigns one or more

IRB members experienced in working with the specific vulnerable population.

2. When appropriate expertise is not available among members of the IRB assigned to review the proposed research activities, the IRB will obtain consultation from experts with relevant expertise and knowledge to assist in further evaluation of the scientific design and to provide an in-depth review of the study. If appropriate expertise is unavailable at a meeting, discussion of the protocol will be deferred until such time as appropriate expertise may be obtained.
3. The IRB will defer review until necessary expertise and in-depth review can be obtained through the current membership or consultation.

II. PROCEDURES

- A. An initial application submitted for either full board or expedited review by the IRB must provide adequate documentation to demonstrate the methodology and procedures are consistent with generally accepted scientific principles in the discipline.
- B. Each application must also include a Statement of Assurance which includes the electronic signature of the Principal Investigator's department chair or his/her designee indicating concurrence with the scientific merit of the proposal and that the research study has the resources necessary to protect participants. These resources include: adequate time for the researchers to conduct and complete the research; adequate number of qualified staff; adequate facilities; access to a population that will allow recruitment of the necessary number of participants; availability of medical or psychosocial resources that participants might need as a consequence of the research.
- C. The application will be assigned to an appropriate member of the IRB for primary review of the Chair will seek outside consultation to provide an in-depth review.
- D. In addition, if a member of the primary review team cannot adequately evaluate the scientific merit and scholarly validity of an assigned protocol, (s)he will notify the Chair to discuss the use of another member of the IRB or whether it is necessary to obtain a consultant to assist in the review or request that the investigator provide additional information and/or be present for IRB discussion.

III. REFERENCES

- A. [Master in Clinical Science Research](#)
- B. [Research Navigation Services in the SC Clinical and Translational Research Center \(SCTR\)](#)



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|--|-------------|--------------------------|
| Policy Name: State Laws Affecting Human Subjects Research | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 1.5 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

In addition to federal laws and regulations, human research activities conducted by MUSC investigators must comply with all laws in the state in which the research is being conducted. In general, when federal and state laws differ, the more restrictive law prevails.

The Principal Investigator has the responsibility for ensuring that a study protocol complies with all Federal, State and Local regulations and statutes governing human subjects' research. The Medical University of South Carolina has the responsibility to advise and counsel its investigators on the relevant Federal Regulations and statutes, as well as, State statutes governing human subjects' research and to assist investigators with compliance through its University's policies and procedures. The General Counsel's office and the State Attorney General's office are charged with the responsibility to provide timely consults to researchers regarding relevant State and Federal statutes. The General Counsel's office provides notice and interpretations of other state's laws that may apply to specific research projects or activities. Interpretation and guidance is also provided by the office on the ethical standards for human subjects research to ensure awareness and compliance

II. LAWS SPECIFIC TO SOUTH CAROLINA

South Carolina is specific in addressing who may consent on behalf of an incompetent person. The IRB must approve the informed consent process and the person who will provide consent for research procedures.

Disclosure of genetic testing results is covered by South Carolina law and disclosure of test results requires written informed consent from the individual or his/her legal representatives. IRB informed consent templates provide suggested language for investigator's guidance when preparing informed consent documents involving genetic testing.

When research involves the possibility of mandatory reporting to a third party, regardless of the research subject's consent, the participant must be informed of the information that may be disclosed.

III. RELEVANT SECTION DETAIL – SOUTH CAROLINA STATUTES:

A. SECTION 15-1-320 – Age of Consent

Minors in State laws mean persons under age of 18 years.

B. SECTION 44-66-30 – Adult Health Care Consent

1. Persons unable to consent:

Persons who are unable, whether temporarily or permanently, to make an informed consent, may have their health care decisions made by another within a legally prescribed priority listing, and with the patient's wishes and best interests (to the extent possible known and determined) as the basis for consent of health care decision-making.

The following is a summary of the priority listing for persons able to make health care decisions for those unable to consent (either to provide or withhold consent);

- Court appointed guardian;
- Attorney with durable power of attorney related to health care decisions;
- Individual authorized by another statute;
- Spouse – unless legally separated, with provisions;
- Parent or adult child;
- Adult sibling, grandparent, adult grandchild; and
- Other relative (by blood or marriage) believed by health care professional, to have close personal relationship.

2. Exceptions:

- Where persons of equal decision-making priority disagree, another authorized person may petition the court for further action including appointment of a new guardian;
- Where it is known that the persons as prescribed in the priority listing are not available, able or willing to decide on behalf of the patient; and
- Where there is actual knowledge that the persons as prescribed in the priority listing were not approved by the patient to act on their behalf.

C. SECTION 38-93-30 (2006) Privacy of Genetic Information

1. Confidentiality; disclosure restrictions and exceptions.

All genetic information must be confidential and must not be disclosed to a third party in a manner that allows identification of the individual tested without first obtaining the written informed consent of that individual or a person legally authorized to consent on behalf of the individual.

2. Genetic tests; informed consent required; exceptions.

It is unlawful to perform a genetic test on tissue, blood, urine, or other biological sample taken from an individual without first obtaining specific informed consent to the test from the individual, or a person legally authorized to consent on behalf of the individual, unless the test is performed for use in a study in which the identities of the persons from whom the genetic information is obtained are not disclosed to the person conducting the study.

3. Tissue from live donor

South Carolina law mandates that genetic information obtained from any tests or from this research be kept confidential. Results of the research will not be given to the individual or his/her doctor. To help protect the individual's privacy, these reports will not be put in his/her health record. South Carolina law prohibits any insurer using this information in a discriminatory manner against the individual or any member of his/her family in issuing or renewing insurance coverage for the individual or his/her family. South Carolina state law further prohibits sharing genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board and then all steps must be taken to protect the individual's identity.

4. Tissue from nonliving donor

South Carolina law mandates that genetic information obtained from any tests or from this research be kept confidential. Results of the research will not be given to individual. To help protect privacy, these reports will not be put in the deceased's health record. South Carolina law prohibits any insurer using this information in a discriminatory manner against the individual or any member of his/her family in issuing or renewing insurance coverage for the individual or his/her family. South Carolina state law further

prohibits sharing genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board and then all steps must be taken to protect the individual's identity.

IV. In areas of conflict between federal and state statutes, the more stringent statute will prevail

V. REFERENCES:

[SECTION 15-1-320 – Age of Consent](#)

[SECTION 44-66-30 – Adult Heathcare Consent Act](#)

[SECTION 38-93-30 \(2006\) Privacy of Genetic Information](#)



| | | |
|---|-------------|-------------------|
| Policy Name: Communicating Conflict of Interest (COI) among IRB, ORSP and University Research COI Committees | | |
| Approved | | |
| Effective Date: 09/15/2012 | Page 1 of 2 | Section: HRPP 1.6 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

Disclosures of individual and institutional Conflicts of Interest (COI) are received through a variety of avenues. These may be received through the Annual COI Disclosures, the Institutional Review Board (IRB), the Office of Research and Sponsored Programs (ORSP), and/or by a variety of MUSC Officers and administrators who request a review for potential or real conflicts and are initially reviewed by the Conflict of Interest Office. Disclosures of significant financial interests related to research are forwarded for review by the Research COI Committee, which includes membership from the staff of the ORSP and the IRB.

It is this Committee's responsibility to review the requests in a timely manner, to maintain confidentiality, and to communicate their recommendations, findings and actions to the requesting unit and/or impacted unit in either detailed or summary form as appropriate.

The IRB is notified of any disclosure involving human subjects received by the Research COI Review Committee.

II. PROCEDURE

- A.** Upon disclosure of a financial interest in the eIRB initial protocol application (Human Research Conflict of Interest Disclosure Form) an electronic notice is sent to the Conflict of Interest Office. The COI Officer initiates the review and coordinates the necessary documents between the researchers and the Research COI Committee Chair.
- B.** The chair of the Research COI Committee determines whether an administrative review is appropriate or if full committee review is warranted and notifies the IRB by written communication.
- C.** After review, the Research COI Committee communicates its decision to the MUSC IRB. If the study is approved, the COI Office issues approval in the eIRB system. If a COI management plan is required, the Committee approved plan is provided to the IRB.

- D.** For new studies undergoing full board review, the COI management plan will be made available to the IRB members for review prior to full IRB approval of the protocol. For studies that were initially reviewed by a convened board and requiring continuing full board review, amendments to add or update related financial interests will also undergo full board review if determined to be a potential conflict of interest. Financial interests that are added to studies that do not otherwise require full board review, and that are determined to be potential conflicts of interest, can be reviewed using the expedited process.
- E.** If an existing financial interest changes or a new financial interest is developed or acquired during the course of an ongoing study, it is the responsibility of the PI to update the IRB application within 30 days of the event in order to initiate the COI review procedure just described.
- F.** All management plans related to sponsored research developed by the Research COI Committee are provided to ORSP plans involving human subjects will also be provided to the MUSC IRB. The Conflict of Interest Office is responsible for recording and monitoring COI management plans with relevant outcomes reported to various parties including the IRB and ORSP.
- G.** The IRB has the final authority to determine whether the approved management plan for any disclosed conflict of interest allows research protocols involving human subjects to be approved. The convened IRB will make this determination for studies requiring full board review. This determination may be made by the expedited reviewer for studies that do not otherwise require full board review.



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|--|-------------|--------------------------|
| Policy Name: Mentor, Department and Ancillary Reviews | | |
| Approved | | |
| Effective Date: 10/01/2014 | Page 1 of 3 | Section: HRPP 1.7 |
| Replaces Policy: | | |

I. Policy

All protocols require Departmental Review and Approval prior to receipt by the IRB. All submitted studies are automatically routed to the individual(s) designed by the Principal Investigator's College/Department/Division (that of the Mentor for Mentored-PIs) for review and approval. Designated individuals will issue electronic approval or request information/clarification from the research team.

Protocols submitted by Mentored-PIs require review and approval by the mentor prior to receipt by the IRB. Protocols will automatically be routed to the Mentor selected by the PI for review and approval. The Mentor will issue electronic approval or request information/clarification from the research team.

Additional ancillary reviews or notifications of an MUSC research application occur when review and approvals are required from research sites, or when the research itself involves certain activities that require specialized review.

Based upon information provided by the Research Staff in the eIRB SmartForm Application, mentor, departmental reviewers and other ancillary offices impacted by the research will receive automatic email notification from the eIRB.

II. Timing of Ancillary Review and Approval

There are 3 classes of ancillary review and approval:

1. **Review Prior to Receipt by the IRB:** Review and approval by the Mentor (for Mentored-PIs) and division/department/college approvers are required prior to receipt of the protocol by the IRB.

In one additional case, ancillary review and approvals must be completed prior to the protocol receipt by the IRB. This is when an investigator-initiated (non-independently funded) protocol indicates use of the Hollings Cancer Center (HCC) or inclusion of cancer patients in the study population.

2. **Concurrent with IRB Review:** Ancillary review and approval occurs concurrently with the IRB review and approval. Upon approval of the protocol **and** receipt of all ancillary approvals, the IRB administrator will release the study.

3. **Notification Only:** Ancillary notification is for information purposes only and no approval is required.

III. Ancillary Department Selection and Review

| Ancillary Department | SmartForm Selection Criteria | Timing of Review |
|--|---|---|
| Conflict of Interest Committee | COI Questions 1.1, 1.2, 1.3, 1.4 or 3.1 are Yes | Concurrent with IRB Review |
| Division/Department/College | Division of PI (or Mentor for Mentored PIs) | Review Prior to Receipt by IRB |
| Grants and Contracts Administration (GCA) | Participant Remuneration Checked on Study Subjects SmartForm | Notification Only |
| GI Fellows | PIs department is 2220301 | Notification Only |
| Institutional Biosafety Committee (IBC) | Vaccine Trials OR Recombinant DNA OR Transplantation on Application Checklist | Concurrent with IRB Review |
| Investigational Drug Services (IDS) | IDS as Study Site | Notification Only |
| Mentor | PI is a Mentored-PI on eIRB Registration | Review Prior to Receipt by IRB |
| Office of Research and Sponsored Programs (ORSP) IRB I and II IRB III | All Studies All Studies other than WIRB WIRB Studies | Notification Only Concurrent with IRB Review Review Prior to Submission to WIRB |
| Protocol Review Committee Sponsored Protocols | HCC as Study Site Or Cancer Patients checked on Application Checklist | Concurrent with IRB Review |
| Protocol Review Committee Investigator Initiated Protocols OR No Funding | HCC as Study Site Or Cancer Patients checked on Application Checklist | Review Prior to Receipt by IRB |
| Radiation Safety | Use of Ionizing Radiation on Application Checklist | Concurrent with IRB Review |
| SCTR/Research Nexus | SCTR Research Nexus as Study Site | Notification Only |
| Simulation Center | Simulation Center as Study Site | Concurrent with IRB Review |
| University Compliance | All Studies | Notification Only |
| VMAC R&D Committee | VAMC as Study Site | Notification Only |



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|---|-------------|-------------------|
| Policy Name: Responsibilities, Ethical Principles, Authority and Independence of the IRB | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 4 | Section: HRPP 2.1 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. RESPONSIBILITIES AND ETHNICAL PRINCIPLES

MUSC Institutional Review Boards for Human Research (IRB) shall provide ethical and scientific review and continuing oversight of the human subject's research of the MUSC and the VAMC. The IRBs shall operate in full compliance with all applicable federal, state, and local laws and regulations.

Research at MUSC is guided by the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, generally known as the "Belmont Report". Research with humans conducted at MUSC is subject to prospective IRB review and approval when the institution's employees or agents intervene or interact with human subjects; when the institution's employees or agents obtain individually identifiable private information about human subjects for the purposes of research and/or when the institution is the recipient of a federal award to conduct human research even if all human research activities are performed elsewhere.

The responsibility for the protection of the rights and welfare of human subjects is shared both by the institutions and the investigators who conduct the research.

B. AUTHORITY AND INDEPENDENCE

1. Scope of Authority

The Medical University of South Carolina's (MUSC) Institutional Review Boards were established and empowered by the President of MUSC to act as the Institutional Review Boards (IRBs) for MUSC and the Ralph H. Johnson Veterans Medical Center (VAMC).

Specifically, the Institutional Review Boards have the authority to:

- a) Decide whether research submitted for review is human subjects research as defined by and subject to federal regulations;

- b) Review, and have the authority to approve, require modification in, or disapprove all research activities, including proposed changes in previously approved human subject research;
- c) Review and determine exempt status from 45 CFR 46.101 and 21 CFR 56.104;
- d) Suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants and report such violation and suspension to organizational officials;
- e) Conduct initial review and continuing review of approved research (not less than once per year), and reporting IRB findings to the investigator and the Institution;
- f) 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;
- g) Request audit by the University Compliance Office;
- h) Monitor the consent process;
- i) Require timely progress reports from investigators; and
- j) Report to the Office of Human Research Protections (OHRP) and, if applicable, the local district Food and Drug Administration (FDA) (21 CFR 56.108b) any significant or material finding or action, including:
 - (1) Unanticipated problems involving risks to subjects or others;
 - (2) Serious or continuing noncompliance with federal regulations or IRB requirements; and
 - (3) Suspension or termination of IRB approval

In exercising this authority, the MUSC IRBs shall communicate all decisions regarding human-subjects research and clinical investigations to investigators and to the Institution through the MUSC Office of Research Integrity (ORI) and the VAMC Research and Development Office.

2. **Independence**

The MUSC IRBs shall exercise independence as the entities authorized to oversee human-subjects research for MUSC and VAMC. Consistent with federal regulation (45 CFR 46.112 and 21 CFR 56.112), research that has been reviewed and approved by the IRB may be subject to further review and disapproval by organizational officials. As well, the VA Associate Chief of Staff for Research may choose to undertake additional review of any or all VA associated studies as they come through the IRB review process. The Associate Chief of Staff or the VA Research and Development Committee may disapprove any VA associated study, even if the IRB has granted approval. No one, however, may approve research if it has been disapproved by the IRB.

Ralph H. Johnson VAMC Research and Development administrative officials including, but not limited to the Associate Chief of Staff for Research and development (ACOS) and the Administrative Officer to the Associate Chief of Staff for Research (AO/ACOS) are prohibited from serving as voting members of the IRB.

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.

3. Undue Influence

Anyone who has concerns about undue influence or coercion (e.g., someone outside of the IRB seeks to influence the outcome of the IRB review of a research activity) should report these concerns to the IRB Program Director, IRB Chair, the Organizational Officials or to the University Compliance Officer. If the concern is related to the IRB Program Director, IRB Chair, or Organizational Officials, the reports should go to the University Compliance Officer. Concerns regarding the University Compliance Officer should be reported directly to the University General Counsel. Anonymous concerns may also be reported to the University Compliance Hotline.

Concerns regarding undue influence or coercion shall be documented. Appropriate University Officials will promptly investigate any reports and report their findings to the ORI Director, IRB Program Director, and/or other Organizational Officials. Immediate steps shall be taken, as necessary, to remedy any concerns or to take remedial actions as necessary based on the findings.

C. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".



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|--|-------------|--------------------------|
| Policy Name: Functions of the IRB | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 4 | Section: HRPP 2.2 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

The Institutional Review Boards of MUSC have the responsibilities, Ethical Principles, Authority and Independence as specified in HRPP Guide 2.1.

B. Functions of the IRB

The IRBs are responsible for ensuring the following:

1. subjects are adequately informed of the nature of the study;
2. subjects' participation is voluntary;
3. risks to subjects are minimized and reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result from the studies;
4. risks and benefits of the study are evenly distributed among the possible subject population;
5. adequate provisions for monitoring research activities are in place to protect the safety of research participants;
6. adequate provisions are in place to protect the privacy of research participants and to maintain the confidentiality of research data;
7. informed consent is sought for prospective participants;
8. initial and continuing review of all human research protocols under the purview of the IRB;
9. written reports conveying the findings and actions of the IRBs are provided to the investigator, the Organizational Officials and the Director -VA Research and Development as appropriate;
10. studies are evaluated to determine if they require review more often than annually;

11. studies are evaluated to determine if they need verification from sources other than the investigators that no material changes have occurred since previous IRB review;
12. changes in approved research are not initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to subjects and others;
13. prompt reporting of IRB board determinations to appropriate Organizational Officials, OHRP, FDA, and appropriate sponsors or agencies of unanticipated events involving risks to subjects or others, and/or serious or continuing noncompliance with regulations governing research involving human subjects or the requirements of the IRB;
14. IRB approval of studies in violation of policy are suspended or terminated;
15. adequate additional protections are provided for vulnerable populations used as subjects in research;
16. studies are evaluated to determine if an IND is required when drugs are used in research;
17. studies are evaluated to determine if devices meet the definition of a significant risk device or a non-significant risk device according to guidance provided by the FDA; and,
18. consult and monitor the emergency use of an IND and IDE test article.

C. Interaction with Sponsors

MUSC requires a written and signed contract/agreement from all sponsors of proposed research activities conducted by the University and its affiliates. All such contracts and funding agreements include language that obligates MUSC and the investigators to follow the protocol, applicable regulations, and ethical principles and guidelines related to the protection of human subjects in research.

D. Memorandum of Understanding

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".



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|---|-------------|--------------------------|
| Policy Name: Membership of the IRB | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 9 | Section: HRPP 2.3 |
| Replaces Policy: 08/01/2012 | | |

I. POLICY

A. Introduction

The Institutional Review Boards of MUSC have the responsibilities, Ethical Principles, Authority and Independence as specified in HRPP Guide Section 2.1 and function as specified in HRPP Guide Section 2.2.

B. Membership – General

Each MUSC IRB is composed of at least five members with varying backgrounds to ensure complete and adequate review of research activities commonly done at the institution. The IRB composition may not consist entirely of one profession. The IRB must have at least one member whose primary interest is scientific, one member whose primary interest is in a non-scientific area, and at least one member who has no affiliation with MUSC and has no immediate family member affiliated with MUSC. Each IRB has at least one member who represents the perspective of the research subjects. In order to ensure that the integrity of the review process is not compromised by competing business interests, individuals involved in research development do not serve as members of the IRB.

C. Ethnic Diversity and Appropriate Expertise

Members include both men and women and members of various ethnic groups. The membership includes individuals with the expertise to review the breadth of research conducted at MUSC including vulnerable subjects, research involving neonates, children, pregnant women, mentally disabled individuals, and persons with impaired decision-making capacity. A qualified member is available to serve as the “prisoner representative” as needed.

D. Designated and Alternate Members

Designated and trained alternates are used to supplement membership. The IRB roster will list the regular member and specify alternate(s) who are authorized to substitute for each regulator member. Alternate members will have qualifications comparable to those of the regular members and will serve in the same representative capacity as the member for whom they

substitute. Alternates may attend any IRB meeting, but their vote will only count when serving as the substitute for the regular member.

E. Documentation of IRB Membership

The IRB minutes will document each alternate's status, vote, and attendance as they relate to IRB actions and quorum requirements. When an alternate attends a meeting as a substitute for a regular member, the alternate's participation counts toward the quorum requirements.

F. MUSC IRB and the Ralph H. Johnson VA Medical Center

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

The MUSC IRBs serve as the IRBs for the Ralph H. Johnson VA Medical Center. Furthermore,

1. Each IRB includes two or more VA employees who hold a minimum of 5/8th VA-compensated appoints to serve as voting members unless a waiver is obtained from the chief research and development officer. These individuals serve as full members of the IRB and review non-VA research and all research matters brought to the Boards. At least one VA member must be present during full board review of VAMC human subjects research. These representatives are appointed to the IRB board by the VAMC Medical Center Director following VA Handbook 1200.05.
2. The VA IRB Liaison and/or research compliance officer serves as a non-voting consultant to all the boards and attends every IRB meeting to provide guidance regarding VA regulations. The VA IRB Liaison and/or research compliance officer may not serve as a voting or non-voting member of the IRB.

II. PROCEDURES

A. Recruitment and Selection of Members

0. Affiliated physician, scientist and nonscientist members shall be recruited by the Vice President for Research and the ORI Director

through the departmental chairs or units or through current IRB members.

1. Persons not affiliated with MUSC shall be recruited through current members or the volunteer department of various community agencies or groups. These may be physicians, scientists, and nonscientist representing the local community.
2. New members shall be recruited as needed to ensure that the memberships of the IRBs continues to include individuals with varying backgrounds and the necessary experience or expertise to review the scope of the biomedical and behavior research conducted by MUSC and VAMC

B. Member Designations

Members shall be designated as either: (1) physician-scientists, other scientist or nonscientists; (2) affiliated or unaffiliated; and, (3) voting member or alternate voting member.

1. Physician-Scientists are members who have a medical degree. Other Scientists are members who have substantive training or experience in a scientific discipline or a scientific method, while nonscientists are those members without substantive training or experience in these areas.
2. Affiliated
 - a) members, or their immediate family members, who are affiliated with any component of the Medical University of South Carolina. "Immediate family member" is defined as spouse, domestic partner, child, parent or sibling. "Affiliated" is defined as having an employment relationship with, a professional relationship with, a paid consultant relationship with, a trustee/governing board member relationship with, or being a student of the entity or component.
 - b) Unaffiliated refers to members, or their immediate family members, who are not affiliated with any component of the Medical University of South Carolina.
3. Voting Members
 - a) those who are required to vote or abstain from voting on each research activity considered by the IRB panel when they are present for the discussion and vote.

- b) Alternate Voting Members are those who are required to vote or abstain from voting on each research activity considered by the IRB panel when they are present for the discussion and are substituting for a regular member.
4. Ex-officio Members are those who may be appointed to the IRB depending on the relevance of their office and their expertise and experience. Ex-officio members are not voting members of the IRB

C. Appointment and Reappointment

1. The IRB Chairs, Co-chairs, Vice- Chairs, and members will be appointed by the Vice President for Research for three year terms. They may serve consecutive terms.
2. The IRB Chair must have been a member of the MUSC IRB for at least two years and participated in research as an investigator. The Vice President for Research is responsible for appointing a replacement if a Chair cannot complete the three year term for any reason. The Chairs are familiar with regulatory requirements and ethical considerations related to human research. When appointing an IRB Chair or Vice-Chair the Vice President considers the following factors: academic appointment and position of leadership; experience with IRB and human subjects research protection issues; clinical expertise; willingness to commit the time required; and skills involved in presiding over committee affairs. The competency of the Chairs is supplemented by educational opportunities such as attending the annual national PRIM&R human research protections conference and workshops, participating in MUSC IRB related workshops, and other opportunities as designated in the Quality Improvement Initiatives within the Human Research Protection Program of MUSC HRPP Guide Section 10.3.
3. An IRB Chair or Vice-Chair may be compensated for his/her duties.
4. VA representatives to the IRB are appointed by the Ralph H. Johnson VAMC Medical Center Director at least every three years. The appointment letters are retained by the Research & Development (R&D) committee of the VAMC

D. Resignation

Any member of the IRB may resign through a written resignation submitted to the ORI Director and Chair of that IRB.

E. Suspension or Removal of Members

Any member of the IRB can be removed by the ORI Director or Chair of the IRB for failure to perform functions and responsibilities, provided that such member is given reasonable notice of the grounds for the suspension or removal and an opportunity to be heard.

F. Periodic Review of Membership

The membership shall be reviewed at least annually to determine 1) if the membership continues to include individuals with varying backgrounds, experience and scientific/scholarly expertise needed to review the scope of the research conducted by MUSC and VAMC and 2) if members are able to fulfill the responsibilities of the IRB.

MUSC recognizes that membership on the IRB boards is voluntary and the members provide an essential service to MUSC. With this in mind, it is the intent of MUSC that the reviews of IRB membership serve multiple purposes. In addition to those 2 goals above, the review provides a platform for members to assess their ability to fulfill their responsibilities and identify how MUSC can strengthen the skills and abilities of our members to fulfill their responsibilities.

Annually, each IRB Chair and Vice-Chair will complete a self-evaluation of his/her performance and provide this to the IRB Program Manager. This evaluation covers the following areas: leadership, preparedness, knowledge of regulations and regulation procedures, and identification of areas for improvement. The Director of ORI and the IRB Program Manager will review these self-evaluations and then meet individually with each IRB Chair and Vice-Chair in order to provide performance feedback and evaluation of Board effectiveness. Such feedback and discussion will include Board metrics, attendance, Board composition, member performance, administrative support, and other issues as appropriate. This process will also provide an additional mechanism for the Chair and Vice-Chair to provide input on overall operations and suggestions for continuing education and quality improvement. Each Chair and Vice-Chair will receive a letter summarizing the overall discussion and feedback.

Annually, each Board member will complete a self-evaluation of his/her performance and provide this to the IRB Program Manager. This evaluation covers the following areas: preparedness, knowledge of regulations and regulation procedures, attendance, identification of areas for improvement, and timeliness of receipt of meeting materials. The Director of ORI and the IRB Program Manager will discuss these self-evaluations with the relevant Administrator, Chair, and Vice-Chair from each IRB. Based on these discussions and member self-evaluations, the Director of ORI and IRB Program Manager may schedule meetings with any members if concerns

come to light. This process also provides an additional mechanism for the IRB members to provide input on overall operations and suggestions for continuing education and quality improvement. All members receive a letter summarizing the evaluation, comments, suggestions and feedback.

After completion of each review, the ORI Director will convey in writing to the Vice President for Research a summary of the IRB Membership Review.

G. Liability of IRB Members

IRB members and alternates fulfill their administrative and institutional service responsibilities to the University, in part, by serving on an IRB committee. Accordingly, the University will indemnify IRB members in the event of a legal dispute relating to the actions of the committee, provided that the IRB member has acted in good faith and in accordance with federal requirements, state and local laws and University policy.

H. Membership Records

Information on membership for each IRB panel is maintained by the Office of Research Integrity and includes:

1. Name;
2. Degrees;
3. Status (i.e., physician-scientist, other scientist or non-scientist);
4. Expertise
5. Affiliation with the Medical University of South Carolina or the VAMC, if any, by the member or immediate family member.
6. Contact information
7. Position on IRB
8. Membership status
9. Representative capacity
10. Alternate members and the primary members or class of primary members for whom each alternate member could substitute.

The Office of Research Integrity shall be responsible for updating the membership roster and IRB registration information as needed when membership changes and submitting the updated information to OHRP as required by the Institutions' FWAs. IRB rosters shall be retained a minimum

of five (5) years and shall be made available upon request when applicable to the NIH and FDA for inspection and copying onsite during normal business hours. Individual membership records shall be retained by the Office of Research Integrity a minimum of five (5) years from date of last service.

Curriculum vitae/resumes are on file for all members and alternates.

I. Use of Consultants

The IRB administrator, the IRB chair, and/or any voting member may request that additional expertise be made available to supplement the expertise of the Board members. The decision to use a consultant will be documented on the IRB administrator checklist. The Chair and Director of the IRB are responsible for securing this expertise. The required expertise will be sought among the MUSC faculty if available and without a conflict of interest in accordance with *IRB Member and IRB Consultant Conflict of Interest Policy (Section II.L below)*. If the expertise is not available within the MUSC, external consultants will be secured. The Chair or designee will specify the concerns/questions requiring expert review and will notify the principal investigator that additional expertise has been secured to review the protocol and/or related documents. The IRB Administrator will ensure the expert has all the materials required to review and address the concerns/questions. Depending on the request and need for the additional expertise, the chair will ask the expert(s) to discuss concerns/questions with a Board member, document his/her review, and/or attend the relevant convened Board meeting, but will not be allowed a vote.

J. Member Orientation, Education and Training

1. Orientation

The Office of Research Integrity shall provide new members with the MUSC IRB Governance and Operating Procedures, all IRB policies and relevant Federal and State regulations.

2. Education and Training

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.

Continuing Education and Training

Members are required to take Refresher course 101 of the Collaborative IRB Training Initiative (CITI) program for biomedical or

social and behavioral research every three years. All members shall receive copies of various IRB-related publications and new and updated guidance documents from the FDA, OHRP or other governing agencies. Additional education and training opportunities are available as designated in the HRPP Program Guide Section 10.3 "Quality Improvement Initiatives within the Human Research Protection Program of MUSC".

K. Responsibilities of Members

1. Chair(s) and Co-Chair(s)

The responsibilities of the Chair(s) and Co-Chair(s) include but are not limited to the following:

- a) Preside over convened meetings of the IRB;
- b) Call special meetings when necessary;
- c) Assure appropriate assignment of reviews to IRB reviewers;
- d) Review of exempt or expedited submissions and determination of appropriate review levels;
- e) Review of reported problems and determining whether they are unanticipated problems involving risks to subjects or to others;
- f) Advise investigators and study team members;
- g) Recommend committee members for appointment to the IRB;
- h) Make decisions in emergency situations to protect subjects and remain in compliance with regulations;
- i) Inform IRB and University Officials of developing problems;
- j) Designate Vice-Chair or experienced IRB members to perform expedited review procedures either by permanent assignment or on an ad hoc basis;
- k) Appoint subcommittees of the IRB;
- l) Relate concerns of the IRB staff and members to administration regarding issues in human research review;
- m) Serve as liaisons with the University Committees;
- n) Perform all regulatory duties;

- o) Educate the University community regarding human research protections; and
- p) Maintain a working knowledge of federal human subjects regulations through continued education and training.

2. Vice-Chair(s)

The responsibilities of the Vice-Chair(s) are to:

- a) Preside convened meetings of the IRB in the Chair's absence;
- b) Assist the Chair with review procedures as delegated;
- c) Chair Subcommittees;
- d) Perform all duties of the Chair in the Chair's absence; and
- e) Maintain a working knowledge of federal human subjects regulations through continued education and training.

3. Members

The responsibilities of the Members are to:

- a) Attend meetings and plan to be present for the entire meeting;
- b) Contact the IRB Administrator if unable to review for a meeting and arrange their replacement from the alternate reviewer list;
- c) Examine all review materials in preparation for the convened meeting to which they are assigned;
- d) Contact investigators as necessary to resolve questions and concerns and notify the IRB Administrator of these discussions and outcomes;
- e) Present primary reviewed protocols to the Board as requested;
- f) Advise the IRB Administrator and the Board of any conflict or perceived conflict of interest with any business of the IRB and to refrain from reviewing materials, participating in the discussion and voting when a conflict of interest is identified;
- g) Participate in subcommittee activities;
- h) Protect the confidentiality of all materials provided and all business conducted;

- i) Acquire and maintain a working knowledge of federal human subjects regulations through education and training requirements for IRB members; and,
- j) Act as the Chair's designee as required.

L. IRB Member and IRB Consultant Conflict of Interest Policy

Federal regulations prohibit a member of the institutional review board (IRB) or consultant to the IRB from participating in the initial or continuing review of any project in which the member or consultant has a "conflicting interest," except to provide information at the IRB's request in accordance with 45 CFR 46.107(e)

Definitions for the following terms may be found in HRPP Guide Section 1.3 – Definitions of terms:

- **Conflict of interest in science**
- **Financial conflict of interest**

IRB members complete the **IRB Member Conflict of Interest Statement** annually. At the start of every Board meeting, Board members will be asked to disclose any conflict of interest they may have with the business before the Board. This discussion will be documented in Board meeting minutes and as well as actions taken to minimize the impact of this conflict.

Any Board member who is a member of the research team of a study presented to the IRB for initial review, continuing review and/or modification will leave the Board room during discussion of the study and during the Board members voting process. This includes the roles of principal investigator, co-investigator, mentor and consultant. IRB members with a conflict of interest will not be counted toward quorum during discussion of the conflicted item. This action will be documented in the Board meeting minutes.

IRB Consultants complete the **IRB Consultant Conflict of Interest Statement** upon acceptance of the request for providing consultant services. If, upon review of the **IRB Consultant Conflict of Interest Statement**, the IRB Administrator and/or Chair, an actual or perceived conflict is identified, the consultant will be replaced with an alternate consultant. At the start of the board meeting in which the individual is providing consulting services, the consultant will disclose any conflict of interest they may have with the protocol before the board for which the IRB consultant is providing services.

Individuals who are responsible for business development at the Medical University of South Carolina are prohibited from:

- Serving as members or ex-officio members on the IRB.
- Carrying out day-to-day operations of the review process.



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| Policy Name: Approval of Research Activities by the IRB | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 3 | Section: HRPP 2.4 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

The Institutional Review Boards of MUSC have the responsibilities, Ethical Principles, Authority and Independence as specified in HRPP Guide Section 2.1, function as specified in HRPP Guide Section 2.2 and are comprised of a membership as specified in HRPP Guide Section 2.3.

B. Approval of Research Activities

In order for the IRB to approve research, all of the following requirements below must be satisfied (46.111 and 21 CFR 56.111). These review criteria are used for initial, continuing review, and review of modifications

1. 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.
2. Risks, physical, psychological, social and economic, are reasonable relative to anticipated benefits.
3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
4. Compliance with all requirements (MUSC policies and to the extent required by §46.116 and 21 CFR Part 50) 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.
5. Documentation of informed consent is required, in accordance with, and to the extent required by MUSC policies and §46.117 and 21 CFR 50.27.

6. A Data and Safety Monitoring Plan, when appropriate, is included to assure the safety of the human subjects, and the validity of the data generated.
7. 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.
8. Provisions are adequate to protect the privacy of subjects and maintain confidentiality of the data.
9. Research deemed to be greater than minimal risk will undergo full board IRB review and approval. Research deemed to be minimal risk may be reviewed by the expedited review or may be exempt from IRB approval.
10. When a VA study involves “usual or standard of care,” in the protocol or a separate document in the IRB application the researcher must clearly designate the individual or entity (e.g., the appropriate research personnel versus the subject’s health care provider) responsible for relevant aspects of both the research and the usual care.
11. When following Department of Defense regulations, surveys performed on Department of Defense personnel must be submitted, reviewed, and approved by the Department of Defense after the research protocol is reviewed and approved by the IRB.

In addition, for a study to be approved by the MUSC IRB, the study must be scientifically sound, ethically appropriate and meet the federal regulatory criteria for approval.

C. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good

Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html))

D. Memorandum of Understanding

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

II. PROCEDURES

A. Duration of Approval

1. Unless renewed, a protocol is active for one year. The expiration date, the last day the protocol is approved, is calculated as 365 days after approval. The calculation of the approval period is based on the date of the convened meeting at which the IRB approves the protocol and not on the date when the reviewer approves any requested modifications.
2. For all approved research protocols, including initial reviews, continuing renewals and amendments, the IRB may determine that the research risk is of significant magnitude meriting review more frequently than on an annual basis. Examples of increased risk include sensitive issues (HIV and AIDS), vulnerable populations (school children) and safety (protocol deviations and AEs).

B. Notification of Investigators

Through the eIRB system, the IRB provides the investigator with notification of decisions to approve or disapprove research and of modifications required to secure IRB approval of the research activity; the notification includes rationale for the decision and the investigator is given an opportunity to respond in person or in writing. If the research protocol is approved, the investigator is notified through the eIRB system of the following requirements: 1) only IRB approved copies of consent document(s), questionnaire(s), letter(s), and advertisement(s) may be used; 2) IRB approval must be obtained if any modifications or changes to the protocol and consent document(s) prior to initiation of the proposed changes; 3) reporting requirements for any unanticipated problems experienced; and, 4) expiration date of IRB approval.

C. Notification of the Institution

The MUSC Organizational Officials have access to IRB meeting minutes, as do the VA Associate Chief of Staff for Research and the VA Research and Development Committee.

D. Review and Approval by Other Committees/Departments

The submission will automatically be routed to appropriate departments following HRPP Program Guide Section 1.7.

E. HIPAA Privacy Review

MUSC IRBs are designated by MUSC to review authorization for use and disclosure of protected health information involved in research protocols and to grant waivers of, or alteration to, such authorizations using the standards and procedures specified in the HIPAA Privacy regulations (45 CFR Parts 160, 164 – specifically 45 CFR 164.508 and 164.512).



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|--|-------------|--------------------------|
| Policy Name: Convened Meetings of the IRB | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 9 | Section: HRPP 2.5 |
| Replaces Policy: 05/15/2012 | | |

I. POLICY

A. Introduction

The Institutional Review Boards of MUSC have the responsibilities, Ethical Principles, Authority and Independence as specified in HRPP Guide Section 2.1, functions as specified in HRPP Guide Section 2.2 is comprised of a membership as specified in HRPP Guide Section 2.3 and approves research activities as specified in HRPP Guide Section 2.4.

B. Convened Meetings

The IRBs shall meet regularly with meetings scheduled for the entire calendar year and posted on the IRB website. Members shall be informed of the meeting schedule prior to the end of the previous calendar year. When required, at least one member who is knowledgeable about or experienced in working with identified vulnerable populations or as the prisoner representative will be present. Members must contact the IRB office if they are unable to review for a meeting, and must find their replacement from the alternate list. In consultation with the Chair, the IRB Administrator will assign initial protocols and protocol amendments to primary reviewers, taking into consideration the knowledge of and experience required to review the research. The application, including agenda and materials related to the research is sent electronically through the eIRB to the Primary Review Group between two and three weeks prior to the convened meeting. The meeting agenda is sent electronically through the eIRB to all IRB members (including those to participate via teleconference) the Friday prior to the meeting.

C. Primary Reviewers

Each Primary Review Group includes at least one scientific member and one non-scientific member as well as other reviewer(s). No reviewer will review a study if he/she has a conflict of interest. The IRB Chair, in consultation with the IRB 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 posted in the eIRB system for use by the reviewers. The Administrator will

request Reviewer critiques by a deadline. The primary and secondary reviewers shall perform an in-depth review of all materials provided to them.

D. Members Not Assigned As Reviewers

Through the eIRB system, members who are not assigned as the primary reviewers have access to all components of the study including the Review Application, Human Subject document, and Informed Consent Document(s) and any advertisements for review at the same time that primary reviewer groups receive their assignments.

E. Quorum

The meeting will be called to order when the Chair has confirmed with the IRB Administrator that a Quorum has been achieved. Quorum is documented in the meeting minutes. A quorum of the membership of the IRB, including at least one physician-scientist and at least one member whose primary concerns are in nonscientific areas, must be met before a meeting can be convened. The presence of more than one-half the voting membership plus one shall constitute a *quorum*. Quorum shall be maintained for the discussion and vote on each research activity on the agenda. Members not present for, or recused from, the discussion shall not be counted towards the quorum. If required members (e.g. non-scientific) leave the room, quorum is lost. If quorum is lost during a meeting, the IRB cannot take vote until the quorum is restored. In the event an IRB member must participate by teleconference, the member will log into the eIRB system prior to the meeting and the minutes of the convened IRB meeting will reflect that the member participated by teleconference.

At least one of the VA members has to be present during the review of VA research.

At least one member who represents the general perspective of subjects is present at convened meetings. This is accomplished by requiring the members as part of quorum, as documented in the meeting minutes.

F. Guests

Guests are permitted to attend IRB meetings at the discretion of the IRB Chairperson and will be instructed that meeting discussions are confidential and cannot be disclosed to others.

G. Discussion and Vote

During the Board meeting, each initial study is presented by the Chair and/or Primary Reviewer(s), discussed and voted on individually. The

Principal Investigator will be present if requested by any Board member or if the Chair/Administrator thinks the Investigator needs to be present to clarify issues/concerns. The Board may approve, table, disapprove, or require modifications to secure approval. Members will vote verbally or by a show of hands (depending on the Chair's preference). If the Board requests minor modifications which do not substantially impact the risk/benefit analysis, the Board may approve the study contingent on final review and approval by the Chair or the Chair's Designee. No required changes to the informed consent document will be deferred to the Chair's or Chair's Designee approval unless the Board has stipulated the wording of these changes. Changes that are substantive in nature must be brought back to the full Board at a convened meeting.

H. IRB Meeting Minutes

The Administrator prepares Minutes of the convened meeting, which are approved by the Chair. Minutes show attendance at meetings and actions taken by the Board including frequency of continuing review. Minutes document the vote on all IRB actions including the number voting for, against, recusing and those abstaining.

Specifically, the Minutes shall include:

0. Voting members (or alternates) present; (documented by sign-in sheet)
1. Voting members (or alternates) absent; and (documented by sign-in sheet)
2. Voting members (or alternates) participating via teleconference (videoconferencing not in use at MUSC);
3. Staff and guests, including consultants, present;
4. Action voted by the IRB;
5. Separate deliberation of each action;
6. Unless explicitly stated, research undergoing full board IRB review and approval is deemed to be greater than minimal risk and research undergoing expedited review or deemed exempt from IRB approval is deemed to be minimal risk.
7. The names of IRB members leaving a meeting during discussion of an action due to a conflict of interest and indication that the conflicting interest was the reason for the absence;
8. Number of votes for, against, and abstaining from voting;

9. Members attending but not present for the discussion and vote;
10. Replacement of a primary member by an alternate member;
11. Recusals of voting members;
12. For initial and continuing review, the IRB approval period, i.e., one year or less;
13. Findings and determinations of the IRB required by regulation including, when applicable, waiver or alteration of the consent process, research involving pregnant women, human fetuses and neonates, research involving children, and research involving prisoners;
14. Justification for any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document.
15. The rationale for significant risk/non-significant risk device determinations or the device is exempt from the IDE regulations;
16. Deliberations of non-compliance and stipulated remedial action will include the rationale for determination of the non-compliance to be serious or continuing non-compliance;
17. Summary of the discussion of controversial issues and their resolution;
18. Modification required and/or additional information requested by the IRB;
19. Substantive modifications and/or clarifications relevant to regulatory criteria will be placed on the agenda of the next IRB convened meeting for review and approval or disapproval;
20. Chair or designee approval of research (VA and MUSC), approved in previous IRB meetings pending addressing minor modifications, and,
21. Basis for requiring changes or disapproving the research.

In addition, for VA research, the IRB minutes shall document:

1. the determination of the level of risk,
2. a summary of the justification for including non-veterans as subjects,
3. a summary of the discussion when real social security numbers (SSNs) scrambled SSNs, or the last four digits of SSNs will be used in the study

- summary needs to include the security measures that are in place to protect the SSN instances embedded in the study, and
- 4. documentation of approval in the minutes of the first IRB meeting occurring after the date of the approval.

Minutes shall be available for review by the IRB at the next convened meeting and provided to the VAMC Research and Development Office within three weeks of the meeting date. Upon request, IRB minutes will be provided to Organizational Officials of other institutions who, by appropriate IRB Authorization Agreement, rely on the MUSC for IRB review. Minutes shall be retained by the Office of Research Integrity for at least five (5) years, and shall be available upon request to authorized representatives of DHHS and, when applicable, the NIH and FDA for inspection and copying onsite during normal business hours.

Once approved at an IRB meeting, minutes may not be altered by anyone, including a higher authority.

I. Guidance Material for IRB Members Available On-Line and During IRB Meetings

Appendix A contains the verbiage of posters permanently displayed in the IRB conference room where all convened IRB meetings are held. The information is also on the IRB website <http://academicdepartments.musc.edu/research/ori/irb/>

J. Memorandum of Understanding

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

K. Use of Technology

- a) Laptops – University owned and OCIO maintained laptops will be made available to board members attending a convened meeting in person. Members may also bring their own laptops. Valid Netid and Passwords are required for access from all laptops to MUSC systems (including eIRB and ERMA) and are entered into both Shibboleth gateway to MUSC Secure or MUSC Guest as well as into the eIRB and ERMA systems.
- b) Teleconferencing – board members may teleconference into a convened meeting. While on teleconference, the board member is considered part of quorum.

- c) Projection Systems – IRB Administration will utilize a laptop to projection system setup to display the agenda items under consideration.

The process for obtaining consent must incorporate all of the following:

- The investigator will obtain the legally effective informed consent of the participant or the participant's legally authorized representative.
- Consent will be sought only under circumstances that provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate.
- Consent will be sought only under circumstances that minimize the possibility of coercion or undue influence.
- The information that is given to the participant or the representative shall be in language understandable to the participant or the representative.
- The informed consent does not include any exculpatory language through which the participant or the representative is made to waive or appear to waive any of the participant's legal rights.
- The informed consent does not release or appear to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

Additional Considerations:

- ***For FDA-regulated Research:***
 - A statement that notes the possibility that the Food and Drug Administration may inspect the records.
- ***For research involving more than minimal risk:***
 - An explanation as to whether any compensation is available if injury occurs.
 - If compensation is available, what it consists of, or where further information may be obtained.
 - An explanation as to whether any medical treatments are available if injury occurs.
 - If medical treatments are available if injury occurs, what it consists of, or where further information may be obtained.

Information that must be provided as part of the interaction with the participant *and* in the documentation of the consent process, unless waived or altered:

- A statement that the study involves research.
- An explanation of the purposes of the research.
- The expected duration of the participant's participation.
- A description of the procedures to be followed.
- Identification of any procedures which are experimental.
- A description of any reasonably foreseeable risks or discomforts to the participant.
- A description of any benefits to the participant or to others which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant.
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained
- An explanation of whom to contact for answers to pertinent questions about the research.
- An explanation of whom to contact for answers to pertinent questions about the research participant's rights.
- An explanation of whom to contact in the event of a research-related injury to the participant.
- Contact information for the research team for questions, concerns, or complaints.
- Contact information for someone independent of the research team for problems, concerns, questions, information or input.
- A statement that participation is voluntary.
- A statement that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled.
- A statement that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

Criteria for Approval of Research

Additional Considerations:

- ***For Initial Review:***
 - Should review be obtained more often than annually?
 - If this is a multi-site research study, is the management of information that might be relevant to the protection of participants adequate?

 - ***For Continuing Review:***
 - Should review be obtained more often than annually?
 - Should verification be obtained from sources other than the investigator that no material changes have taken place since prior IRB review?
 - Is the consent document accurate and complete?
 - If information has arisen that might affect the willingness of participants to continue to take part in the research, will it be provided to those participants?

 - ***For Review of Modifications to Previously Approved Research:***
 - If information has arisen that might affect the willingness of participants to continue to take part in the research, will it be provided to those participants?
-

Belmont Report

The unifying ethical principles that form the basis for the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research:

- **respect** for persons: protecting the autonomy of all people and treating them with courtesy and respect and allowing for informed consent;
- **beneficence**: maximizing benefits for the research project while minimizing risks to the research subjects; and
- **justice**: ensuring reasonable, non-exploitative and well-considered procedures are administered fairly (the fair distribution of costs and benefits.)



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|---|-------------|--------------------------|
| Policy Name: Retention of Review Activities Records of the IRB | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 2.6 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

The Institutional Review Boards of MUSC have the responsibilities, Ethical Principles, Authority and Independence as specified in HRPP Guide Section 2.1, functions as specified in HRPP Guide Section 2.2 is comprised of a membership as specified in HRPP Guide Section 2.3, approves research activities as specified in HRPP Guide Section 2.4 in convened meetings as specified in HRPP Guide Section 2.5.

B. Federal Regulations for Retention of IRB Records

HHS regulations (45 CFR 46.115(b)) and FDA Regulations (21 CFR 56.115) require that IRB records be retained for at least 3 years. This includes protocols cancelled without participant enrollment. Research records from the ERMA system are scanned and stored electronically on a secure MUSC server. Access to these records is limited to ORI personnel and other personnel as designed by the Institutional Official.

New studies in the eIRB system remain in the eIRB system which is maintained on a secure server owned by HSSC.

Research records should be retained for a sufficient minimum period to allow evaluation and repetition by others of the results and to investigate an allegation of research misconduct. Usually [unless granted an exception by the Department of Health and Human Services (HHS) or the Office of Research Integrity (ORI)], this minimum period is six years.

C. Department of Veterans Affairs

For VAMC studies, all records, including the investigator’s research records, must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA’s Records Control Schedule (RCS 10-1). If a VA protocol is cancelled without participant enrollment, IRB records are maintained for at least five years after cancellation. The local VA Research and Development Committee will have access to all IRB records related to VA research.

D. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GCP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

E. Memorandum of Understanding

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

F. Inspection of Records

All records must be accessible for inspection and copying by authorized representatives of HHS and FDA at reasonable times and in a reasonable manner. A log of stored paper records is maintained in the IRB office for retrieval if documents are needed for audit purposes.



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| Policy Name: Management of the IRBs | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 2.7 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

Human research protection activities are overseen by the Program Director of the MUSC IRB who reports to the Director of the Office of Research Integrity and the MUSC Associate Provost for Research.

B. Appropriate Number of IRBs

MUSC will maintain an appropriate number of IRBs to accomplish timely and thorough review of MUSC's human subjects research activities. Establishment of IRBs will be based on the volume and types of research activities engaged in by MUSC.

II. PROCEDURES

Each IRB is supported by qualified and dedicated staff possessing the skills required to support the research activities assigned to their Board.

A. IRB Program Director

The IRB Program Director will be appointed by the Director of the Office of Research Integrity. The responsibilities of the Program Director include but are not limited to:

1. Manage the IRB Staff;
2. Ensure there are necessary resources required to perform regulatory functions;
3. Supervise orientation and training of all new members and ensure appropriate continued training is provided to IRB staff and members;
4. Act as the liaison with all University/ Medical Center departments/ divisions;
5. Coordinate with the University Compliance Office, the Office of Research and Sponsored Programs, and the Office of Grants

Accounting regarding compliance on regulations and policies associated with new, continuing, and competing proposals involving human subjects;

6. Provide advice on regulatory compliance to University Officials and Committees;
7. Administer policy on the protection of human subjects and advise on appropriate revisions in policy and procedures;
8. Advise IRB member on review requirements and criteria for approval;
9. Advise investigators and study team members on all matters related to compliance with the protection of human subjects related to IRB requirements; and,
10. Educate the University community regarding human research protections.

B. IRB Administrators

The responsibilities of the IRB Administrators include but are not limited to:

1. Review IRB submissions and keep IRB members aware of current regulations and policies/procedures;
2. Interpret and apply federal and state laws, regulations, policies, and guidelines related to human subjects research;
3. Prepare correspondence on IRB deliberations and contingencies for approval of research activities;
4. Develop and present materials and training materials for IRB members and research teams;
5. Provide orientation and training to new staff members and IRB members;
6. Prepare and distribute Board meeting agenda and attend meetings of the IRB; and,
7. Prepare minutes within the time frame specified.

The competency of all the staff is supplemented by educational opportunities as designated in the HRPP Program Guide Section 10.3

“Quality Improvement Initiatives within the Human Research Protection Program of MUSC.”

C. Review of Resources

During the annual assessment of budgets and fiscal needs, the Director of the Office of Research Integrity and the Associate Provost for Research meet with the Program Director of the MUSC IRB to discuss resource requirements. At that time a formal assessment of the upcoming fiscal year is made. Issues are addressed regarding staffing and financial resources for the support of the IRB chairs, education and training, office operations, and new initiatives.

The volume of materials processed by the IRB is reviewed annually and as required to determine need for additional staffing or changes in procedures to increase efficiency and maintain an adequate level of support for all Boards and human research activities conducted at the University. This allows the Associate Provost for Research to maintain an accurate understanding of the level of work and resource requirements of the IRB and the IRB chairs.



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|--|-------------|-------------------|
| Policy Name: Human and Not Human Research Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 5 | Section: HRPP 3.1 |
| Replaces Policy: Effective 12/01/2009 | | |

I. POLICY

A. Introduction

The IRB must approve any undertaking in which an MUSC faculty, staff, or student (i.e., an employee or agent) conducts non-exempt human research.

B. Statement

This policy statement provides information for determining whether an activity is research involving human participants and covered by the Federal Regulations. In general, any activity that meets either (a) the Department of Health and Human Services (DHHS) definition of both “research” and “human subject” or (b) the Food and Drug Administration (FDA) definitions of both “clinical investigation” and “human subjects” is considered human research and requires review and approval by the MUSC IRB.

Unidentified Cell lines and unidentified tissue specimens are human subjects as defined by FDA when the research involves *in vitro* diagnostic device studies.

C. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

II. DEFINITIONS

As used in this document, human-subjects research encompasses activities that meet the DHHS definitions of *research* and *human subject* and/or the FDA definitions of *clinical investigation* and *human subject*. These definitions are found in HRPP Program Guide Section 1.3 – Definitions of terms.

- A. Clinical Investigation (FDA)
- B. Human Subject (DHHS)
- C. Human Subject (FDA)
- D. Identifiable Information
- E. Interaction
- F. Intervention
- G. Private Information
- H. Research (DHHS)

III. PROCEDURES

- A. It is the responsibility of each investigator to seek IRB approval prior to initiation of any research involving human subjects or conducting any clinical investigation.
- B. It is the responsibility of each investigator to obtain any and all required approvals by mentors, faculty departments and ancillary departments, as appropriate, as detailed in HRPP Program Guide Section 1.7 - “Mentor, Department and Ancillary Reviews”.
- C. The investigator is responsible for making a preliminary decision regarding whether the activities meet either (a) the DHHS definitions of both “research” and “human subjects” or (b) the FDA definitions of both “clinical investigations” and “human subjects”.
- D. Steps and criteria for evaluating an activity to determine whether the activity is human research:
 - 1. **Step 1:** Is the activity “Human Research” according to DHHS regulations?
 - a) **Criterion 1:** The activity is research per 45 CFR 46.101(d) if **either** are true:
 - (1) it is part of a systematic investigation (including research development, testing and evaluation) to test a hypothesis and permit conclusions to be drawn, usually described in a formal protocol that sets forth

an objective and a set of procedures designed to reach that objective; **or**,

- (2) it is designed to (e.g., the primary purpose) contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships, or published in medical journals as research).
- (3) if either (1) or (2) are true, proceed to **Criterion 2**.
- (4) if neither (1) or (2) are true, the activity is not “Human Research” according to DHHS regulations. Proceed to **Step 2** to determine whether the activity is “Human Research” according to FDA regulations.

b) **Criterion 2**: The research involves human participants per 45 CFR 46.101(f) because:

- (1) the investigator will obtain data about living individuals; **and**
- (2) the investigator will obtain this data through intervention or interaction with those participants; **or**
- (3) the information obtained by the investigator is both private information **AND** identifiable information.
- (4) if the statements in **Criterion 2** are true, the activity is human research according to DHHS regulation. Proceed to Step 2 to determine whether the activity is human research according to FDA regulations.
- (5) if the statements in **Criterion 2** are not true, the activity is not human research according to DHHS regulations. Proceed to **Step 2** to determine whether the activity is human research according to FDA regulations.

2. **Step 2**: Is the activity “Human Research” according to FDA regulations?

a) **Criterion 1**: The activity involves an FDA regulated test article because at least one of the following statements are true per 21 CFR 50.3(c) and 21 CFR 56.102(c):

- (1) the activity involves the use of a drug, other than the use of a marketed drug in the course of medical practice; **or**
 - (2) the activity involves the use of a device to evaluate safety or effectiveness of that device; **or**
 - (3) data from the activity will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-regulated product.
 - (4) if any of the above are true, proceed to **Criterion 2**.
 - (5) if none of the above are true, the activity is not Human Research according to FDA regulations.
- b) **Criterion 2**: The activity involving an FDA-regulated test article involves human participants per CFR 50.3(g) and 21 CFR 56.102(e) because at least one of the following statements are true:
- (1) the test article will be used on one or more humans; **or**
 - (2) the data obtained from controls will be submitted to, or held for inspection by the FDA in support of a marketing or research application for an FDA-regulated product; **or**
 - (3) the data obtained from use of a device on tissue specimens will be submitted to, or held for inspection by, the FDA in support of a marketing application or research application for an FDA regulated product.
 - (4) if any of the above are true, the activity is human research according to FDA regulations.
 - (5) if none of the above are true, the activity is not Human Research according to FDA Regulations.
3. **Step 3**: Summary of “Human Research” determinations (DHHS & FDA).
- a) DHHS – If the activity is considered research (Step 1, criterion 1) and involves human participants (Step1, criterion 2), it is considered human research according to DHHS regulations and requires IRB approval.

- b) FDA – If the activity involves an FDA regulated test article (Step 2, criterion 1) and involves human participants (Step2, criterion2), it is considered human research according to FDA regulations and requires IRB approval.
- 4. Investigators proposing activity which is “research” per 45 CFR 46.102(d) but does not involve obtaining information about living individuals per 45 CFR 416.102(f), may request for “Not Human Research” determination by the IRB by completing the “Not Human Research” application in eIRB.

E. Use of Cell Lines Obtained from Commercial Sources

- 1. Federal regulations (45 CFR 46.102(f)) defines a human subject as a living individual about whom an investigator (professional or student) conducting research obtains:
 - a) Data through intervention or interaction with the individual; or
 - b) Identifiable private information.
- 2. Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information to meet the criterion of human subject.
- 3. The Office of Human Research Protections has further clarified that “non-identifiable” material must be submitted to a repository (e.g. ATCC) without any identifiable private data or information. That is, no codes or linkers of any sort may be maintained, either by the submitter or by the repository, that would permit access to identifiable private data or information about the living individual from whom the material was obtained.
- 4. If either of the above criteria [1 a) or 2 b)] is met, then an application for Exempt Status MUST be submitted and approved by the IRB prior to use of the cell line.
- 5. If neither of the above criteria are met, then an application to the IRB is NOT required.

- F.** The Principal Investigator will submit the application for Not Human Research by indicating on the “Human Subjects Research” eIRB SmartForm page the basis for requested determination. The applicable justification will be indicated on the subsequent SmartForm page “Not Human Subjects Research”. The protocol is then uploaded on the following SmartForm page.

IV. REFERENCES

- A.** [OHRP Human Subject Regulations Decision Charts](#) – (Note: These decision charts do not address requirements of other organizations, such as the Food and Drug Administration, National Institutes of Health, other sponsors, or state or local governments.)
1. Chart 1 – Is an Activity Research Involving Human Subjects?
 2. Chart 2 - Is the Human subjects Research Eligible for Exemption?
 3. Chart 3 - Does Exemption 45 CFR 46.101(b)(1)(for Educational Settings) Apply?
 4. Chart 4 – Does Exemption 45 CFR 46.101(b)(2) or (b)(3)(for Tests, Surveys, Interviews, Public Behavior Observation) apply?
 5. Chart 5 – Does Exemption 45 CFR 46.101(b)(4) (for Existing Data, Documents, records and Specimens) apply?
 6. Chart 6 – Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) apply?
 7. Chart 7 – Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) apply?
 8. Chart 8 – May the IRB Review be done by Expedited Procedures?
 9. Chart 9 – May the IRB Continuing Review by done by Expedited Procedures?
 10. Chart 10 – May Informed Consent be Waived or Consent Elements be Altered under 45 CFR 46.116(d)?
 11. Chart 11 – May Documentation of Informed Consent be Waived under 45 CFR 46.117(c)?



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|--|-------------|--------------------------|
| Policy Name: Exempt Research Review Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 6 | Section: HRPP 3.2 |
| Replaces Policy: Effective 09/15/2016 | | |

I. POLICY

A. Introduction

MUSC has designated the MUSC IRB as the reviewer for the determination of “exemption” from the requirements for continued IRB review and monitoring. The determinations of exemption may be made by IRB administrative staff knowledgeable about this area of federal regulation, the IRB Chair or Vice Chair, or an IRB member. The IRB may not create new categories of exempt research.

B. Responsibilities of IRB Reviewer in Reviewing Exempt Research

1. Reviewers of exempt research are subject to the HRPP Program Guide Section 1.6 “IRB Governance and Operations Policy and Procedures” Subsection 4.11 *IRB Member Conflict of Interest Policy*.
2. No exempt research may proceed without written IRB approval.
3. While the Principal Investigator may request a particular category of exemption, the final determination will be made by the IRB administrative staff, the IRB Chair or Vice Chair, or an IRB member.

C. Regulatory Criteria for Exempt Research

1. The regulations found at 45 CFR 46.101(b) and 21 CFR 50.104 provide the criteria for studies that may be exempt from IRB review and approval.
2. Regardless of the exempt status, the MUSC IRB requires that any research involving human subjects be conducted in an ethical manner with scientific rigor and respect for subjects.
3. The conduct of exempt research is subject to all applicable MUSC policies, IRB policies, and appropriate federal and state laws and applicable Health Insurance Portability and Accountability Act (HIPAA) regulations.
4. When reviewing exempt research applications, IRB reviewers will give special consideration to research that may raise ethical

consideration and evaluate whether the research upholds MUSC's ethical standards. When conducting such reviews, issues such as the level of risk, the equitable selection of subjects and provisions to maintain the privacy interests of participants and confidentiality of the data must also be adequately addressed. If there are interactions with participants, the IRB should determine whether there should be a consent process that will disclose such information as the activity involves research, a description of the procedures, the participation is voluntary and the name and contact information for the researcher.

5. The Principal Investigator is responsible for assuring that the research is carried out in an ethical manner that includes appropriate subject protections.
6. A new application must be submitted before a Principal Investigator can proceed with any modifications to an exempt research study. Certain changes may disqualify the research from exempt status; therefore, Principal Investigators should consult with the IRB whenever questions arise about whether planned changes to an exempt study may change the required level of IRB review.
7. Exempt studies are expired by the IRB five years after the initial date of approval. The Principal Investigator must submit a new application to extend the study.

D. Memorandum of Understanding

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. DETERMINATION OF EXEMPTION AND REVIEW PROCEDURES

A. HHS Exempt Research Categories (45 CFR 46.101(b))

Unless otherwise required by department or agency heads, HHS Regulatory Provisions allow exemption from federal policy for the protection of human subjects when the only involvement of human subjects falls within one or more of the categories below:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special educational strategies, or (ii) research on the effectiveness of or the comparison among

instructional techniques, curricula or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observations of public behavior; unless: (i) information is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability or reputation. (The Department of Veterans Affairs (VA) also includes loss of insurability in this category.)

The only research activities involving children that may fall under this exemption are those involving educational tests or observation of public behavior where the Principal Investigators do not participate in the activity being observed.

To be exempt, these activities must also meet the condition that the data are recorded without individual identifiers, or the condition that disclosure of the recorded responses would not place the subjects at risk of criminal or civil liability or be damaging to their financial standing, employability, or reputation.

3. Research not exempt under 2 above may be exempt if: (i) the human subjects are elected or appointed public official or candidates for public office; or (ii) federal statute(s) require(s) with exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter (e.g., Department of Justice or National Center for Educational Statistics).
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 Principal Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. To qualify for this exemption, the data, documents, records or specimens must be in existence before the project begins.
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: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to

those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

DHHS Guidance for this category of exempt research stipulates:

- a) The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
 - b) The research or demonstration project must be conducted pursuant to specific federal statutory authority.
 - c) There must be no statutory requirements that the project be reviewed by an IRB
 - d) The project must not involve significant physical invasions or intrusions upon the privacy of participants.
 - e) The exemption should have authorization or concurrence by the funding agency.
6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level 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.

NOTE: None of the exemption categories in the HHS regulations for research involving human subjects apply to research involving prisoners.

B. FDA Exempt Research (21 CFR 56.104)

The FDA provides only three types of exemption:

1. Research started before July 27, 1981, and either did not require FDA approval before that date, or, was subject to requirements for IRB review prior to that date, and remains subject to review by and IRB which meets FDA requirements.
2. Emergency use of a test article, provide any such use is reported to the IRB within five (5) working days and any future use of the test article at the institution is subject to IRB review.

3. The taste and food quality evaluation provided in category six of the HHS regulations.

NOTE: For VA- Regulated Research: Human subjects research cannot be qualified as exempt under this policy if any disclosure of the participant's responses outside of the research could reasonably place the participants at risk of loss of insurability.

III. PROCEDURES

- A. The Principal Investigator identifies the exemption category and submits supporting data as appropriate.
- B. The IRB administrative staff, IRB Chair, Vice Chair or IRB member will conduct a review of the project to determine if it qualifies for exempt status according to IRB policy and human subjects research regulations. Request for revisions and/or clarifications will be entered electronically along with the study team responses.
- C. If there are no questions/concerns, or if responses are satisfactory, and the research as described on the application fits the exempt criteria, the Reviewer will electronically approve the application and the approval letter will be generated.
- D. If the reviewer makes the decision that the research does not fit the exempt criteria, then the IRB staff will notify the study staff that exempt status has not been approved. The study staff will be provided with the rationale for this decision and of the need to submit the research study for expedited or full board review.
- E. The applications submitted for exempt consideration are evaluated based upon the DHHS and FDA criteria for exempt research determinations in subsection 3.
- F. At each meeting, minutes of the previous meeting are available to all IRB members. Exemption determinations are included in the "Report of Expedited, Exempt, Acknowledged Items" of the minutes.

IV. REFERENCES

- A. [HHS Exempt Research Categories \(46.106\(b\)\)](#)
- B. [FDA Exempt Research \(21 CFR Part 56.104\)](#)



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|---|-------------|-------------------|
| Policy Name: Expedited Review of Research Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 5 | Section: HRPP 3.3 |
| Replaces Policy: Effective 09/15/2015 | | |

I. POLICY

A. Introduction

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 and 21 CFR 56.110. The review will normally be performed by the Chair, Vice-Chair or IRB member with extensive service on the IRB. If necessitated by unique circumstances in the area of research under consideration (i.e., vulnerable population or novel procedures), the reviewer may solicit input from another IRB member with relevant experience. When reviewing non-exempt human-subjects research and clinical investigations using the expedited review procedure, the reviewer(s) are subject to *IRB Member Conflict of Interest Policy* detailed in **HRPP Guide Section 2.3 Membership of the IRB**.

B. Limitations to the Use of Expedited Review

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.

C. IRB Approval Process

The Chair or designee may approve a protocol meeting the requirements of expedited review (documented by completion of the Expedited Review Form) but may not disapprove a protocol meeting these requirements. Any protocol submitted that should be considered for disapproval will be sent to a meeting of the convened IRB for consideration.

D. Reporting of IRB Approval

Protocols approved by the expedited process will be reported to the full board at a convened meeting. Any board member may request further consideration of any protocol approved by the expedited process

II. DEFINITIONS

As used in this document, human-subjects research encompasses activities that meet the DHHS definitions of *research* and *human subject* and/or the FDA definitions of *clinical investigation* and *human subject*. These definitions are found in HRPP Program Guide Section 1.3 – Definitions of terms.

- A. Research (DHHS)
- B. Human Subject (DHHS)
- C. Clinical Investigation (FDA)
- D. Human Subject (FDA)
- E. Minimal Risk

III. APPLICABILITY TO CONSIDER EXPEDITED REVIEW

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 (45 CFR 46.110; 21 CFR 56.110):

IV. CATEGORIES OF RESEARCH THAT MAY BE REVIEWED BY THE IRB THROUGH AN EXPEDITED REVIEW (45 CFR 46.111)

1. Clinical studies of drugs and medical devices only when condition (1) or (2) 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 (1) an investigational device exemption application (21 CFR Part 812) is not required; or (2) 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, non-pregnant 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: Hair and nail clippings in a nondisfiguring manner; deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; permanent teeth if routine patient care indicates a need for extraction; excreta and external secretions (including sweat); uncannulated saliva collected either in an unstimulated fashion; placenta removed at delivery; amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; 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; mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; 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: 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: weighing or testing sensory acuity; magnetic resonance imaging; electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, eletroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; 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 DHHS regulations for the protection of human subjects 45 CFR46.101 (b) (2) and (b) (3). This listing refers only to research that is not exempt.)

V. PROCEDURES

A. Initial Determination for Expedited Review

1. The Principal Investigator submits the protocol indicating request for review using the Expedited Procedure, indicates the review Category(s) and submits supporting data as appropriate.
2. When the IRB receives an application that is prepared in such a way that the proposed research procedures are unclear or large components of the application are missing, reviewers will be unable to provide meaningful comments and guidance. In such cases, the application will be returned to the PI with the status of Not Ready for Review, and recommendations for additional resources and guidance will be provided to the PI.
3. 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, the PI/ study communication coordinator leads in eIRB. is notified that that IRB approval of the study will not be released until documentation that all study personnel have completed required education is received in the IRB office.
4. The IRB Chair or designee will conduct a review of the project to determine if it qualifies for review using the expedited procedure according to IRB policy and human subjects research regulations. Request for revisions and/or clarifications will be entered electronically along with the study team responses. The Chair or designee will complete the IRB Reviewer Checklist for Expedited Initial Application and electronically submit this document along with review notes and decisions.

5. If there are no question/concerns, or if responses are satisfactory, and the research as described on the application fits criteria for review by the expedited process, the Reviewer will electronically approve the application and the approval letter will be generated.
6. If the reviewer makes the decision that the research does not fit the criteria for review by the expedited procedure, then the IRB staff will notify the study staff that the protocol does not meet criteria for review by the expedited procedure. The study staff will be provided with the rationale for this decision and of the need to submit the research study for full board review.
7. The applications submitted for review by the expedited procedure are evaluated based upon the DHHS and FDA criteria for expedited review research determinations in 45 CFR 46.110 et al, 21 CFR 56.110 et al and accompanying guidance documents.
8. At each meeting, minutes of the previous meeting are available to all IRB members. Expedited determinations are included in the "Report of Expedited, Exempt, Acknowledged Items" of the minutes.

VI. MATERIAL PROVIDED TO THE REVIEWER

- A. IRB Application and the Principal Investigator Statement of Assurance
- B. Informed Consent or Waiver of Informed Consent
- C. Protocol
- D. HIPAA Authorization or HIPAA Waiver of Authorization (if applicable)
- E. Budget
- F. Advertisements (if applicable)
- G. Questionnaires and Surveys (if applicable)
- H. Conflict of Interest Disclosure (if applicable)

VII. CHECKLISTS

- A. IRB Reviewer Checklist for Expedited Initial Application
- B. IRB Reviewer Checklist Informed Consent
- C. Special Subject Populations Checklist if applicable
 1. Children
 2. Cognitively Impaired or Persons Unable to Consent
 3. Pregnant Women, Fetuses, Neonates
 4. Prisoners
- D. If applicable, checklist addenda for
 1. Department of Defense,
 2. Department of Education,
 3. Department of Energy,
 4. Department of Justice,

5. Environmental Protection Agency

VIII. REFERENCES

- A. [Office for Human Research Protections \(OHRP\) - Expedited Review Categories](http://www.hhs.gov/ohrp/policy/expedited98.html) <http://www.hhs.gov/ohrp/policy/expedited98.html>
- B. FDA Expedited Review Categories – <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm119074.htm>



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|---|-------------|-------------------------|
| Policy Name: Full Board Initial Review Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 6 | Section: HRPP3.4 |
| Replaces Policy: 01/28/2016 | | |

I. POLICY

A. No human research will be initiated without prospective IRB review and approval.

B. Required Elements

The protocol submitted to the IRB must include all elements from the MUSC protocol template. The protocol format is:

1. Objectives/specific aims,
2. Background,
3. Intervention to be studied (if applicable),
4. Study Endpoints (if applicable),
5. Inclusion and Exclusion Criteria/ Study Population,
6. Number of Subjects,
7. Setting,
8. Recruitment Methods,
9. Consent Process
10. Study Design / Methods
11. Specimen Collection and Banking (if applicable)
12. Data Management
13. Provisions to Monitor the Data to Ensure the Safety of Subjects (if applicable)
14. Withdrawal of Subjects (if applicable)
15. Risks to Subjects
16. Potential Benefits to Subjects of Others
17. Sharing of Results with Subjects
18. Drugs or Devices (if applicable)

C. FDA Regulated Products

All studies involving FDA regulated products will be reviewed and approved in accordance with FDA regulations.

D. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H.

Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards”.

II. PROCEDURES

A. Submission by the Principal Investigator

The Principal Investigator submits the protocol for “Full IRB Review”, ensures relevant information (including Conflict of Interest) has been completed and documentation appropriate to the study has been uploaded. In performing this submission, the Principal Investigator electronically signs the Principal Statement of Assurance Form.

B. The submission will automatically be routed to appropriate departments following HRPP Program Guide 1.7.

C. Processing by IRB Administration

1. Upon receipt of an application, the application is checked by the IRB staff for completeness. If additional items are necessary to complete the submission, the IRB staff will note the items and return the study to the Principal Investigator/study communication coordinator leads in eIRB.
2. When the IRB receives an application that is prepared in such a way that the proposed research procedures are unclear or large components of the application are missing, reviewers will be unable to provide meaningful comments and guidance. In such cases, the application will be returned to the PI with the status of Not Ready for Review, and recommendations for additional resources and guidance will be provided to the PI.
3. 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, the PI/ study communication coordinator leads in eIRB. is notified that that IRB approval of the study will not be released until documentation that all study personnel have completed required education is received in the IRB office.
4. The IRB Administrator administratively reviews the eIRB application for regulatory compliance and adherence to established guidelines.

D. Assignment of Reviewer

1. The IRB Administrator will assign initial protocols to primary reviewers.

- a) Each Primary Review Group will include someone with the relevant expertise and knowledge is included to conduct an in depth review.
 - b) No Board member who may have a conflict of interest is assigned to a study as primary reviewer.
2. If an IRB member notifies the Administrator that he/she does not feel competent to review a protocol/amendment assigned, the material will be reassigned.
 3. The IRB Administrator will ensure the prisoner representative is a primary reviewer for any initial protocols involving prisoners and is a reviewer for any amendments and continuation applications for protocols involving prisoners; the prisoner representative will be a voting member of the convened meeting where these documents are discussed

E. Use of Non-IRB Members with Expertise

1. The IRB Administrator, chair, and/or any voting member may request additional expertise when reviewing a protocol.
2. The chair or designee will contact an individual with the expertise requested.
3. The required expertise will be sought among the MUSC faculty if available and without a conflict of interest.
4. The chair or designee will indicate the concerns/questions requiring expert review.
5. The IRB Administrator will ensure the expert has all the materials required to review and address the concerns/questions.
6. Depending on the request and need for the additional expertise, the chair will ask the expert(s) to discuss concerns/questions with a Board member, document his/her review, and/or attend the relevant convened Board meeting.

F. Review Material for IRB Members

1. The complete application is available to all IRB members through the eIRB system. The IRB Administrator will select the primary reviewers and upload the appropriate IRB reviewers' checklists. The eIRB system will send a review request to the primary reviewers containing a link to the protocol in the eIRB system. The application consists of the following items when applicable to the study:

- a) Study Application Smartfoms,
 - b) Study protocol,
 - c) Investigator drug brochures,
 - d) The consent documents or waivers of consent documents,
 - e) HIPAA or HIPAA waiver document,
 - f) Advertisements,
 - g) Questionnaires and Surveys,
 - h) Conflict of Interest Disclosure, and
 - i) Drug and/or Device smartforms.
2. The checklists received by the primary reviewers for assessment to ensure consistency and completeness are (as appropriate to the specific study):
- a) IRB Reviewer Checklist (Full Board Review)
 - b) Informed Consent Document Checklist
 - c) Special Subject Populations Checklist if applicable
 - (1) Children
 - (2) Cognitively Impaired or Persons Unable to Consent
 - (3) Pregnant Women, Fetuses, Neonates
 - (4) Prisoners
 - (5) If applicable, checklist addenda for Department of Defense, Department of Education, Department of Energy, Department of Justice, Environmental Protection Agency.
3. The IRB Administrator sends the agenda to selected IRB members. IRB members receive an email to link to the agenda of the protocols under initial review for the scheduled meeting.
4. The application submission is generally assigned 3 weeks prior to the next scheduled Board meeting.

G. Review Criteria - The primary reviewers are assigned to assess the following:

- 1. risks to the subjects have been minimized by using sound research design, and, whenever appropriate, using procedures already being performed on the subject for diagnostic or treatment purposes,
- 2. risks, including physical, psychological, social and economic risks, are reasonable relative to anticipated benefits,
- 3. selection of subjects is equitable,
- 4. the informed consent process and document are in compliance with MUSC policies and federal regulations,
- 5. provisions are adequate to protect the privacy of subjects and confidentiality of data,
- 6. 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, and
7. the recommended frequency of continuing review.

H. Documentation of Primary Review

1. Using the designated review procedure, the primary reviewer enters reviewer comments.
2. The Administrator requests the reviewers' critiques by a stated deadline.
3. The primary reviewers finalize their reviews by categorizing their recommendation as approval, conditional approval, or disapproval and summarize the suggested modifications that may be required for the study to achieve an acceptable benefit/risk ratio.
4. The IRB staff summarizes the reviewers' comments and discusses these comments with the reviewers and IRB Chair as necessary for clarification.

I. Communication between IRB Administration and PI prior to meeting

1. The IRB staff sends all comments to the study communication leads electronically. A date of when their response is due is given based on when the comments were received.
2. The IRB Administrator checks the study team's response and marks the changes to correspond with the comments and uploads the response with the agenda for the Board's review.
3. The IRB Chair reviews the Principal Investigator's response and seeks additional information from reviewers and/or the Principal Investigator when necessary to clarify issues/concerns.
4. Principal Investigator responses that come in after the agenda has been sent out will be reviewed by the Chair when possible to determine if additional information would be useful; all complete investigator responses will be presented to the Board at the meeting.

J. Convened IRB

1. During the Board meeting, each initial study is presented by the Chair and/or Primary Reviewer(s), discussed and voted on individually. The Principal Investigator will be present if requested by any Board member or if the Chair/Administrator thinks the Investigator needs to be present to clarify issues/concerns.

2. The Board may approve, table, disapprove, or require modifications to secure approval. If the Board requests minor modifications which do not substantially impact the risk/benefit analysis, the Board may approve the study contingent on final review and approval by the Chair or the Chair's Designee. No required changes to the informed consent document will be deferred to the Chair's or Chair's Designee approval unless the Board has stipulated the wording of these changes. Changes that are substantive in nature must be brought back to the Full Board at a convened meeting.

K. Communication between the Institutional Review Board and the Office of Research and Sponsored Programs

If the study is sponsored by a Corporate or Industry sponsor, the Approval form and Informed Consent are reviewed by the Office of Research and Sponsored Programs. ORSP will review the approved consent sponsor commitment language against the sponsor/MUSC contract and notify the Administrator by email once the contract negotiations are complete and the study can be released

L. Post-IRB Communication with the PI

1. For approved studies, the IRB administrator completes the following activities:
 - a) The informed consent(s) is/are electronically stamped with the approval date.
 - b) The HIPAA Authorization and advertisements are electronically stamped with the approval date.
 - c) An approval letter is prepared. This letter includes the following: **Electronic Signature:** *This document has been electronically signed by the IRB Chairman through the HSSC eIRB Submission System authorizing IRB approval for this study as described in this letter.*
 - d) The approval is electronically issued in the system.
2. For studies requiring modification, the IRB administrator completes the following activities:
 - a) The IRB reviewers' comments and requirements are summarized.
 - b) A letter from the Chair or Chair's Designee notifying the PI/study team that the IRB requires changes to the study is prepared.
 - c) The letter is sent to all study communication leads.

3. If the Board Tables the study, the IRB Administrator completes the following activities:
 - a) The IRB reviewer's comments and requirements are summarized
 - b) A letter from the Chair or Chair's Designee notifying the PI/Study team that the IRB has tabled the study is prepared.
 - c) The letter is sent to all study communication leads.
 - d) The PI may be invited to attend the next meeting.
4. If the Board disapproves the study, the IRB Administrator completes the following activities:
 - a) The IRB reviewers' comments and requirements are summarized.
 - b) A letter from the Chair or Chair's Designee notifying the PI/study team that the IRB has disapproved the study is prepared.
 - c) The letter is sent to all study communication leads.
5. For changes submitted by the study team in response to IRB request:
 - a) If the study modifications are minor in nature, the IRB Administrator will forward to the Chair or the Chair's designee for review.
 - (1) If the Chair finds the modifications acceptable, the Chair will indicate approval and the IRB Administrator will complete the steps in **L.1** above.
 - (2) If the Chair determines additional modification are necessary, the Chair will indicate changes required and the IRB Administrator will complete the steps in **L.2** above.
 - b) Study Team responses to substantive modifications due to being tabled or disapproval are presented to the Full Board for review, discussion and vote at a convened meeting.
6. If a study has been disapproved and 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. The Principal Investigator will be notified of the date, time and place of the meeting.

M. Duration of Approval

1. Unless renewed, a protocol is active for one year. The expiration date, the last day the protocol is approved, is calculated as no more than 365 days after approval. The calculation of the approval period is based on the date of the convened meeting at which the IRB approves the protocol and not on the date when the reviewer approves any requested modifications.
2. For all approved research protocols, the IRB may determine that the research risk is of significant magnitude meriting review more frequently than on an annual basis.



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| Policy Name: Continuing Review Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 6 | Section: HRPP 3.5 |
| Replaces Policy: 09/15/2016 | | |

I. POLICY

A. Introduction

Full Board review and approval is required for studies that initially went through review at a convened meeting of the IRB. Continuing review of ongoing research may be expedited when the initial review of the protocol qualified for expedited review, as well as the following:

1. (Expedited Category 8) (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
2. (Expedited Category 9) Unless the IRB or sponsor required full review: continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories 2 through 8 of the expedited review categories do not apply and 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.

B. IRB Continuing Review

The IRB will conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. The same criteria used for initial review of protocols will be followed during protocol renewal review. This evaluation will include subject accrual and current status of all study participants, any study revisions (amendments) that have been approved by the IRB since the last review, any unanticipated problems, any subject complaints, any conflicts of interest, and any new information or findings relating to the risk/benefit assessment. The informed consent process or document also be reviewed to determine if it is still acceptable or whether new information needs to be included as a result of the information provided to the IRB at the time the Continuing Review.

C. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

D. VA Studies

Continuing review of research that are VA studies will address requirements of VHA 1200.05.

II. PROCEDURES

A. Notification to Principal Investigator

At 60 and 45 days prior to the protocol's expiration date, a reminder of approval expiration will be sent to the Principal Investigator and/ or study contact person.

B. Submission Deadlines

Full Board Studies: A completed continuing review must be received by the IRB one month prior to the date at which it needs to be reviewed.

Expedited Studies: A completed continuing review must be received by the IRB one month prior to the expiration of the study.

C. Regulatory Compliance Review

1. IRB Administration

a) When received, the continuation application is assigned to the appropriate IRB staff member who:

(1) Documents receipt of the application

(2) Reviews the application for completeness, accuracy, regulatory compliance and congruency with previous applications. If the application is incomplete or if it is noted that there are some discrepancies with what has been reported in the past, the IRB staff will contact the study coordinator regarding the deficiencies.

Incomplete or incorrect applications may need to be returned electronically to the study contact for editing.

- b) Study personnel listed on the application are checked against the Compliance Office database to ensure that the required institutional training has been completed. The IRB will notify Principal Investigator in writing that continuation approval will not be released until documentation is received by the IRB that the training has been completed.
- c) Once the administrative review is complete, the application is sent to the Primary Reviewer (IRB Chair/Vice-Chair) for review. The IRB Reviewer Checklist for Continuing Review Full Board and expedited Protocols is sent to the primary reviewer for reference in completing the review.

D. Review by the Primary Reviewer (Chair/Vice-Chair)

- 1. The Primary Reviewer will review the entire application, including the following, as applicable:
 - a) The initial application and previous continuing review applications,
 - b) Study protocol,
 - c) A summary of all adverse events reports,
 - d) Data safety monitoring reports,
 - e) Investigator drug brochures,
 - f) The current consent document(s), and
 - g) Any conflict of interest disclosures.
- 2. Any questions or concerns of the Primary Reviewer are summarized and submitted electronically to the study team.
- 3. The Primary Reviewer will review the PI response, which will be prepared by IRB staff for review with the continuing review application at the meeting. If the primary reviewer is unable to resolve issues with the study team, the Principal Investigator may be invited to attend the Board meeting.

E. Materials Provided to the convened IRB

The Continuing Review Application and any additional documents submitted by the study team in support of the renewal application are sent to all members of the board prior to the meeting, and are presented for review and discussion during the meeting.

F. Convened IRB

1. The continuation application submitted by the Principal Investigator and reviewed by the primary reviewer is included in the agenda distribution. The entire study protocol and minutes from the meeting at which the protocol was reviewed initially are available to all members upon request.
2. During the meeting, each continuation application is presented by the chair and/or primary reviewer(s), discussed and voted on individually. The chair and/or primary reviewer will present additional pertinent information regarding the studies applying for continuation such as recent published events. The Principal Investigator will be present if requested by any Board member or if any issues from the review remain unresolved or require clarification.
3. The Board may approve the continuing review. They may also request an independent audit of the study, require additional information regarding any of the Principal Investigator's responses on the application, and/or require substantive changes to the protocol. If there are concerns that have not been addressed, the Board may approve the study for a period less than one year, and have the modifications come back to an upcoming convened meeting. The PI can also be contacted by telephone during the meeting to answer any questions. If approved, the Board will stipulate the frequency of future continuation review. The Board may also suspend or terminate a study if there are serious concerns about the safety of subjects or noncompliance.
4. If the Board needs clarification on something that does not substantially impact the risk/benefit ratio, the Board may approve the continuation contingent on final review and approval by the Chair or the Chair's Designee. No required changes to the informed consent document will be deferred to the Chair's or Chair's Designee for approval unless the Board has stipulated the wording of these changes.

G. Post-IRB Meeting

1. If the continuation is approved without substantive changes, the IRB staff will prepare the approval for release and send documentation of approval to the study team.
2. If the continuation application requires further modifications that are minor in nature, IRB staff will notify the study staff in writing. When revisions are received, the IRB Chair will review them. If acceptable, the approval will be released.

3. If the Board suspends or terminates the study, the Chair will notify the Principal Investigator in writing that the continuation of the study has not been approved and to stop all research related activities including new enrollment, unless currently enrolled subjects will be placed at risk. This action by the Board will be reported to the appropriate agencies including FDA and OHRP, as applicable. The Vice President for Research and the Department Chair will be copied on the correspondence. The Board will work with the Principal Investigator on an appropriate plan in the event that stopping research-related activities will place the currently enrolled subjects at risk.

H. Expedited Continuing Review

The IRB Reviewer completes the Continuing Review Full Board and Expedited Review Protocols Reviewer's Checklist and electronically submits these documents along with review notes and decision upon completion of the review.

I. Reporting of IRB Approval

Continuing Reviews approved by the expedited process will be reported to the full IRB board at a convened meeting. Any board member may request further consideration of any protocol approved by the expedited process.

J. Expiration of IRB Approval

If the continuation application is not submitted prior the IRB deadline date or does not address the IRB's concerns, IRB approval of the study may expire.

1. IRB staff will send written notification to the Principal Investigator (Letter of Expiration) informing the Principal Investigator that the IRB approval has expired and all research activities must stop, including recruitment, advertisement, screening, enrollment, consent, intervention, interactions, and collection of private identifiable information. The Department Chair will be copied on this correspondence.
2. Interventions and interactions on current participants may continue only when the IRB, the IRB Chair or designee finds an overriding safety concern or ethical issue involved such that it is in the best interests of individual participants.
3. The Principal Investigator is requested to sign the letter indicating receipt of notification of approval expiration. If the Principal Investigator wishes to continue the study, he/she must submit a continuation application for review at the next convened meeting.

K. VA Protocols

1. **Continuing Review Information Provided by PI** - In addition to the above information, the continuing review will include
 - a) The number of participants considered as members of specific vulnerable populations and
 - b) An assurance that all serious adverse events and unexpected adverse events have been reported as required.
2. **Expiration of IRB Approval** - If an investigator does not provide continuing review information to the IRB or the IRB has not approved a protocol by the expiration date:
 - a) The IRB notifies the investigator to submit immediately to the IRB chair, a list of research participants for whom stopping research activities will cause harm.
 - b) The IRB Chair must determine within two business days whether or not interventions or interactions on current participants may continue This determination by the IRB Chair is made with appropriate consultation with the local VA Chief of Staff.

III. CHECKLISTS

- A. IRB Reviewer Checklist for Continuing Review Full Board and Expedited Protocols

IV. REFERENCES

- A. [45 CFR 46.109 \(e\)](#)
- B. [21 CFR 56.108 \(a\)\(1\)](#)
- C. [21 CFR 56.109 \(f\)](#)
- D. [Office for Human Research Protections \(OHRP\) – Expedited Review Categories](#)
- E. [FDA Expedited Review Categories](#)



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|--|-------------|--------------------------|
| Policy Name: Modifications to Approved Research Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 7 | Section: HRPP 3.6 |
| Replaces Policy: 05/30/2014 | | |

I. BACKGROUND

IRB review is an ongoing process. Federal regulations require that IRBs have written procedures for ensuring prompt reporting to the IRB of any changes in approved research and for ensuring that such changes are not implemented without prior IRB approval, except when necessary to eliminate apparent immediate hazards to subjects. The IRB must be notified immediately of any changes made to protect subjects' immediate safety.

II. POLICY

- A. All changes to currently approved research must be approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the human subjects.
- B. Minor changes to currently approved research may be reviewed by expedited review procedures. Examples of amendments that may be considered minor include advertisements, personnel changes and other, low risk changes. Additionally, changes to protocols that have previously been reviewed under the expedited review procedures may be reviewed under the expedited review procedures as long as these changes do not increase the risk level of the study.
- C. The criteria for approval of changes to previously approved research are the same as those for initial review. The IRB must determine that, in light of the proposed changes, the research continues to satisfy 45 CFR 46.111 and/or 21 CFR 56.111, as applicable.

III. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

IV. PROCEDURES

- A. Submitting a Modification to the IRB for Review

1. All proposed modifications to study submissions must be submitted via the amendment process in the appropriate electronic system (either eIRB or ERMA) prior to instituting the change.
2. Examples of modifications that must be submitted include, but are not limited to, changes in:
 - a) Study Personnel
 - b) Enrollment numbers
 - c) Duration of study
 - d) Recruitment methods
 - e) Consent form
 - f) Investigator Brochure or device information
 - g) Study design, methods, procedures, or randomization
 - h) Adding or dropping an arm of the study
 - i) Questionnaires, surveys, interview scripts, advertising
 - j) Funding
 - k) Data and Safety Monitoring plan
3. Investigators must provide the IRB with complete descriptions of the modifications, including the rationale(s) for the modifications and the anticipated impact upon current and future subjects, as well as revised versions of those study materials affected by the modifications. This could include modifications to the protocol, informed consent, HIPAA authorizations and eIRB/ERMA application as applicable. The Principal Investigator electronically submits requests for modifications. Changes in any document must be clearly marked in this submission and the appropriate associated paperwork uploaded with the submitted amendment.

B. Initial Review and Level of Review

1. Upon receipt of a modification request, IRB staff and/or a Chair will pre-review the submission to determine the appropriate level of IRB review required.
 - a) Modifications containing minor changes in previously approved research may be forwarded to the Chair or his/her designee for consideration under the expedited review

procedures. The Chair has discretion to forward such changes to the full board for review if appropriate.

b) Modifications that represent more than a minor change will be forwarded to the full board for review. PI's should review the meeting deadlines prior to submitting a full board amendment. Modifications to research initially eligible for expedited review may be reviewed using expedited procedures. However, modifications that render a research study ineligible for expedited review under the applicable regulatory categories will be reviewed by the full board.

c) Some modifications, such as study staff changes (other than the PI) or fixing typos or formatting errors in study documents, are not considered changes in the research. They still must be submitted through the eIRB/ERMA for administrative purposes, but may be approved administratively by designated IRB staff. The following are considered administrative changes which can be approvable by designated IRB staff:

- (1) deletion of study staff
- (2) Addition of study staff other than principal investigators
- (3) Change in contact information (ERMA only)
- (4) Title change that does not reflect a change in the study
- (5) Corrections of typographical errors/reformatting of unchanged text
- (6) Errors in the eIRB smartforms as confirmed by the study team and IRB staff

2. All modifications will undergo initial evaluation by MUSC IRB staff to make sure the submission is complete and correct and the changes are consistent with the applicable administrative and regulatory requirements.

3. The convened IRB, or the IRB Chair/designee using expedited review procedures, will determine whether the research, in light of the proposed changes, continues to satisfy the applicable criteria for approval. This includes determining whether the proposed changes reflect new information that may relate to a subject's willingness to continue participation, thus warranting re-consent or notification of subjects.

4. Approval of a modification to a study does not result in a change to the approval period for the study.
5. The IRB or IRB staff will provide investigators with written notice of approval (including administrative approval where appropriate), required modifications to secure approval.

C. Full Board Amendment Review

1. Once the determination is made that the amendment requires full board review, the IRB Staff reviews the amendment for completeness and forwards the amendment to the Primary Reviewer (Chair, the Vice Chair, or Chair's designee). S/he reviews the amendment for compliance with the criteria for approval of research.
2. The amendment application is distributed to all IRB members by the IRB Staff prior to the convened meeting. The amendment application consists of the following items:
 - a) the amendment application;
 - b) a red-line version of the informed consent and protocol indicating changes as applicable
 - c) information which would relate to participant's willingness to continue participation; and
 - d) other supporting documents (summary request from sponsors, new surveys and questionnaires etc.).
3. All IRB members are expected to review all modified documents in sufficient depth to discuss the information at the convened meeting.
4. Using the designated review procedure, the IRB Staff will provide comments regarding the administrative review of the application. The Primary Reviewer (the Chair, Vice-Chair or the Chair's Designee) will enter his/her review comments and recommendation of approval, required changes, or disapproval to the on-line application. If the recommendation is for additional changes or disapproval, IRB Staff will send the reviewer's comments to the study communication leads for response prior to the Board meeting. In addition to the above material, the designated reviewers also receive a red-line version of the protocol indicating changes.
5. In addition to the above material listed in III.C.2. above, Board members will receive a red-lined version of the documents being revised by the amendment. Reviewing members can send any

questions/concerns to the Administrator or Chair prior to the convened meeting.

D. Reporting of IRB Approval

1. Protocols approved by the expedited process will be reported to the full IRB board at a convened meeting. Any board member may request further consideration of any protocol approved by the expedited process.

E. IRB Convened Meeting

1. The Primary Reviewer's recommendations are included in the agenda distribution.
2. During the meeting, each full Board amendment is presented by the Chair and/or Primary Reviewer(s), discussed and voted on individually. The Principal Investigator will be present if requested by any Board member or if the Chair/Administrator thinks the Investigator needs to be present to clarify issues/concerns.
3. In evaluating the proposed amendment, IRB members and staff consider OHRP, FDA and, as relevant, VA regulatory criteria.
4. In addition to the application material submitted by the Principal Investigator, the IRB may request additional information, e.g. DSMB reports, sponsors reports, journal articles etc., which may be relevant to the participant's willingness to continue participation.
5. If the IRB determines that the information presented in the amendment application and associated documents would affect a participant's willingness to continue participation, the IRB will request the Principal Investigator contact and reobtain the participants' consent.
6. When the amendment is the result of an immediate change initiated without IRB approval in order to eliminate apparent immediate hazards to participants, the IRB will review the facts surrounding the hazard in order to determine that the benefits of such change outweighed the risks inherent in instituting such change without IRB approval and that the change was consistent with ensuring the participants' continued welfare. An example would be the Principal Investigator reading a scholarly scientific article reporting the deleterious effects of a drug dose, which, had not been previously reported.
7. The Board may approve, require further modifications to secure approval, table, or disapprove an amendment to a study. If the Board requests minor changes which do not substantially impact the

risk/benefit analysis, the Board may approve the amendment contingent on final review and approval by the Chair or the Chair's Designee.

8. Final review and approval of Board-requested changes to study documents may be deferred to the Chair's or Chair's Designee.

F. IRB Administration Responsibilities Post-Meeting

1. If the amendment is approved at the meeting, the IRB Staff releases the approval to the Principal Investigator.
2. If applicable, the new version of the informed consent/HIPAA authorization is date stamped with the amendment approval date. A new version of the amended informed consent/HIPAA authorization document, with an original IRB approval stamp, is released to the study contact. The previously approved version becomes "obsolete".
3. For amendments in which the Board has approved contingent upon completion of requested minor changes which do not substantially impact the risk/benefit analysis, the IRB Staff will notify the study contact electronically of any required changes. When revisions are received in the IRB office, they will be reviewed and if acceptable, the approval will be released.
4. If modifications are substantive in nature or if the Board tables or disapproves the amendment, the IRB Staff/Chair will notify the study contact in writing outlining the Board's requirements.

G. Substantive Modifications Required by the IRB

1. Principal Investigator's responses to an amendment tabled due to substantive modifications or rewrites are presented to the Full Board for review, discussion and vote at the earliest possible convened meeting. If approved, the IRB Staff will release the approval using the above outlined process.

H. Responsibilities and Assurances

1. It is the responsibility of the Investigator as attested in the Principal Investigator assurance, that no modification will be made to the approved research without IRB approval except in circumstances necessary to eliminate apparent immediate hazards to participants.
2. In addition, the University Compliance Office performs for cause and routine random audits of research records. One focus of these audits is the determination that study modifications either occurred subsequent to IRB approval or were initiated in order to eliminate

apparent immediate hazards to participants with subsequent review and approval by the IRB.

3. Furthermore, the training completed by research staff emphasizes the need for IRB approval of all research activities.



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|---|-------------|-------------------|--------------------|
| Policy Name: Case Reports Policy | | | |
| Approved | | | Date: 11/01/08 |
| Effective Date: 02/20/09 | Page 1 of 2 | Section: HRPP 3.7 | Policy Number: N/A |
| Replaces Policy: N/A | | | Dated: N/A |

I. POLICY

A. Introduction

In an academic medical center it is not unusual for unique and interesting clinical cases to be written up as case reports for publication in medical journals or presentation at medical or scientific meetings.

B. Scope

This policy clarifies whether case reports require IRB review and approval at the Medical University of South Carolina.

II. Regulations

A. The Federal Policy for the Protection of Human Subjects (45 CFR 46.102(d)) defines "research" as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

B. Research requires IRB approval prior to be conducted.

III. Medical University of South Carolina Institutional Review Board Position

A. It is the policy that the publication of case reports of three or fewer patients is NOT considered human-subject research and does NOT typically require IRB review and approval because case reporting on a small series of patients does not involve the formulation of a research hypothesis that is subsequently investigated prospectively and systematically for publication or presentation. Therefore three or less case is not considered research but rather a clinical exercise.

B. A case series (more than 3) meets the definition of research.

C. If the journal requires a written statement, the IRB will send to the investigator a form letter that states:

“The IRB received your request (dated ‘x’), concerning a case report you wish to publish. The Medical University of South Carolina IRB has

determined that a case report (3 or fewer patients) does not produce generalizable knowledge, nor is it an investigation of an FDA regulated product. IRB review is not required for this activity.”

- D.** Confidentiality: Patient confidentiality should be respected in all clinical situations involving identifiable medical information from patients. All clinicians are reminded of the following:

Names, dates of birth, social security numbers, and other "codes" or combinations of identifiers, which might easily allow someone to identify a subject, should never be used in publications or external presentations.



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|--|-------------|--------------------------|
| Policy Name: Quality Improvement Projects Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 3.8 |
| Replaces Policy: Effective 10/01/2010 | | |

I. POLICY

A. Introduction

Quality Improvement (QI) activities are done to improve quality of programs, improve services, or improve the provision of medical care, customer service, etc. QI projects are usually done for internal purposes only. However, some QI projects may fall under the federal definition of human subject's research, and therefore may require IRB review.

B. Requirements

To determine whether QI activities involving human participants or individually-identifiable data must be submitted to the IRB, consider the definition of research. This policy defines when a QI project involves research and is subject to IRB review.

II. DEFINITIONS

Definitions for the following terms may be found in the HRPP Program Guide Section 1.3 – Definitions of terms:

A. Research – DHHS and FDA Definitions

B. Human Subject – DHHS and FDA Definitions

III. PROCEDURES

A. Overview of the differences between QI and Research

| | Research | QI |
|---------------|--|--|
| Purpose | To test a hypothesis OR to establish clinical practice standards where none are already accepted | To assess or improve a process, program, or system OR to improve performance as judged by established/accepted standards |
| Benefits | Knowledge sought may or may not benefit current subjects, but may benefit future patients | Knowledge sought directly benefits a process/ program/ system, and may or may not directly benefit patients |
| Risks/Burdens | May put subjects at risk | Does not increase risk to patients, with exception of possible privacy/confidentiality concerns |
| Methods | Systematic data collection | Systematic data collection |
| Analysis | Statistically prove or disprove hypothesis | Compare a program/process/system to an established set of standards, or to establish internal benchmarks |
| Result | Answer a research question | Improves or creates a program/ process/system that results in greater safety, efficiency or satisfaction |

B. Issues to Consider

1. What often distinguishes QI activities from research is whether the activities are intended or designed to develop or contribute to generalizable knowledge. For purposes of this policy, "generalizable knowledge" is information (findings) that can be applied to populations or situations beyond those being immediately studied.
2. If there are no intentions to develop or contribute to generalizable knowledge, IRB review is not required.
3. If QI activities are a systematic investigation AND will develop or contribute to generalizable knowledge, IRB review is required. It is important to note that at the onset, many QI projects have only local (organizational) improvement intentions, but during the process of data collection or

analysis, it becomes clear that findings could be generalizable or benefit others. IRB review should occur when there is an intention to make findings generalizable.

4. When an IRB Chair, designee or IRB staff member cannot in all fairness decide or agree on whether a submission is research or QI, that application may be referred to the full board for discussion and vote.

C. The QI project must be submitted to the IRB if any of the following are true:

1. there is an intent to use the data to contribute to generalizable knowledge,
2. there is a random assignment of participants to compare outcomes,
3. the activities are not normally done as part of standard operating procedures,
4. results will be used to apply knowledge to other programs outside the institution,
5. the project is subject to peer review (designed to be used outside of the institution),
6. anonymity of participants cannot be assured, or
7. the activities involve more than minimal risk to participants.

D. If an investigator is unsure as to whether or not the project meets, or does not meet, the definitions above, please consult with the IRB.



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|--|-------------|--------------------------|
| Policy Name: Review of Research Involving Drugs or Biological Drug Products Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 4 | Section: HRPP 4.1 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

This policy defines the use of drugs and biological drug products in human clinical research settings. MUSC policy requires that investigators obtain approval of and adhere to FDA regulations regarding 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. Principal investigators must provide the IRB with sufficient information for evaluation of the drug’s effectiveness and analysis of risk.

II. DEFINITIONS

As used in this document, human-subjects research encompasses activities that meet the DHHS definitions of **research** and **human subject** and/or the FDA definitions of **clinical investigation** and **human subject**. Definitions for the following terms may be found in HRPP Program Guide Section 1.3 - Definitions of terms:

- A. **Research**
- B. **Human subject**
- C. **Intervention**
- D. **Interaction**
- E. **Private information**
- F. **Clinical investigation**
- G. **Botanical drug products**
- H. **Investigational new drug**
- I. **Radioactive drug**
- J. **Sponsor**
- K. **Sponsor-investigator**

III. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

IV. PROCEDURES

- A. The Principal Investigator indicates in the study application that drugs will be used in this research study.
- B. When a Principal Investigator wishes to conduct a project which may utilize an Investigational Drug, unless the criteria listed in section D are met, the IRB staff will confirm that there is an IND and that it is a valid IND number. This will occur by reviewing the protocol to check for the IND number or by review of an IND acknowledgement letter from the FDA.
- C. If the research involves a MUSC investigator-sponsored IND submission, the Principal Investigator indicates this in the application and uploads a completed FDA form 1571 with all required attachments. If the study is not a MUSC investigator-initiated study, the Principal Investigator uploads FDA form 1572 and a current curriculum vitae.
- D. The PI will complete the drug information section of the application when the research involves the use of drug which is exempt from the 21 CFR 312.2 FDA requirement for an IND:
 - 1. Exemption 1:
 - a) The drug product is lawfully marketed in the United States.
 - b) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.
 - c) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product.
 - d) The investigation does not involve a route of administration or dosage levels or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.
 - e) The investigation is conducted in compliance with 21 CFR 50 and 56.
 - f) The investigation is conducted in compliance with requirements of 21 CFR 312.7.
 - 2. Exemption 2:

- a) A clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following:
 - (1) Blood grouping serum.
 - (2) Reagent red blood cells.
 - (3) Anti-human globulin.
 - b) The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.
 - c) The diagnostic test is shipped in compliance with 21 CFR 312.160.
 - 3. Exemption 3:
 - a) A drug intended solely for test in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.160.
 - 4. Exemption 4:
 - a) A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.
- E.** If the principal investigator states that use of the marketed drug(s) in a manner not currently approved by the FDA does not significantly create risk to subjects, current supporting literature must be uploaded into the eIRB.
- F.** One PharmD or MD IRB member as a primary reviewer of a protocol involving the use of a marketed drug(s) in a manner not currently approved by the FDA.
- G.** The IRB Chair may consult with the PharmD or MD IRB members prior to the convened meeting. Additional supporting literature may be requested or the PI may be asked to attend the meeting to discuss the use of the drug(s).
- H.** The Board will make the decision if the principal investigator must query the FDA regarding the need for an IND given the nature of the research and the drug(s) use.
- I.** The Board may table the protocol or approve the protocol with the contingency that the approval will not be released until documentation from the FDA is received, that an IND is not required, or an IND number is received. The Board's discussion and decision will be documented in the

meeting's minutes. The IND goes into effect 30 days after the FDA receives the IND, unless the investigator-sponsor receives earlier notice from the FDA.

- J.** All inpatient studies must be coordinated through the Investigative Drug Services and the investigator is responsible for following all procedures as defined in "Research Involving Investigational Medications Conducted within MUSC Medical Center Policy and Procedures".
- K.** The PI is responsible for assuring the investigative drugs are only used in the IRB approved research study and under the direction of the study investigator.
- L.** Outpatient studies may be coordinated through the Investigational Drug Services but if the PI can provide adequate storage and control over the distribution of investigational drug supplies, the investigator(s) may be exempt from the pharmacy handling requirement and would thus assume responsibility for the services that would have been provided by the IDS. These areas may also be audited by the IDS at any time to assess compliance. The PI is responsible for assuring the IRB there are appropriate plans for inventory control, storage, monitoring and dispensing of the test articles (drugs, biologics, or devices).
- M.** Investigational drugs for Treatment IND, compassionate use and other emergency uses will be handled by the Investigative Drug Services upon request.
- N.** The PI or appropriate member of the research team will obtain informed consent and the consent form will identify the test article as investigational and will also inform the participants that the FDA may inspect the research records.

V. PROCEDURES SPECIFIC TO VA RESEARCH

- A.** The Principal Investigator is responsible for informing the investigational pharmacy service that the IRB and R&D Committee approvals have been obtained. The Principal Investigator is responsible for ensuring that the research does not commence until the investigator provides to the Pharmacy Service:
 - 1. Documentation of IRB and any other relevant approvals;
 - 2. A copy of VA Form 10-9012 (if applicable);
 - 3. A copy of the current approval protocol;
 - 4. A copy of the consent document for each participating subject with all appropriate signatures;

5. Documentation of IRB continuing review approval;
 6. Copies of sponsor-related correspondence specific to the drugs as appropriate and
 7. Copies of all correspondence addressed to the researcher from the FDA specific to the investigational drugs as appropriate.
- B.** The investigator informs the chief, pharmacy service, the research pharmacy when applicable, and the IRB in writing with a study involving investigational drugs has been suspended, terminated, or closed.
- C.** The investigator complies with all dispensing requirements.
- D.** The investigator complies with all documentation requirements and make relevant records accessible to the investigational drug pharmacist when requested.

VI. REFERENCES

- A.** Code of Federal Regulations Title 21 : [21 CFR 312](#)



| | | |
|---|-------------|--------------------------|
| Policy Name: Single Emergency Use of an Investigational Drug Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 4 | Section: HRPP 4.2 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

This document outlines the policy and procedures established by MUSC for single emergency use of an investigational drug.

B. Single Use of an Investigational Drug

A physician may use an investigational drug one time under the following circumstances and meeting the following requirements.

1. The physician must document in writing that:
 - a) The participant is confronted by a disease or condition that was life threatening.
 - b) The situation necessitates the use of the investigational article.
 - c) No standard acceptable treatment is available.
 - d) There is not sufficient time to obtain IRB approval.
2. The emergency use will be reported to the IRB within five working days. The physician must provide the IND if the investigational drug has one. Any subsequent use of the investigational product at the organization must have prospective IRB review and approval.

C. Informed Consent

Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with and to the extent required by 21 CFR 50 and informed consent will be appropriately documented, in accordance with and to the extent required by 21 CFR 50.27.

D. Single Use of an Investigational Drug if Informed Consent is Not Required

Prior to use of the investigational drug, if informed consent is not required, all of the following must be true and certified in writing by both the treating

physician and a physician who is not otherwise participating in the clinical investigation.

1. The participant is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from the participant.
3. Time is insufficient to obtain consent from the participant's legal representative.
4. No alternative method of approved or generally recognized therapy providing equal or greater likelihood of saving the life of the participant is available.

The above written certification will be submitted to the IRB within five working days after the use of the test article.

E. Single Use of an Investigational Drug when Immediate Independent Determination of a Physician is Unobtainable

If the treating physician is unable obtain the independent determination of a physician because the immediate use of the test article was, in the investigator's opinion, required to preserve the life of the participant and there was insufficient time, the treating physician will:

1. Certify in writing prior to use of the test article:
 - a) The participant is confronted by a life-threatening situation necessitating the use of the test article.
 - b) Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from the participant.
 - c) Time is insufficient to obtain consent from the participant's legal representative.
 - d) No alternative method of approved or generally recognized therapy providing equal or greater likelihood of saving the life of the participant is available.
2. After the use of the test article, a physician who is not otherwise participating in the clinical investigation will certify in writing within five working days after use of the article agreement with all of the above conditions.

3. The written certifications from both physicians will be submitted to the IRB within five working days after the use of the test article.

F. IRB Responsibilities

1. If physicians provided prior notifications of their intent to use a test article in an emergency or their intent to invoke the exception to the requirement to obtain consent, the IRB chair or designee will review the notification to determine whether the circumstances would follow FDA regulations.
2. The written description of the emergency requiring the drug and the rationale for selecting the drug will be received by the IRB Members at the next convened meeting of the IRB.

G. Research Participant

The emergency use of a test article or the outcomes of the emergency may be considered research and the person receiving the test article may be a study participant. The FDA may require data from an emergency use to be reported in a marketing application.

VA and DHHS regulations pertaining to research involving human subjects do not permit data obtained from patients to be classified as human subjects research, nor may the outcomes of such care be included in any report of a research activity subject to VA regulations pertaining to research involving human subjects.

H. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. DEFINITIONS

Definitions for the following terms used in this document may be found in HRPP Program Guide - Section 1.3 Definitions of Terms

- A. Emergency use**
- B. Severely debilitating**
- C. Legal representative or Legally Authorized Representative**

III. PROCEDURES

- A.** The requesting PI will contact either the IRB administrator or chair and present the nature of the emergency prior to administering an investigational drug for emergency treatment.
- B.** The PI will submit a written clinical summary describing the nature of the emergency and the rationale for selecting the investigational drug for treatment; this summary will be reviewed by the IRB chair; the chair will contact the PI as needed to discuss the request.
- C.** The IRB administrator and chair will jointly decide there is inadequate time to convene a meeting of the IRB allowing the exemption from prospective IRB review.
- D.** The PI will contact the drug manufacturer regarding obtaining the drug under the manufacturer's IND.
- E.** The IRB administrator will prepare a letter for the chair's signature acknowledging awareness of the emergency use but not approving the emergency use. *This letter also states that any subsequent emergency use of the investigational drug requires IRB prospective review and approval.
- F.** If the drug does not yet have an Investigational Drug IND, the PI must contact the FDA to obtain authorization for the drug to be shipped; the PI will document this authorization.
- G.** The PI will document that informed consent was obtained and from whom.
- H.** If informed consent is waived because:
 - 1. the patient is confronted by a life-threatening condition;
 - 2. the patient cannot give informed consent;
 - 3. time is not sufficient to obtain informed consent from an appropriate surrogate;and, there is no other comparable treatment to save the individual's life, the PI administering the Investigational Drug and an independent physician will document that each condition is met respectively.
- I.** The PI using an investigational drug for emergency treatment must submit to the IRB within 5 working days a written clinical summary describing the nature of the emergency and the rationale for selecting the investigational drug for treatment if not previously submitted to the IRB during initial contact with the IRB.

- J. The written description of the emergency requiring the drug and the rationale for selecting the drug will be received by the IRB Members at the next convened meeting of the IRB.

***Note:** Neither the IRB or the FDA would deny the emergency use of an investigational drug to another individual if the only obstacle is lack of sufficient time for a convened IRB to prospectively review and approve the use.

IV. REFERENCES



| | | | |
|--|-------------|-------------------|--------------------|
| Policy Name: Review of Research Involving Medical Devices Policy and Procedures | | | |
| Approved | | | Date: 09/15/2012 |
| Effective Date: 09/15/2012 | Page 1 of 7 | Section: HRPP 4.3 | Policy Number: N/A |
| Replaces Policy: 01/27/2012 | | | Dated: N/A |

I. POLICY

A. Introduction

This document describes the policies and procedures for conducting studies involving investigational new *devices* at MUSC Hospitals & Clinics (MUSC) as well as the secure storage of those devices and new biologics, in keeping with the policy of MUSC's Human Research Protection Program (HRPP).

B. Federal Regulations

Clinical investigations of investigational medical devices at MUSC are subject to Federal regulations and are required to comply with Investigational Device Exemption (IDE) regulations as outlined in FDA document 21 Code of Federal Regulations (CFR) 812 and 21 CFR 814, unless exempted under certain specified conditions. All principal investigators (PI) are expected to fulfill all of the responsibilities delineated in the FDA regulations, other federal and State laws and regulations relating to clinical research and MUSC policies and procedures.

C. Storage and Control

Investigational devices under the control of principal investigators and used at MUSC must be procured, stored, secured, dispensed, and monitored in accordance with the MUSC Human Research Protection Program (HRPP) and specific device requirements.

D. Approval for Use

Investigational devices may only be used after research studies and associated documentation have been approved by the MUSC Institutional Review Board (IRB) and any other governing committees, excluding the exemption which permits emergency use of an investigational device on a one-time basis per institution without IRB review and approval [21 CFR 56.104(c)].

E. Classification of Devices

Devices are classified as a Significant Risk Device [21 CFR 812.3m] or Non-significant Risk (NSR) Device, unless EXEMPT from the regulations for Investigational Device Exemptions (IDE).

1. Device studies require review and approval by the MUSC IRB.
2. NSR device studies require MUSC IRB review and approval with regard to informed consent, record keeping, and study monitoring.
3. If a principal investigator (PI) proposes the initiation of a NSR device investigation to the IRB, and if the IRB agrees the device study is NSR and approves the study, the investigation may begin immediately, without submission of an IDE application to the FDA.

Note: If the IRB disagrees with a claim the device is non-significant risk or agrees with the claim and disagrees with the investigator's rationale, the rationale for the IRB's determination will be documented in the IRB meeting minutes.

1. 4. Any safety and efficacy data collection on a significant risk device for other than approved indication requires an IDE in advance of IRB approval

F. Administration of Policy

Contact the Chairman of the Safety Committee (Safety Officer) and/or consult the IRB in situations where guidance is required in administering this policy.

II. DEFINITIONS

Definitions for the following terms may be found in the HRPP Program Guide Section 1.3 – Definitions of terms:

- A. Custom Device**
- B. Emergency Use**
- C. Investigational Device**
- D. Investigation Device Exemption (IDE)**
- E. Medical Device**
- F. Non-Significant Risk (NSR) Device Study**
- G. Significant Risk (SR) Device Study**

III. PROCEDURES

A. Informed Consent

The Principal Investigator is required to obtain informed consent from the research participant or their legally authorized representative, unless the

FDA requirements for exception from informed consent are met [21CFR 50.23(a)]. Note: A note in the medical record will serve to notify hospital personnel that the patient is a research participant in a clinical study involving an investigational device.

B. Responsibilities of the Principal Investigator

1. **Prior to Use** – Prior to use of the investigational device for any reason, the PI must:
 - a) Submit a scientific protocol and all required initial and continuing documentation to the appropriate IRB committee and follow all applicable policies of the MUSC HRPP, including, but not limited to, record keeping by the PI under 21CFR 812.140(a).
 - b) Adhere to the IDE regulations [21 CFR 812]. Research investigations involving NSR devices must adhere to the abbreviated requirements at 21 CFR 812.2(b).
 - c) Obtain IRB approval for research as well as the MUSC informed consent from the research participant or their legal representative [45 CFR 46.116].
 - c) d) Forward IRB acknowledgement of approval to the manufacturer and/or sponsor.
2. **During Use** – During the use of the investigational device, the PI must:

Provide secure and controlled access storage for each investigational device through the MUSC clinical department where they will be utilized (e.g., OR, Cardiac Catheterization Laboratory) that satisfies storage requirements (e.g., controlled temperature, sterile conditions) and maintains proper control of the device for security, storage, inventory, dispensing and disposal purposes;

 - b) Ensure proper dispensing and utilization of investigational devices as defined in the research protocol to those authorized to receive and use it. Note: The PI is responsible for the education of co-investigators, study personnel, and hospital personnel who prescribe, distribute, or administer the investigational device.
 - c) Protect the rights, safety, and welfare of the research participants enrolled in the study.

- d) Maintain complete records as required by the policy of the MUSC HRPP.
 - e) Use investigational devices only in approved research protocols.
 - f) Maintain records of receipt, use or disposition (including retrieval of unused product) of the investigational device. Records should include the type and quantity of the device, the dates of receipt, the batch number or code mark, the names of all persons who received, used, or disposed of each device, and why and how many units of the device have been returned to the sponsor, repaired, or otherwise discarded.
3. **After Use** – After use of the investigational device the PI must return or dispose of the device in accordance with the manufacturer's specifications.
4. **Throughout** - Through the MUSC sponsoring department, in conjunction with the manufacturer or vendor sponsor of the device, the PI must:
- a) Provide for the ongoing security, inventory, and dispensing of the investigational device to appropriate personnel for use by following the MUSC HRPP and MUSC policies, regulations and procedures.
 - b) Perform quality audits to insure security, integrity, and inventory of the investigational device.

C. Responsibilities of the MUSC Clinical Department

The MUSC clinical department where the device will be utilized will cooperate with and assist the Principal Investigator in obtaining secure and controlled access storage in the clinical department for each investigational device satisfying its storage requirements (e.g., controlled temperature, sterile conditions) and maintain proper control of the device for security, storage, inventory, dispensing, and disposal purposes.

D. Adverse Event Reporting

1. The Principal Investigator who holds an IDE or a device with NSR has responsibilities for reporting adverse events associated with use of an investigational device.
- a) The Principal Investigator must report any adverse effect to the sponsor and the IRB *within 10 days of discovery*.

- b) The sponsor is required to evaluate the specific adverse event and investigate under a sponsor's monitoring requirements [21 CFR § 812.46(b)].
 - c) The sponsor must then report its findings to the FDA, to all participating investigators, and to (all) reviewing IRB committee(s) within 10 working days after the *sponsor* receives notice of the adverse effect.
2. The Principal Investigator must also follow *all* MUSC reporting policies pertaining to Adverse Event Reporting, and must participate in any investigation and/or quality review.
 3. The PI of a study using an investigational radiology device must also report any adverse event to the MUSC Clinical Radiation Safety Committee, which reports to the MUSC Administrative Panel on Radiological Safety.

E. Custom Devices for Clinical Research – Investigational Device Exemption (IDE)

Clinical application of custom and/or investigational devices must satisfy all of the requirements of *FDA 21 CFR part 812, Investigational Device Exemptions*. Custom devices are *exempt* unless the device is being used to determine safety or effectiveness for commercial distribution [21 CFR 812.2(c)(7)]. A custom device is as follows [21 CFR 812.3(b)]:

1. The device necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician.
2. The device is not generally available to, or generally used by, other physicians or dentists.
3. The device is not generally available in finished form for purchase or for dispensing upon prescription.
4. The device is not offered for commercial distribution through labeling or advertising.
5. The device is intended for use by an individual patient named in the order of a physician and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician in the course of professional practice.

IV. LEGAL AUTHORITY/REFERENCES

- A. [CDRH, 21 CFR § 812 and § 814, Investigational Device Exemptions, Center for Devices and Radiological Health, Food and Drug Administration](#)
- B. [FDA, Department of Health and Human Services \(DHHS\), as reported in the Federal Register, Volume 62, No. 181, September 18, 1997](#)
- C. [FD&C Act](#)



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|--|-------------|--------------------------|
| Policy Name: Medical Devices Risk Determination Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 5 | Section: HRPP 4.4 |
| Replaces Policy: Effective 01/27/2012 | | |

I. POLICY

A. Introduction

This guide section details the policies and procedures established at MUSC for evaluating the risk in use of medical devices in human subjects research.

B. Regulations

1. The IRB will determine if an investigational device is a “significant risk” (SR) or a “non-significant risk” (NSR).
2. A SR device will have a documented IDE number issued by the FDA before used in human research.
3. Off-label use of a marketed device in human research requires documented FDA review of the proposed use within the context of the research.
4. A protocol using a NSR device may be expedited if it fits the definition of “minimal risk” and fits one of the federally defined categories of research that may be approved by expedited review (21 CFR 56.110).

II. DEFINITIONS

Definitions of the following terms used in this section may be found in HRPP Guide Section 1.3 – Definition of terms

- A. Medical Device**
- B. Investigational Device**
- C. Investigation Device Exemption (IDE)**
- D. 510K device**
- E. Significant Risk Investigational Device**
- F. Non-significant Risk Device**
- G. Medical Device Class**

III. MAJOR DIFFERENCES BETWEEN SIGNIFICANT RISK AND NONSIGNIFICANT RISK DEVICE STUDIES

A. *Significant Risk (SR) Device Studies*

1. SR device studies must follow all the IDE regulations at 21 CFR 812.
2. SR device studies must have an IDE application approved by FDA before they may proceed.

B. *Non-significant Risk (NSR) Device Studies*

1. NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b).
2. These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion. However, there is no need to make progress reports of final reports to FDA.
3. NSR device studies do not have to have an IDE application approved by FDA.
4. Sponsors and IRBs do not have to report the IRB approval of an NSR device study to the FDA. Thus the IRB's NSR determination is important because the IRB serves as the FDA's surrogate for review, approval, and continuing review of the NSR device studies. An NSR device study may start at MUSC as soon as the MSUC IRB reviews and approves the study and without prior approval by the FDA.

IV. PROCEDURES

A. Principal Investigator Submission

1. The Principal Investigator conducting research that involves use of a medical device selects "Investigation of medical device, instrument, machine, computer program or other device, FDA approved or non-FDA approved, including HUD" on the Application Checklist SmartForm page in the IRB application submission.
2. The Principal Investigator will complete the appropriate Device Smartform application pages if the research involves an investigational device provided by a sponsor/investigator sponsor; the Principal Investigator will submit documentation of the IDE number issued by the FDA to the sponsor and a current curriculum vitae. The IRB Administrator will confirm that there is an IDE and the IDE number is valid by review of the required FDA correspondence stating the IDE #.
3. The Principal Investigator will complete the appropriate Device Smartform application pages if the research involves the use of a device approved by the FDA as a 510k device.

4. If the Principal Investigator is requesting the IRB to determine if an investigational device is a NSR, the Principal Investigator will complete the appropriate Device Smartform application page and include the following:
 - a) an explanation as to why the device is a NSR including supporting literature evaluating the risks,
 - b) reports of prior investigations of the device if available,
 - c) names of other IRBs which have reviewed the proposed study and what device determination was made, and
 - d) the FDA's assessment of the device if an assessment was made.

B. IRB Determination

1. The IRB will make the SR or NSR determination for a study by convened meeting. The IRB reviews reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria, monitoring procedures, and any other information the IRB deems necessary to make its decision.
2. The IRB is not required to make a SR/NSR determination for studies involving devices that meet the criteria for exemption from the IDE regulations.
3. The IRB may request that the PI consult with the FDA for an opinion as appropriate.
4. If the IRB determines the study is SR, then the IRB notifies the investigator who notifies the sponsor. The sponsor notifies the FDA that the IRB has made an SR determination. The PI may not conduct the study until the FDA approves the sponsor's IDE application.
5. When research is conducted to determine the safety or effectiveness of a device, where the device is not a significant risk device, the IRB staff, the convened IRB, or the reviewer using the expedited procedure determines whether:
 - a) The device has an IDE issued by the FDA. The IDE for each device must be supported by one of the following:
 - The sponsor protocol imprinted with the IDE number
 - A written communication from the sponsor documenting the IDE number

- A written communication from the FDA documenting the IDE number (required if an investigator listed on this protocol holds the IDE)

OR

- b) The device fulfills the requirements for an abbreviated IDE [Criteria in 21 CFR 812.2(b)(1)]
- The device is not a banned device.
 - The sponsor labels the device in accordance with 21 CFR 812.5.
 - The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.
 - The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived.
 - The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
 - The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
 - The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
 - The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

OR

- c) The device fulfills one of the IDE exemption categories [Criteria in 21 CFR 812.2(c)]:
- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
 - A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28,

1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

- A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
 - 1) Is noninvasive.
 - 2) Does not require an invasive sampling procedure that presents significant risk.
 - 3) Does not by design or intention introduce energy into a subject.
 - 4) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
 - A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
 - A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.
6. If IRB determines that the study is NSR, there is no requirement for submission of an IDE application to the FDA. The PI conducts the study in accordance with abbreviated IDE requirements.
 7. If the FDA has made the SR or NSR determination prior to IRB review, the IRB is not required to make this determination; the FDA's determination is final.
 8. The IRB may approve or disapprove the proposed research based on local context and its responsibilities to protect human subjects in research even when approval of the device has been granted by the FDA.
 9. IRB staff document the decision of the IRB (both risk determination and approval), including a description of the reason (s) for the Board's decision, in the meeting minutes.

III. REFERENCES

- A. [FDA Guidance: Significant Risk and Non-significant Risk Medical Device Studies](#)
- B. [21 CFR 50](#)
- C. [21 CFR 56.110](#)
- D. [21 CFR 809](#)
- E. [21 CFR 812](#)



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|--|-------------|--------------------------|
| Policy Name: Emergency Use of an Investigational Device Policy and Procedures | | |
| Approved | | |
| Effective Date: 05/08/2013 | Page 1 of 3 | Section: HRPP 4.5 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

A. Introduction

The following details the policy and procedures established by MUSC for emergency use of an investigational device.

B. IDE Requirement

The emergency use of an Investigational Device requires an IDE.

C. IRB Consultation

The emergency use of an Investigational Device requires consultation with the IRB prior to use.

D. Informed Consent

The emergency use of an Investigational Device requires documented informed consent of the patient. If the patient is unable to give informed consent, informed consent may be obtained from a legal representative, spouse, parent or sibling in that order.

E. Waiver of Informed Consent

Documented informed consent may be waived only if ALL of the following conditions are documented including certification that all four conditions are present by another MD not directly involved in the patient's care:

1. The patient is confronted by a life threatening event;
2. Informed consent cannot be obtained because the patient cannot communicate or is not cognitively competent to give consent;
3. Time is not sufficient to obtain consent from an authorized surrogate; and
4. No alternative approved therapy is available with equal or greater likelihood of saving the individual's life.

(Note: IRB may **NOT** approve planned emergency research that is subject to VA Regulations)

F. Reporting of Use

The MD using an Investigational Device for emergency treatment must submit a written report to the IRB within 5 working days of the device's use.

G. Single Use Limitation

**A specific Investigational Device may be used only once as an "emergency" by an institution; subsequent use must be prospectively reviewed and approved by the IRB

H. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. DEFINITIONS

Definitions for the following terms used in this document may be found in HRPP Program Guide Section 1.3 - Definitions of Terms:

A. Emergency use

B. Legal representative or Legally Authorized Representative

III. PROCEDURES

A. The requesting MD will contact either the IRB administrator or chair and present the nature of the "emergency" prior to investigational device for emergency treatment.

B. The MD will submit a written clinical summary describing the nature of the "emergency" and the rationale for selecting the device for treatment; this summary will be reviewed by the IRB chair; the chair will contact the MD as needed to discuss the request.

C. The IRB administrator and chair will jointly decide if there is inadequate time to convene a meeting of the IRB allowing the exemption from prospective IRB review.

- D. The MD will contact the device manufacturer regarding obtaining the device under the manufacturer's IDE.
- E. If the manufacturer holding the IDE requires "IRB authorization", the IRB administrator will prepare a letter for the chair's signature acknowledging awareness of the emergency use but not "approving" the emergency use.
- F. If the device does not yet have an IDE or if the device is to be used for a purpose other than that authorized with the IDE, the MD must contact the FDA to obtain authorization for the device to be shipped; the MD will document this authorization.
- G. The MD will document that informed consent was obtained and from whom.
- H. If informed consent is waived because: 1) the patient is confronted by a life-threatening condition; 2) the patient cannot give informed consent; 3) time is not sufficient to obtain informed consent from an appropriate surrogate; and, there is no other comparable treatment to save the individual's life, the MD using the Investigational Device and an "independent" MD will document that each condition is met respectively.
- I. The MD using an Investigational Device for emergency treatment must submit to the IRB within 5 working days a written clinical summary describing the nature of the "emergency" and the rationale for selecting the investigational device for treatment if not previously submitted to the IRB during initial contact with the IRB.
- J. The written description of the emergency requiring the device and the rationale for selecting the device will be reviewed at the next convened meeting by IRB members.
- K. The MD will be notified in writing that any subsequent emergency use of the investigational device requires IRB prospective review and approval.

***Note:** Neither the IRB or the FDA would deny the emergency use of an investigational device with an IDE to another individual if the only obstacle is lack of sufficient time for a convened IRB to prospectively review and approve the use.



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| Policy Name: Humanitarian Use Device Policy and Procedures | | |
| Approved | | |
| Effective Date: 05/08/2013 | Page 1 of 2 | Section: HRPP 4.6 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

A. Introduction

A humanitarian use device (HUD) is defined by the FDA as a device intended to benefit patients in the treatment and diagnosis of disease or conditions that affect or is manifested in fewer than 4,000 individuals in the US per year.

B. Regulations

Designation of a device as a HUD is determined by the Office of Orphan Products Development. Use of an HUD within its approved labeling does not constitute research.

C. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. PROCEDURES

- A.** Informed consent is not required when treating or diagnosing a patient under an HDE, but prospective informed consent should be obtained when feasible. Patient labeling information may also provide information about the potential risks and benefits of the HUD and informs patients about the humanitarian use of device and that effectiveness for the labeled indication has not been demonstrated in previous clinical trials.
- B.** After the Humanitarian Device Exemption (HDE) has granted FDA approval, IRB approval must also be approved prior to its use.
- C.** Principal Investigators must submit an application to the IRB including a copy of the HDE application submitted to the FDA, documentation of FDA approval, any consent document that may be used, and the patient labeling information.

- D. Initial IRB approval must be performed at a convened meeting of the Board. The IRB may approve use of the HUD without restrictions or may require review on a case-by- case basis. Applications to the IRB should describe the approximate number of the patients the investigator anticipates will be treated or diagnosed with the device.
- E. Unless the IRB determines full board's review is necessary, continuing review and approval of the use of the device (not to exceed one year) may be conducted using expedited review procedures.
- F. All unanticipated problems and adverse events involving the use of a HUD should be submitted to the IRB in accordance with policies and procedures involving the use of investigational devices under an IDE application.

G. Off-Label Use of Humanitarian Use Device

Prior FDA approval for an emergency use of a HUD is recommended. If this is not feasible, FDA recommends that the procedures in the Expanded Access of Unapproved Devices be used as guidance. **(Note: IRB may NOT approve planned emergency research that is subject to VA Regulations)**

H. Future Research Designed to Obtain Marketing Approval

If the holder of HDE develops a research protocol designed to collect safety and effectiveness data to support marketing of the device, the investigational study must receive prior IRB review and approval. While an Investigational Device Exemption (IDE) is not required if the device is used within the FDA approved HUD labeling, IDE regulations must be followed and consent must be obtained from prospective participants in accordance with the IRB approved application. **(Note: IRB may NOT approve planned emergency research that is subject to VA Regulations)**



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|---|-------------|--------------------------|
| Policy Name: Unanticipated Problems and Adverse Events Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 9 | Section: HRPP 4.7 |
| Replaces Policy: Effective 08/01/2012 | | |

I. INTRODUCTION

This policy defines the policies and procedures of MUSC for addressing unanticipated problems involving risks to research participants or others (UPIRSOS).

MUSC investigators are required to promptly report to the IRB if there are unanticipated problems during the course of the research that involve risks to subjects or to others. MUSC IRB will not review reports of adverse events, whether at MUSC or external sites, unless those reports constitute unanticipated problems involving risks to subjects or others.

See letter to the research community and sponsors posted at <http://academicdepartments.musc.edu/research/ori/irb/Documents/Magruder%20Letter%20October%201%202010.pdf>

II. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

III. DEFINITIONS

According to federal guidance, an unanticipated problem involving risks to subjects or others (UPIRSOS) refers to any incident, experience, or outcome that:

- is unexpected (in terms of nature, severity, or frequency) given: (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- is related or possibly related to a subject’s participation in the research; and

- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

Adverse event or adverse experience (AE) is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms and occur most frequently in the context of biomedical research, although they can occur in the context of social and behavioral research.

- Internal adverse event is an adverse event experienced by subjects enrolled by the investigator(s) at MUSC or at a site for which MUSC has oversight.
- External adverse event is an adverse event experienced by subjects enrolled by investigators at other institutions engaged in a multi-site clinical trial.

Serious Adverse Event (SAE) is any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

- results in death;
- is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in a persistent or significant disability/incapacity;
- results in a congenital anomaly/birth defect; or
- any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

Unexpected Adverse Event as defined by the FDA, is any adverse event, the specificity or severity of which is not consistent with the current Investigator Brochure; or, if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended.

Possibly related to the research refers to the reasonable possibility that the adverse event, incident, experience or outcome may have been associated with the procedures involved in the research (modified from the definition of associated with use of the drug in FDA regulations at 21 CFR 312.32(a)).

Related to the research refers to an incident, experience or outcome that is likely to have resulted from participation in the research study.

IV. DECIDING IF AN EVENT MEETS THE CRITERIA FOR UNANTICIPATED PROBLEM INVOLVING RISK TO SUBJECTS OR OTHERS

A. Is it unexpected?

An event is unexpected if it occurs in one or more subjects or others participating in a research protocol, and the event's nature, severity, or frequency is not consistent with either:

- the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in; (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document; and (b) other relevant sources of information, such as product labeling and package inserts; or
- the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

B. Is it related or possibly related to a subject's participation in the research?

Events that are related or possibly related to participation in the research may be caused by one of the following:

- The procedures involved in the research;
- An underlying disease, disorder, or condition of the subject;
- Other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject.

In general, events that are determined to be at least partially caused by the procedures in a study would be considered related to participation in the research, whereas events determined to be solely caused by the subject's condition or state of illness or other circumstances clearly outside of the study would be considered unrelated to participation in the research

C. Does it suggest that the research places subjects or others at greater risk of harm than was previously known or recognized?

Adverse events that are: 1) unexpected, 2) related or possibly related to participation in research, and 3) serious are the most important subset of adverse events representing unanticipated problems, because such events always suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. These events warrant consideration of substantive changes in the research protocol and/or informed consent process/document or other corrective actions in order to protect the safety, welfare or rights of subjects.

If the answers are that the event is a) unexpected, b) related or possibly related and c) serious, it is a UPIRSOS and should be reported to the MUSC IRB.

Other adverse events that are unexpected and related or possibly related to participation in the research, but not serious, would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. These events should also be reported, for consideration of changes or corrective actions.

Determining whether a particular incident, experience, or outcome is unexpected and whether it is related or possibly related to participation in the research may be difficult. When making this assessment, the investigator should take into consideration whether substantive changes in the research protocol or informed consent document, or other corrective actions may be warranted in order to protect the safety, welfare, or rights of subjects or others. Generally, if the problem is considered an unanticipated problem involving risks to subjects, substantive changes to the protocol and/or consent form may be warranted.

Examples of unanticipated problems that should be reported to the IRB, even though they are not adverse events, include:

- Publication in the literature, safety monitoring report (e.g., DSMB report), interim result, or other finding that indicates an unexpected change to the risk/benefit ratio of the research;
- Breach in confidentiality resulting from a disclosure of confidential information or from lost or stolen confidential information, that may involve risk to that individual or others;
- Complaint of a participant or family member that indicates an unanticipated risk;
- Laboratory or medication errors that may involve potential risk to that individual or others;
- Change in FDA labeling because of adverse consequences or withdrawal from marketing of a drug, device, or biologic used in a research protocol;
- Disqualification or suspension of investigators;
- Accidental or unintentional change to the IRB-approved protocol that involves risks or has the potential to recur;

- Deviation from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant
- Any deviation from the IRB-approved protocol that increases the risk or affects the participant's rights, safety, or welfare.

Note: "Harm" does not need to occur for an event to be an unanticipated problem; an unanticipated problem places subjects or others at increased risk of harm.

V. REQUIRED REPORTING OF UNANTICIPATED PROBLEMS

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs)

Investigators must report to the IRB any unanticipated problem involving risk to subjects or others. The reported information must include: a description of the event, the date of occurrence, whether it is a local or outside report, how the event affected the rights, safety or welfare of the subject or others, current status of MUSC subjects, and any planned changes or modifications to the project as a result of the event.

Reports from the investigator to the IRB must be submitted no later than 10 working days after the event or notification to the investigator that the event has occurred.

When a research study includes investigational drugs or devices, some unanticipated problems may also meet the definition of an unexpected adverse drug experience (serious or otherwise), or an unanticipated adverse device effect. MUSC investigators and research staff are expected to be familiar with the various requirements for reporting of adverse events and UPIRSOs.

When a UPIRSO report is filed with IRB, the staff will compare the content of the report with the previously approved project materials such as applications, informed consent document(s), protocols, investigator brochures, or other supporting documents to determine whether this event appears to meet the definition of an unanticipated problem involving risk to subjects or others. This preliminary determination is forwarded to an expedited IRB reviewer.

The IRB reviews the UPIRSO report by expedited procedures in order to determine whether the criteria for approval under 45 CFR 46.111 and 21 CFR 56.111 are still met. In its review of the UPIRSO report, the IRB may determine that additional safeguards need to be developed within the protocol procedures in order to adequately minimize risks. It may require consent form modifications in order to include additional information about this new risk (already enrolled subjects may or may not need to be provided with this new information). The IRB is also responsible to decide whether the study may continue as it was previously approved given this new information.

When very serious risks of harm or serious harms occur, the IRB may consider suspending its approval of the research as a way of safeguarding the rights and welfare of the subjects.

All reports of unanticipated problems involving risks to subjects or others are filed with the appropriate research study. The investigator will be asked to summarize these reports for the IRB at the time of continuing review.

Adverse Events

FDA regulations and clinical trial agreements require the prompt reporting of Serious Adverse Drug Events and Serious Adverse Device Effects to the Sponsor and to FDA. Sponsors are responsible for reporting these events to investigators at other institutions who are conducting research under the relevant IND or IDE of these events. However, these events only need to be reported to the MUSC IRB (whether they occur at MUSC, or at an external site) when they constitute an unanticipated problem involving risks to subjects or others. While non-UPIRSO adverse events still need to be reported to the Sponsor, who must report them to FDA, they do not need to be reported to the MUSC IRB and the MUSC IRB will not review them. The only exception to this is the requirement that adverse device effects need to be reported by the Sponsor to the IRB. If these constitute UPIRSOs, then the MUSC PI will be required to submit an Adverse Event or UPIRSO report.

A Reportable external adverse event is determined by a Data Safety Monitoring Board (DSMB) or a Central Monitoring Entity (CME) to be:

- a. Unanticipated;
- b. Related or possibly related to participation in research;
- c. Serious or more prevalent than expected; **AND**
- d. The DSMB/CME recommends a specific change to the protocol/informed consent based on the event, for example, modification of inclusion/exclusion criteria, and revision of the informed consent to encompass newly identified risks.

Deaths on Study

Investigators are required to report to the IRB any death of an MUSC research subject within 24 hours of learning about the death, unless the death is expected (e.g., due to disease progression).

Anticipated deaths (e.g., due to disease progression) may be reported at the time of continuing review.

VI. IRB AND OTHER INSTITUTIONAL RESPONSIBILITIES

The assigned IRB staff will review any unanticipated problem reports and forward them to the IRB Chair, or designee, for review.

The Chair, or designee, will review the report including the protocol, informed consent documents, changes already implemented for immediate safety reasons and those proposed, and determine in consultation with the principal investigator if there is a need for immediate action beyond the action taken/recommended by the principal investigator. Appropriate institutional officials and federal oversight agencies will be promptly notified when applicable. Preliminary notification may be sent in some cases.

If the Chair, or designee, decides the research should be suspended to enrollment of new subjects or research activities involving currently enrolled subjects should be suspended given the nature of the unanticipated problem, the Chair or designee will have the IRB Staff suspend the study in the system which will issue an automatic notification to the Principal Investigator with actions to be taken to protect currently enrolled subjects.

All of the pertinent information regarding the unanticipated problem will be reviewed by the Board at a convened meeting. This information may include the protocol, informed consent, as well as any proposed changes to these documents and any additional information such as national/international experiences within the research study if available. The Board may require additional actions. These actions may include:

- revision of the protocol including inclusion/exclusion criteria;
- incorporation of new information into the informed consent;
- implementation of additional data monitoring activities;
- informing currently enrolled participants;
- suspension of enrollment of new subjects;
- suspension of research procedures in currently enrolled subjects;
- notification of previously enrolled subjects of the event and any actions they should take;
- termination of the research; and/or
- notification to current participants when such information may relate to participants' willingness to continue to take part in the research.

The Board's discussion and required actions will be documented in the IRB minutes.

If the Board requires additional actions, the IRB Staff will enter these into the system for automated notification to the Principal Investigator of these changes with a request that these modifications be submitted for IRB review after discussion with the study's sponsor.

The Chair will submit a written report to the Institutional Official(s) copied to the principal investigator within 10 working days after review of the event by the convened Board. This report will include:

- the name of the institution;
- title of the research study;
- the name of the principal investigator;
- number assigned by the IRB and any numbers assigned by another agency/sponsor;
- the IND or IDE number if applicable;
- a detailed description of the unanticipated problem; and
- actions the principal investigator and the IRB have taken or will implement to address the problem and prevent future occurrences.

The Institutional Official(s) will review the event and discuss the report with the IRB chair and the Director of the Office of Research Integrity. The Institutional Official will promptly notify OHRP, the FDA if appropriate, the sponsor, and other agency officials as appropriate within 30 working days of receiving the Chair's report regarding the unanticipated problem including those resulting in IRB suspension or termination of the protocol.

If the research study is a VA protocol, the following will be notified: 1) The Associate Chief of Staff/Research & Development: 2) the VA Privacy Office (when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information). The ACOS-R and VAMC compliance officer will follow the procedures of VAMC Center Policy Memorandum No. 151-16-07 Human Research Protection Program (HRPP), subparts II.E.15 "IRB Review of SAEs and Serious Problems" and II.E.16 "IRB Review of Apparent Serious of Continuing Non-Compliance". Revisions to this SOP will be communicated to the MUSC IRB by the VAMC Compliance Officer and/or VA Liaison.

VII. VA Protocols

If the research study is a VA protocol, the following will be notified: 1) The Associate Chief of Staff/Research & Development: 2) the VA Privacy Office (when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information). The ACOS-R and VAMC compliance officer will follow the procedures of VAMC Center Policy Memorandum No. 151-16-07 Human Research Protection Program (HRPP), subparts II.E.15 "IRB Review of SAEs and Serious Problems" and II.E.16 "IRB Review of Apparent Serious of Continuing Non-Compliance". Revisions to this SOP will be communicated to the MUSC IRB by the VAMC Compliance Officer and/or VA Liaison.

- a. The terms "unanticipated" and "unexpected" refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

- b.** The unfounded classification of a serious adverse event as “anticipated” constitutes serious non-compliance.
- c.** For serious unanticipated problems involving risks to subjects or others, within five business days of becoming aware of any serious unanticipated problem involving risks to subjects or others in VA research, members of the VA research community are required to ensure that the problem has been reported in writing to the IRB. Serious unanticipated problems involving risks to subjects or others include:
 - i.** Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others.
 - ii.** Any work-related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individuals, or leads to serious complications or death.
 - iii.** Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the VA facility’s research projects.
 - iv.** Any data monitoring committee, data and safety monitoring board or data and safety monitoring committee report describing a safety problem.
 - v.** Any sponsor analysis describing a safety problem for which action at the VA facility might be warranted.
 - vi.** Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others.
 - vii.** Any problem reflecting a deficiency that substantively compromises the effectiveness of the VA facility’s HRPP.
- d.** IRB review of serious unanticipated problems and unanticipated serious adverse events in VA research:
 - i.** Within five business days after a report of a serious unanticipated problem involving risks to subjects or others, or of a local unanticipated serious adverse event, the convened IRB or a the chair or designee must determine and document whether the reported incident was serious and unanticipated and related to the research.
 - ii.** “Related” means the event or problem may reasonably be regarded as caused by, or probably caused by, the research.
 - iii.** If the convened IRB or the IRB chair or designee determines that the problem or event was serious, unanticipated, and related to the research, the IRB chair or designee must report in writing the

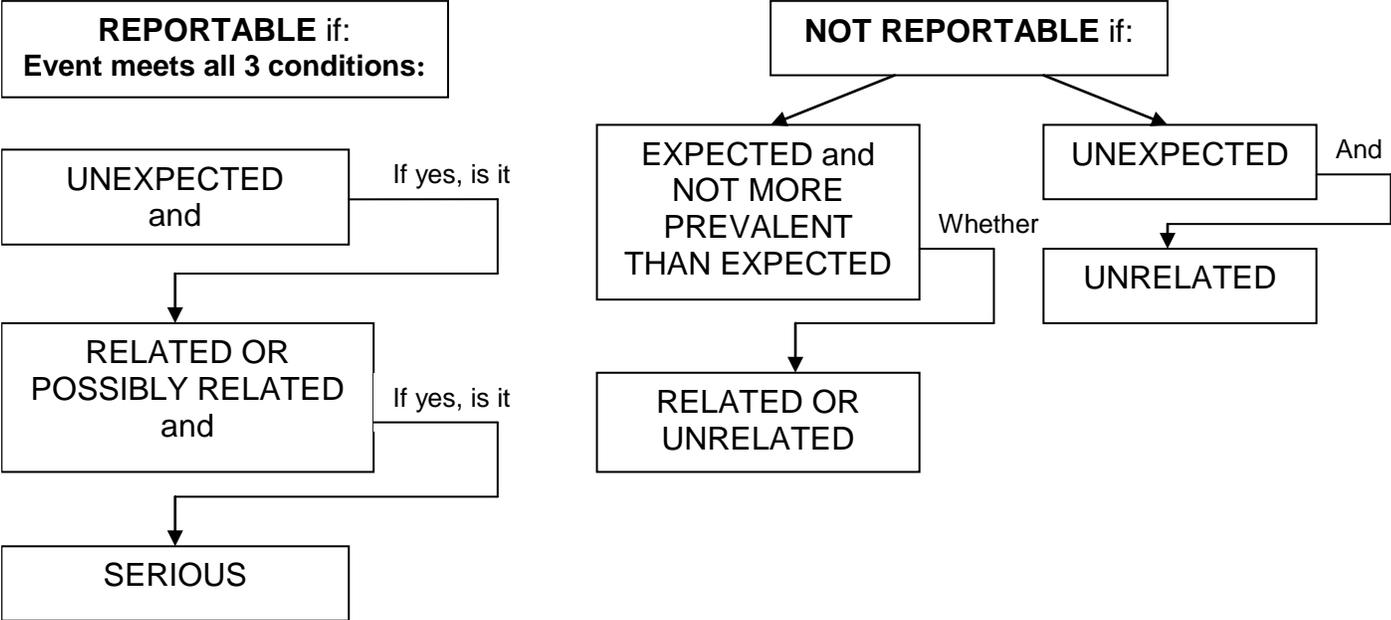
unanticipated problem or event within five business days after the determination to:

1. Medical center director (responsible for reporting to the Office of Research and Development, The Regional Office of Research Oversight and, if the report involves violations of information security requirements, the Information Security Officer),
 2. Associate chief of staff for research and
 3. The Research and Development Committee.
- iv. If the convened IRB or the IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research, a simultaneous determination is required regarding the need for any action (e.g., suspension of activities; notification of subjects) necessary to prevent an immediate hazard to subjects in accordance with VA regulations.
- v. All determinations of the IRB reviewer (regardless of outcome) must be reported to the IRB at its next convened meeting.
- vi. If it was determined that the problem or event is serious, unanticipated, and related to the research, the convened IRB must determine and document whether a protocol or consent document modification is warranted.
- vii. If the convened IRB determines that a protocol or consent document modification is warranted, the IRB must also determine and document:
1. Whether previously enrolled subjects must be notified of the modification.
 2. When such notification must take place and how such notification must be documented.

VIII. REFERENCES

- e. [Office of Human Research Protections \(OHRP\), DHHS, Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, 2007.](#)
- f. Reportable Event Flowcharts (following page)

Reporting Requirements for INTERNAL Adverse Events



***Reporting Requirements for INTERNAL DEATHS**

All internal deaths
during the study or 30 days post termination from study intervention, are
required to be reported as adverse events unless they are expected (i.e.,
due to disease progression).



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|--|-------------|-------------------|
| Policy Name: Management of Non-Compliance Policy and Procedures | | |
| Approved | | |
| Effective Date: 08/08/2013 | Page 1 of 4 | Section: HRPP 4.8 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

A. Introduction

The purpose of this policy is to define the policies and procedures of MUSC for addressing allegations and findings of non-compliance with HRPP requirements.

B. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

C. Investigators, research staff or anyone with allegations of non-compliance or continuing non-compliance regarding human subjects research will report allegations to the IRB or University Compliance Office.

D. In a convened meeting, the IRB will discuss the non-compliance, with reference to all study materials including the protocol and informed consent documents, and decide if the non-compliance is 1) non-serious and/or non-continuing or 2) serious and/or continuing.

E. In situations of non-compliance determined to be neither serious or continuing, the IRB may:

1. issue a letter of guidance/reprimand to the investigator that is copied to the appropriate chair, division director or dean;

2. request the investigator appear at a convened meeting to answer questions of non-compliance;
 3. request the investigator perform a quarterly or semi-annual self-audit of the research study activities and report the findings to the board;
 4. request the investigator and/or research staff complete additional HRPP training;
 5. request that the university compliance office perform an audit of the study protocol and associated activities and provide a written report to the IRB , and/or
 6. initiate any other measures deemed appropriate by the IRB.
- F.** The IRB will report any instance of serious or continuing noncompliance with federal or state regulations governing the protection of human subjects, VHA 1200.5 (for VA protocols) and IRB requirements to the Director, Office of Research Integrity and the Organizational Officials(s) [21 CFR 56.108(b); 45 CFR 46.103(b)(5)].
- G.** The IRB Chair will notify the ORI Director and Organizational Officials(s) within 24 hours if a research study is suspended due to an issue of serious or continuing noncompliance; followed by a written report within 10 working days after review of the event by the convened Board.
- H.** The Organizational Official(s) will notify OHRP, the FDA if appropriate, the sponsor, and other agency officials as appropriate within 30 working days of receiving the Chair's report regarding serious or continuing noncompliance, including those occurrences resulting in IRB suspension/termination of research.
- I. MEMORANDUM OF UNDERSTANDING**

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. DEFINITIONS

Definitions for the following terms may be found in the HRPP Program Guide Section 1.3 – Definitions of Terms

A. Allegation of Non-Compliance

B. Continuing Non-Compliance

C. Non-Compliance

D. Serious Non-Compliance

III. PROCEDURES

A. Investigators, research staff or anyone with allegations of non-compliance or continuing non-compliance regarding human subjects research will report allegations to the IRB or University Compliance Office.

B. The allegation report should include 1) Study Title, 2) HR#, 3) Name of the Principal Investigator, 4) Description of the alleged non-compliance, 5) timeframe, 6) other individuals involved, 7) other relevant information.

C. An allegation, concern, or issue of noncompliance initially will be reviewed by the IRB Program Manager and IRB Chair.

D. The IRB Program Manger and the IRB Chair will conduct a preliminary investigation to determine the nature of the noncompliance including interviewing the individuals involved in the allegation, concern or issue.

E. If the preliminary investigation determines no basis of fact (i.e., there are no documents or statements supporting the allegation) of non-compliance, the IRB Program Manager and the IRB Chair will present the case to the convened IRB for review. The convened IRB may dismiss the allegations as unjustified and take no further action.

F. If the preliminary investigation finds serious evidence (i.e., there are supporting documents or statements) of non-compliance, the IRB Program Manager and the IRB Chair will decide if the nature of the non-compliance warrants immediate suspension of protocol enrollment/participation or other immediate corrective actions.

G. The IRB Chair or their designee will contact the principal investigator responsible for the protocol(s) involved in the issue of noncompliance. If the protocol(s) is suspended to enrollment or continued participation of current subjects, the IRB chair will write a letter to the principal investigator stating the scope of this suspension, the reason for the suspension, and actions that should be taken to protect currently enrolled subjects.

H. The IRB Chair and IRB Program Manager will conduct a full investigation of alleged noncompliance including requesting the University Compliance Office to conduct an audit of the protocol(s). As part of this investigation, the IRB Program Manager and the IRB Chair will determine if subjects were harmed and if subjects were notified of the non-compliance.

- I. All findings will be reported to the Board at the next scheduled meeting. The Board will be provided with written documents used in the investigation. These documents may include an audit report, e-mail correspondence, letters between the IRB and the Principal Investigator. The investigator involved in the allegation of non-compliance will be invited to attend the Board meeting when appropriate.

- J. If the Board decides the evidence supports the determination of “serious” or “continuing” noncompliance, the Board will determine corrective actions which may include:
 - 1. suspension or termination of a particular protocol,
 - 2. suspension of the investigator’s privilege to conduct human subject research with the requirements necessary for the privilege to be reinstated identified,
 - 3. notification of current participants (required when such information might related to participants’ willingness to continue to take part in research),
 - 4. the requirement that no data collected during the research in question may be used for publication, and/or
 - 5. random audits of other research studies to detect if a pattern is present.

The Board may also decide to implement additional corrective actions such as:

- 1. modification of the research protocol,
 - 2. modification of the information disclosed during the consent process,
 - 3. additional information provided to past participants,
 - 4. requirement that current participants re-consent to participation,
 - 5. modification of the continuing review schedule,
 - 6. monitoring of the research, and/or
 - 7. monitoring of the consent process.

- K. The Chair will prepare a letter for the Organizational Official(s) copied to the principal investigator that will include:
 - 1. the name of the institution,

2. title of the research study,
3. the name of the principal investigator,
4. number assigned by the IRB and any numbers assigned by another agency/sponsor,
5. the IND or IDE number if applicable,
6. a detailed description of the noncompliance, and
7. actions the IRB has taken relative to the issue.

L. VA Research

1. Within five business days of becoming aware of any apparent or possible serious or continuing non-compliance, members of the VA research community are required to ensure that the apparent non-compliance has been reported in writing to the IRB.
2. Within five business days of identifying apparent serious or continuing non-compliance based on a consent document audit, regulatory audit, or other systematic audit of VA research, the IRB chair, or designee must provide a written report of the apparent non-compliance directly (without intermediaries) to:
 - a) Medical Center Director,
 - b) Associate Chief of Staff for Research and
 - c) The Research and Development Committee.
3. The IRB must review a report of apparent serious or continuing non-compliance at its next convened meeting.
4. Should the IRB determine that the reported incident constitutes serious non-compliance or continuing non-compliance, within five business days after the determination, the IRB chair, or designee must provide a written report of the determination directly to the following individuals or committees at the Ralph H. Johnson VAMC:
 - a) Medical Center Director,
 - b) Associate Chief of Staff for Research,
 - c) The Research and Development Committee
 - d) Other relevant research review committee.

5. An initial report of an IRB determination that serious non-compliance or continuing non-compliance occurred is required, even where the determination is preliminary or disposition of the matter has not been resolved at the time of the report.
6. The IRB must research a determination that serious or continuing non-compliance did (or did not) occur within 30-45 days after receiving a report of apparent non-compliance.
7. Remedial actions involving a specific study or research team must be completed within 90-120 days after the IRB's determination.
8. Remedial actions involving programmatic non-compliance must be completed within 120-180 days after the IRB's determination, unless remediation requires substantial renovation, fiscal expenditure, hiring, or legal negotiations.
9. Members of the VA research community must report possible serious or continuing non-compliance with VA or other federal requirements related to human research or with IRB requirements or determinations to the Associate Chief of Staff for Research and Development and the IRB within five business days after becoming aware of it.

III. REFERENCES



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|--|-------------|--------------------------|
| Policy Name: Suspension or Termination of IRB-Approved Research Policy and Procedures | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 2 | Section: HRPP 4.9 |
| Replaces Policy: 08/08/2013 | | |

I. POLICY

A. Introduction

This section details the policy and procedures established at MUSC for evaluating IRB-Approved research for possible suspension or termination to comply with the regulatory requirements in 45 CFR 46.103(b)(5)(ii) and 21 CFR 56.108(b)(3) requiring IRBs to have written procedures ensuring prompt reporting to the IRB, appropriate institutional officials, Office for Human Research Protections, and, when applicable, the Food and Drug Administration (FDA), any suspension or termination of IRB approval.

B. MUSC grants the IRB authority to suspend, or terminate approval of human research that is not being conducted in accordance with regulatory requirements of the IRB, institution, state and federal agencies. Such actions may be based on IRB determination of unanticipated problems involving risk to participants, study staff or others. Study termination may also occur for serious or continuing non-compliance or other findings arising from continuing reviews, information from medical literature and/or subject complaints or if the research has been associated with unexpected serious harm to participants.

C. Suspension or termination of IRB approval will generally be determined by a convened IRB. Under emergency circumstances, a board Chair, Vice-Chair or ORI director may immediately suspend a human research protocol. At the next convened IRB meeting, the matter will be reviewed by full board. Actions which the board may take include:

1. lifting the suspension,
2. continuing the suspension or
3. terminating the study.

D. Suspensions and terminations do not include:

Interruptions in research resulting solely from the expiration of a protocol approval period.

E. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. DEFINITIONS

Definitions for the following terms used in this section may be found in HRPP Program Guide Section 1.3 – Definition of Terms:

- A. Sponsored-Imposed Hold**
- B. Suspension of IRB Approval**
- C. Termination of IRB Approval**

III. PROCEDURES

- A.** In circumstances of major concern and with sufficient evidence, the IRB will notify the investigator of the suspension or termination of the human research protocol, possible remediation and of the time and date of the next convened IRB meeting where the protocol will be discussed.
- B.** On occasion, a sponsor may notify the PI of intent to suspend a study. Such sponsor-imposed holds may be made for interim data analysis; inadequate drug availability; response to DSMB report/recommendation; or a pre-planned stopping point, as well as for changes in the potential risk-benefit ratio for participants.
- C.** Following determination of sponsor-imposed hold, suspension or termination, the IRB will take the following actions:
 - 1. ensure that current subjects are notified of the hold, suspension or termination of the study through communication which receive IRB approval;
 - 2. ensure that procedures for withdrawal of enrolled subjects consider the rights and welfare of the subjects, making arrangements for clinical medical care, and/or transfer to another investigator for continued research treatment;
 - 3. ensure the method of informing current participants of the hold, suspension or termination is appropriate to the circumstances (in person contact, telephone call, email, or letter);

4. ensure that subjects are informed of any follow-up procedures permitted or required by the IRB;
5. ensure that any reportable adverse events/unanticipated problems involving risks to subjects or others are reported to the IRB and the sponsor when follow-up of subjects is permitted or required by the IRB and
6. for suspensions or terminations of VA research, the IRB will report the suspension or termination to the local VA facility.

D. Reporting Requirements

1. Whenever the IRB suspends or terminates a research protocol, the IRB Chair will submit a written report to the Organizational Official(s) copied to the Principal Investigator within 10 working days after review of the event by the convened Board. This report will include:
 - a) title of the study;
 - b) the name of the Principal Investigator;
 - c) number assigned by the IRB and any numbers assigned by another agency/sponsor;
 - d) the IND or IDE number if applicable;
 - e) the nature of the event; and
 - f) the findings of the IRB; actions taken by the PI, and/or the IRB to address the issue.
2. The Organizational Official(s) will review the action and discuss the report with the IRB chair and the Director of the Office of Research Integrity. The Organizational Official will notify OHRP, the FDA if appropriate, the sponsor, and other agency officials as appropriate within 30 working days of receiving the Chair's report.
3. If the research study is a VA protocol, any termination or suspension of research (e.g., by the IRB or other research review committee, or by the Associate Chief of Staff for Research or other VA facility official) related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others, must be reported in writing within five business days after the termination or suspension occurs to
 - a) the Associate Chief of Staff/Research & Development,

- b) the Medical Center Director (responsible for reporting to the Office of Research and Development, The Regional Office of Research Oversight and, if the report involves violations of information security requirements, the Information Security Officer),
- c) the Research and Development Committee,
- d) other relevant research review committees, and
- e) the VA Privacy Office (when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information). VA policy for reporting to the VA Office of Research Oversight will be followed.

III. REFERENCES

- A. [45 CFR 46](#)
- B. [21 CFR 56](#)



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|--|-------------|---------------------------|
| Policy Name: Data and Safety Monitoring Plans | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 4.10 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

Investigators develop data and safety monitoring plans as a mechanism for assuring the safety of human subjects and human research data, the validity of data, and the appropriate termination of studies. The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research, clinical research, or clinical investigations funded by the National Institutes of Health (NIH) or regulated by the Food and Drug Administration (FDA)..

B. Scope

This policy specifies requirements for appropriate use and establishment of a data and safety monitoring plan for clinical research protocols to ensure the safety of subjects, the accuracy of data, and the appropriate termination of the study.

C. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html))

II. DEFINITIONS

The definitions for the following terms used in this document may be found in the HRPP Program Guide Section 1.3 - Definitions of terms:

- A. Data and Safety Monitoring Plan**
- B. Data and Safety monitoring Board**

III. GUIDANCE ON DATA AND SAFETY MONITORING PLANS (DSMPs)

- A.** A Data and Safety Monitoring Plan is intended to assure the safety of the human subjects, and the validity of the data generated. The essential elements of the plan include:
 - 1. What data is to be monitored
 - 2. Who is responsible for monitoring and how often
 - 3. Reporting plan for communicating findings to IRB/Sponsor/Federal Agencies
 - 4. Reporting plan for adverse events
 - 5. Endpoints Proposed
- B.** A Data and Safety Monitoring Plan must appropriately consider several criteria including the potential risks, nature, size, and complexity of the research protocol, as well as the subject population. A DSMP is commensurate with the risks involved with the investigation and can involve the principal investigator submitting an annual safety and adverse event report to the IRB, or establishing a formal Data and Safety Monitoring Board (DSMB).
- C.** All multi-site clinical trials, all investigator-initiated Investigational New Drug trials, and all investigator-initiated Investigational Device trials involving interventions that entail potential risk to the participants must have a DSMB included in the Data and Safety Monitoring Plan. The IRB will review and approve the adequacy of Data and Safety Monitoring Plans.
- D.** A DSMB is a formal committee that is established specifically to monitor data throughout the life of a study to determine if it is appropriate, from both the scientific and ethical standpoint, to continue the study as planned. A DSMB may consist of as few as 3 members, but this number should be large enough to include a representation of all needs/skills and experience. The membership of the DSMB cannot have any actual or perceived conflict of interest associated with the study.

IV. PROCEDURES

- A.** The principal investigator will submit a detailed Data Safety and Monitoring Plan as part of the protocol submission to the IRB. If the Data

Safety Monitoring Plan includes a DSMB, the following should be considered regarding DSMB composition: relevant expertise, experience in research, experience as a member of other DSMBs, and a lack of conflict.

- B.** The IRB will review the plan in conjunction with the protocol review to determine the adequacy of the plan to minimize risks to subjects and to support data integrity including the adequacy of interim reporting to the IRB.
- C.** Any modifications in the plan required by the IRB will be communicated in writing to the principal investigator.
- D.** The principal investigator is responsible for submitting the DSMB reports at the time the reports are available to the Investigator, regardless of the timing of the report in relation to the continuing review of the study. These reports should follow the timeframe as specified in the IRB approved protocol.

V. REFERENCES

- A.** [NIH Policy for Data and Safety Monitoring](#)
- B.** [Further Guidance on a Data and Safety Monitoring for Phase I and Phase II Trials](#)



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|---|-------------|---------------------------|
| Policy Name: Human Gene Transfer Studies Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 6 | Section: HRPP 4.11 |
| Replaces Policy: Effective 12/01/2009 | | |

I. POLICY

A. Introduction

Clinical trials involving the transfer of genes into humans must adhere to the same regulations, fulfill the same requirements, and follow the same guidelines as all other human research studies.

B. Regulations

Regulations and guidelines are set out in 45CFR46, 21CFR50, 21CFR56, and other documents from the Office for Human Research Protections (OHRP) and FDA. Additional institutional policies and procedures, local, and/or state laws and federal regulations and guidelines may also be applicable.

C. Specific Guidelines

1. In addition, human studies involving the transfer of genes must also follow the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*. These Guidelines outline responsibilities of institutions, the Institutional Biosafety Committee (IBC), and principal investigators performing this research. If an institution receives NIH funds for recombinant DNA (rDNA) research, all human gene transfer trials at that institution are subject to these Guidelines regardless of the funding of the project.
2. Section III-C of the *NIH Guidelines* covers the basics regarding "Experiments that Require Institutional Biosafety Committee and Institutional Review Board Approvals and Recombinant DNA Advisory Committee (RAC) Review before Research Participant Enrollment". Appendix M, added in 1990, includes additional information on considerations for the design of these protocols and their submission to the NIH Office of Biotechnology Activities (OBA). Section IV IV-B-7-c and -e describe aspects of the responsible conduct of research involving rDNA molecules that must be followed by both basic and clinical researchers.
3. The RAC page <http://oba.od.nih.gov/rdna/rdna.html> on the NIH/OBA web-site provides further assistance with these protocols

in which recombinant DNA molecules are transferred into one or more human research participants. Included are links to:

- a) NIH Guidance on Informed Consent for Gene Transfer Research that can be used by both investigators and the Institutional Review Board for Human Research (IRB);
- b) FAQs on the NIH review process for these trials that includes sections on the NIH, RAC, and submission of protocols; and
- c) May 28, 2002 reminder re: compliance with the *NIH Guidelines* (All of these divisions are available for consultation on design, methodology, statistics, and ethical issues).

II. PROCEDURES

A. General Overview of the Submission and Approval Process

1. The primary investigator i.e. principal investigator (PI) for an original human gene transfer protocol submits Appendix M of the *NIH Guidelines* and other supportive documentation to the RAC for a determination. After review the RAC may notify the PI either that the trial may proceed without additional review or that it will need to be reviewed at a public session. In the first case, any feedback sent to the PI is also available to other investigators, sponsors, the IRB, and the IBC upon request. If there is a public review, a summary letter is sent to the PI, IRB, IBC, and FDA.
2. At the Primary Investigator's institution, IBC and IRB applications may be submitted for review either before or after RAC review. No final decision may be made on IBC submissions until the RAC recommendations are received. Likewise, no final approval may be made on IRB submissions until approval from the institutional IBC is received. The IRB may review the protocol before or after RAC review.
3. Principal investigators for the same trial at an added clinical site (i.e. Secondary investigators) do not need to resubmit Appendix M to RAC. Information on the RAC review process and outcome must be submitted to the IBC at any clinical site to be added as part of the approval process at that site.

B. Initiation of the Human Gene Transfer Trial

1. In the cover letter to NIH/OBA that accompanies Appendix M for original gene transfer submissions, the principal investigator(s)

must identify the IBC and IRB at the proposed clinical trial site(s) that are responsible for local review and approval of the protocol.

2. According to the *NIH Guidelines*, participants cannot be enrolled in the trial until RAC review is complete and IBC, IRB, FDA, and other applicable regulatory authorizations are obtained.
3. If a clinical site is added to a trial that has already been approved by the RAC, the necessary approvals must be obtained from the institutional IBC and IRB at the additional site before enrollment may occur

C. Reporting Requirements

1. Appendix M-I-C of the *NIH Guidelines* specifies reporting requirements that must be fulfilled by the primary investigator, the individual who made the original submission to the RAC for review, as well as any secondary investigators who are responsible for the conduct of the trial at any additional clinical sites. Both primary and secondary investigators may designate another party e.g. the corporate sponsor or the primary investigator to complete the reporting requirements (initial, annual, and safety)
2. With respect to the IRB, the primary investigator(s) must submit a copy of the approved protocol, a copy of the approval, and a copy of the informed consent document to the NIH/OBA no later than 20 days after enrollment of the first participant.
3. Within the same time frame, a copy of the IBC approval must also be submitted to the NIH/OBA.
4. Other documentation that must be submitted for the initiation of a gene transfer clinical investigation is detailed in Appendix M-1-C-1.
5. Documentation to be submitted prior to any enrollment at additional clinical trial sites is listed in Appendix M-1-C-2. At MUSC, the IRB Program Manager will send the IRB approval and IRB approved informed consent document to the NIH OBA prior to their release to the MUSC principal investigator for the trial.
6. Investigators, both primary and secondary, for trials conducted at MUSC, may also be required by the MUSC IBC to submit additional reports to the IBC including internal adverse events at the same time that they are submitted to the IRB and safety reporting involving health care workers and other MUSC personnel that may be related to the study agent.

D. Roles of Institutional Entities in Gene Transfer Trials at MUSC

1. MUSC Office of Research and Sponsored Programs (ORSP)
 - a) Principal investigators record the proposed involvement of human participants in item 8. of the electronic Proposal Data Sheet (ePDS). They record use of microorganisms, recombinant DNA, biotoxins, and Select Agents in section 11. The IBC administrator is able to access these sheets and the corresponding proposals for review in conjunction with the processing of IBC applications associated with gene transfer clinical trials.
 - b) ORSP Grants Administrators can access eIBC approvals and applications/registrations on ERMA for review in conjunction with the processing of applications associated with gene transfer clinical trials.) The ORSP Policies and Procedures Manual includes the roles and responsibilities of PIs including the need to obtain IBC approval for research involving recombinant DNA.

2. MUSC Office of Research Integrity - Institutional Review Board for Human Research (IRB)
 - a) The application checklist portion of the eIRB application has an entry for "Recombinant DNA, gene transfer, infectious agents, select agents or microorganism exposure to human subjects." If this box is checked, the IBC administrator is notified electronically that this study is available for examination. The purpose of the examination is to determine if IBC review and approval is needed for the study.
 - (1) If unnecessary, a statement to this effect will be entered in the "Ancillary Committee Comment" textbox.
 - (2) If necessary, Committee review will occur and the decision noted under "Ancillary Committee Comment".
 - b) IRB administrators would be alerted too of the need follow up with the IBC administrator regarding status of the IBC application for approval and with any questions that they or the Board itself may have regarding biosafety issues. They may request that a representative of the IBC attend the IRB meeting at which the human research application is discussed. Gene transfer trials are subject to the same

human research regulations and guidelines as any other clinical trials.

- 1) Continuing reviews must be submitted at least annually.
- 2) Internal adverse events and other safety reports provided by Data Safety Monitoring Boards (DSMBs) must be submitted by the PI according to institutional (includes federal) requirements. Copies of reports received from DSMBs for all gene transfer clinical trials should be provided to the IBC for its review.
- 3) Amendments must be filed as indicated. The IRB administrator will notify the IBC administrator if any amendments are submitted that are pertinent to biosafety issues e.g. change of personnel and change of rooms. These will then be forwarded to the IBC for review as indicated.

3. MUSC Office of Research Integrity - Institutional Biosafety Committee (IBC)

- a) According to the *NIH Guidelines*, Section IV-B-6, when an institution participates in or sponsors rDNA research, the institution must ensure that: (i) the IBC has adequate expertise and training (using *ad hoc* consultants as deemed necessary) and (ii) all aspects of Appendix M have been appropriately addressed by the PI before it is submitted to NIH/OBA.
- b) Approval must be obtained from the IBC at each institution at which the recombinant DNA material will be administered to humans. This includes those institutions at which the primary investigator will be heading the clinical trial and those additional clinical sites at which secondary investigators will be overseeing the trial.
- c) The IBC is responsible for reviewing the application to use materials that are proposed for use in a clinical trial according to the directives in the *NIH Guidelines*. In addition, the IBC must perform continuing reviews of the use of these materials.
- d) Section 4 Recombinant DNA of the MUSC IBC application inquires in section 4h1 if humans will be exposed *in vivo* to the recombinants named in the application. A text box is available in section 4h4 to record the HR#/PRO# of the study. At this point on the form, the investigator is advised to

refer to the *NIH Guidelines* especially Appendix M and links available at the NIH/OBA web-site.

The IBC administrator is alerted if section 4h1 and/or 4h4 indicates that clinical trials are planned and can then coordinate review efforts with the IRB administrator for the human research application.

- e) The IBC administrator will notify the IRB administrator for the human research application when IBC approval has been obtained and when it is released to the principal investigator. In addition, the IBC administrator will provide the IRB with a copy of the approval letter and, if requested, a copy of the IBC application and any other materials that may be requested.
- f) The IBC provides the following for MUSC Principal Investigators for gene transfer trials:
 - (1) Initial instructions for IBC applications that includes a list of uploads to be submitted as part of the IBC application.
 - (2) A list of reporting requirements for MUSC investigators serving as secondary investigators for gene transfer clinical trials for which MUSC is an added clinical site.
- g) For continuing review, the IBC requires completion of the continuing review form and submission of the same annual reports and other safety reports that are submitted to the IRB for their continuing review process. In addition, the IBC may request that additional information be submitted.
- h) The IBC will review the IBC Termination Form to be submitted by the Principal Investigator at the conclusion of the clinical trial for proper disposal or transfer of any recombinant DNA materials remaining. This form will be copied to the institutional Biosafety Officer (BSO).
- i) The IBC administrator will provide the IRB administrator with pertinent communications and updates on the IBC application/registration associated with each gene transfer clinical trial.
 - (1) The IBC will review

- (a) eIRB initial submissions that involve gene transfer and
- (b) amendments to IRB approved gene transfer studies that could impact biosafety.

4. MUSC University Risk Management/Occupational Safety and Health (OSH)

- a) The institutional Biosafety Officer (BSO) will conduct an inspection of all areas to be used in the storage, processing, or administration of the materials to be used in the clinical trial. If there are any deficiencies, s/he will inform the PI so that they can be corrected. In addition, the BSO will review the safety protocol to be used for this study and request revisions as needed. Once the safety protocol is satisfactory, the BSO will request that it be signed by all individuals who will come in contact with the recombinant material to be used and submitted to OSH. A satisfactory laboratory inspection with correction of any deficiencies and submission of signed, satisfactory safety protocol are necessary for final approval and release of the IBC submission. The BSO will provide written documentation to the IBC administrator when these requirements have been achieved.
- b) Rooms and other areas to be used in the study as identified in section 2a of the eIBC application must be inspected at least every two years by the BSO. If the PI wants to use new space, it must be inspected and a satisfactory inspection achieved before it is used in the study. An amendment requesting addition of the new space must be approved by the IBC. It may also be necessary for equipment e.g. biosafety cabinets to be certified if they are new, have been moved, or possibly have been damaged.
- c) The BSO's web-site should be accessed at <http://musc.edu/biosafety/HGT/SOP> for additional guidance on registering human gene transfer studies.

5. MUSC Medical Center

- a) There are two Medical Center Policies that specifically impact on gene transfer studies: PC-74(C-120) - Management of Gene Therapy and PC-90 (C-153)-Management of HCT/P (Human Cells, Tissues, or Human Cell or Tissue-Based Products) Based Therapy. Portions of

the policies including the IRB and IBC are summarized below.

- b) Policy PC-74 states that “All clinical trial protocols involving investigational gene therapy must be reviewed and approved by the Institutional Review Board (IRB) and the Institutional Biosafety Committee (IBC) before patient recruitment and protocol implementation.” Responsibility for education and training of the hospital personnel falls to the principal investigator “and will follow IBC policies”. The Infection Control Department (ICD) is responsible to establish guidelines and provide or monitor surveillance studies as recommended by the IBC and Infection Control Committee. Either the ICD or BSO can stop any study in which infection control is not being done according to recommendations of the IBC and Infection Control Committee.
- c) Policy PC-90 includes the two responsibilities of the ICD and BSO noted above for policy PC-74. It states that, “All clinical trial products involving investigational HCT/P therapy must be reviewed and approved by the IRB before patient recruitment and protocol implementation.” Additionally, Appendix A must be applied to the policy if “one or more HCT/Ps containing or associated with recombinant DNA” are used. Likewise, Appendix B must be applied if HCT/P is combined with one or more infectious substances as part of the therapy.

III. REFERENCES

- A. [45CFR46](#)
- B. [21CFR50](#)
- C. [21CFR56](#)
- D. [NIH Guidelines for Research Involving Recombinant DNA Molecules \(NIH Guidelines\)](#)
- E. [Recombinant DNA Advisory Committee \(RAC\) of the NIH Office of Biotechnology Activities \(OBA\) web-site](#)
- F. Medical University of South Carolina Policies
 - 1. [PC-74 \(New\) C-120 \(Prior\) –Management of Gene Therapy](#)
 - 2. [PC-90 \(New\) C-153 \(Prior\) - Management of HCT/P \(Human Cells, Tissues, or Human Cell or Tissue-Based Products\) Based Therapy](#)



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|--|-------------|---------------------------|
| Policy Name: Clinical Trials Registration Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 3 | Section: HRPP 4.12 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

The FDA and the International Committee of Medical Journal Editors (ICMJE) each have their own registration requirements. While some of the requirements overlap, there are also significant differences. In order to comply with new laws and preserve the ability to publish in ICMJE journals **both** sets of requirements must be met.

B. FDA Clinical Trials Registration

In September 2007, the FDA Amendment Act expanded the ClinicalTrials.gov requirements previously established in the 1997 FDA Modernization Act (FDAMA) requiring registration of trials testing drugs for life threatening diseases and conditions. This new FDA policy:

1. Expands the types of trials that must be registered to all clinical trials for drugs, devices, and biologics with the exception of Phase I drug trials and small device feasibility studies.
2. Increases the data elements that must be included in the registration.
3. Results of trials must be registered within 3 years of the completion of the primary aim of the study. The process for registration of results is in development

C. ICMJE Clinical Trials Registration

Effective July 1, 2008, the ICMJE revised its policy of June, 2005. The new policy requires the registration of all clinical trials including Phase I and pharmaco-kinetic trials. ICMJE defines clinical trials as:

1. Any human research project that prospectively assigns human subjects to an intervention or comparison group to study the relationship between a medical intervention and a health outcome.

2. ICMJE Signatories: New England Journal of Medicine, Journal of the American Medical Association, Annals of Internal Medicine, The Lancet, The Medical Journal of Australia, The New Zealand Medical Journal, Norwegian Medical Journal, Canadian Medical Association Journal, Croatian Medical Journal, Dutch Journal of Medicine, Journal of the Danish Medical Association

II. PROCEDURES

A. Updating Registrations:

Once a trial is registered, both the FDA and the ICMJE require that registrations be updated as follows:

1. FDA updating requirements:
 - a) Information must be updated at least every 12 months
 - b) Additionally, the registry must be updated within 30 days of any changes in recruitment status or completion of study.
2. ICMJE requires updating study information every six months.

B. Who is responsible for registration?

1. For FDA Registration

The sponsor of the drug or device clinical trial, as defined/identified under the FDA regulations, is responsible for registering the trial. This could be either the company or the investigator.

If the sponsor is the company, the company at its discretion, can delegate the principal investigator as the “responsible party.” This may only be done when “the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements” for submitting information under the law

2. For ICMJE Registration

While anyone involved in the clinical trial could register the trial, in practice this responsibility usually falls with the individual submitting the publication to the ICMJE journal, which is usually the Principal Investigator.

C. Deadline for Registration

Compliance with the ICMJE is only required if publication in one of the relevant journals is planned. In contrast, compliance with the FDA regulations is required for relevant trials. If there is any possibility of submission to an ICMJE journal for publication, ensure compliance with both registration requirements.

D. Registering a Study

The Medical University of South Carolina has established an online Information Sheet detailing the instructions for clinical trials registration. The following Account Application Process must be used for registration. The University has an organizational account with the ClinicalTrials.gov Protocol Registration System (PRS). To request an individual account to enter protocol information, use the following steps:

1. Send an email to ORSP@musc.edu and type "Request ClinicalTrials.gov account" in the subject line.
2. Enter your name and NetID (This will be your user name for the system.) in the subject of the email. You will be contacted when your account is activated.
3. You may request accounts for investigators and assistants. **Keep in mind that only the individual who created the record (the owner) has access to it.** You may preview and print it for checking and distribution. System administrators may also change ownership of the protocol but only the owner has access.
4. Once the account is established you may login in to the registration system using this URL for the PRS login <https://register.clinicaltrials.gov/>. Our Organization name for the login is: **MUSouthCarolina**
5. Once you are in the system, follow the directions to complete the protocol information.

III. Informed Consent Requirement

The Food and Drug Administration (FDA) is amending the current informed consent regulations (21 CFR Part 50) to require that informed consent documents and processes for applicable drug (including biological products) and device clinical trials include a specific statement that clinical trial information will be entered into a databank.

The compliance date of this final rule is March 7, 2012, for clinical trials that are initiated on or after the compliance date.

When seeking informed consent for applicable clinical trials, the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act.

The statement is: "A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

IV. REFERENCES

- A. [MUSC ClinicalTrials.gov Protocol Registration](#)



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|---|-------------|---------------------------|
| Policy Name: Privacy and Confidentiality | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 6 | Section: HRPP 4.13 |
| Replaces Policy: Effective 09/08/2011 | | |

I. POLICY

A. Introduction

All organizations involved in conducting human subjects research must ensure procedures are in place to protect the privacy of subjects and maintain the confidentiality of data.

B. Federal Regulations

The IRB will review proposed research activities in accordance with HIPAA privacy and security regulations at 45 CFR Parts 160, 164. The IRB will determine whether adequate procedures are in place to protect the privacy of participants and to maintain the confidentiality of the data in accordance with federal regulations at 45 CFR 46, 21 CFR 56 and 38 CFR 16, as applicable, or the regulations of federal agencies and applicable state laws.

C. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage](http://research.musc.edu/ori/irb/resources.html) (<http://research.musc.edu/ori/irb/resources.html>)

D. IRB Responsibilities

The IRB must review how investigators are obtaining information and the participant's expectations of privacy regarding the information obtained by the investigator. Investigators must have appropriate authorization to access the subject's or the participant's information.

The IRB must also determine if appropriate protections are in place to minimize the likelihood that confidential information will be divulged. The level of confidentiality should be commensurate with the potential harm from inappropriate disclosure

E. Pertinence of Data Collected

Only data pertinent to answering an IRB approved research question will be collected for human research purposes. When research involves the collection of personally identifiable, sensitive data, consideration should be given regarding the need for obtaining a Certificate of Confidentiality. As detailed on the US DHHS *Certificates of Confidentiality Kiosk Website*, "Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure." Further information may be obtained by reference to the website listed in the References section of this policy guide

F. Prohibition on Use of Subject Identifiers

Unless explicitly approved by the IRB, subject identifiers must not be used as a code to link protected health information to individual subjects. For example, use of consecutive numbers is acceptable.

The following are considered subject identifiers not to be used as a code to link information to a participant:

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: a) the geographic units formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and b) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000).
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

G. Requirements for Appropriate Data Storage Techniques

Electronic research data that is individually identifiable should be, to the extent possible, only stored in appropriately protected repositories/databases with formally established and authorized information systems. In exceptional circumstances, there may be an unavoidable requirement to store electronic research data on an end-user device (including but not limited to: desktop computers, laptops or tablets). In these circumstances, the Investigators shall meet the baseline data protection requirements outlined in the MUSC information security-data protection policy (<http://www.musc.edu/security/policy/data-protection.shtml>).

For example, if a database containing identifiers is stored anywhere other than an MUSC network drive, the database must be encrypted using the OCIO approved encryption technology.

<http://www.musc.edu/infoservices/endpointsecurity/encryption.htm>

Ideally, hardcopy documents with identifiers, such as consent forms and HIPAA authorizations should be stored in a physically separate and secure location from the research data files and associated through an approved linking code.

If data that includes participant identifiers must be transmitted over an untrusted network (including any public network), then the data must be encrypted during transmission, using for example SSL encryption, a secure file transfer protocol, or MUSC SecureMail. For more information on MUSC SecureMail, please see:

<http://www.musc.edu/infoservices/exchange/securemail.html>

Participant identifiers and contact information may only be distributed outside MUSC with mechanisms including, but not limited to: specific informed consent of the participants and IRB approval, via Business

Associates Agreement and/or Data Use Agreement. *For more information please contact the IRB*

H. Study Monitor Access to Research Participant's Study and Medical Records

When site visits are conducted by study monitors, investigators are obligated to maintain the confidentiality of participants enrolled in the study. Access to confidential information must be controlled and managed in a way that does not permit unauthorized access. Access must be authorized by the IRB as part of an approved and authorized by the research participant. Unsupervised access to the complete medical record, access to databases, and access to any other electronic medical record source that contain Protected Health Information which is not related to the research is not allowed.

Study Monitors are not permitted to conduct their visits in an area where unrelated case report forms with subject identifiers and/or other privileged study information (e.g. study materials or trial data belonging to other sponsors) or patient information might be viewed.

II. DEFINITIONS

Definitions of the following terms used in this section may be found in Section 1.3 - Definitions of the MUSC HRPP Program

- A. Privacy**
- B. Confidentiality**
- C. Sensitive information**
- D. Private information**
- E. Identifiable information**

III. PROCEDURES

- A.** The principal investigator will describe the nature of the data to be collected and the plan to protect participant privacy and maintain data confidentiality in the research protocol. This description will include identification of who will have access to data collected, how information will be disclosed, the methods of accessing, storing, and how data will be safeguarded to maintain confidentiality. Any risk to disclosure of identifiable private information of participants and provisions to protect the participant's identity during the course of the research must also be described.

- B. When research involves activities or information of a particularly sensitive or potentially damaging nature, the IRB, in collaboration with the principal investigator, will determine whether the investigator should seek a Certificate of Confidentiality.
- C. The informed consent document and the HIPAA Authorization will specify what collected data will be shared with others, how these data will be shared, and with whom the data will be shared.
- D. The IRB will determine if the data being collected are relevant to answering the research question and the adequacy of the confidentiality and privacy protection plan.
- E. Clinical Databases - Requirements for IRB Approval & HIPAA Authorization
 - 1. Clinical Databases
 - a) Developed for clinical purposes of tracking and monitoring care (not subject to IRB review or approval).
 - b) Allowed by the covered entity's HIPAA notice of privacy practices.
 - c) If an individual wants to query the database for research:
 - (1) IRB approval is required;
 - (2) HIPAA de-identification certification or a HIPAA waiver* is required and;
 - (3) research must present **minimal risk** to privacy of the individuals.
 - 2. Clinical Databases with Possibility of Future Research
 - a) Developed for clinical purposes of tracking and monitoring care but may be used for research purposes at a later time.
 - b) Allowed by the covered entity's HIPAA notice of privacy practices.
 - c) If an individual wants to query the database for research:
 - (1) IRB approval is required;
 - (2) HIPAA de-identification certification or a HIPAA waiver is required; and

- (3) research must present **minimal risk** to privacy of the individuals.

3. Clinical Databases for Research

- a) Developed for the express purpose of research with specific research questions not identified as of yet.
- b) Requires IRB approval **before** the database is initiated.
- c) Requires informed consent and HIPAA authorization from patients/participants to be included in the research database.
- d) When an individual wants to query the database for research:
 - (1) IRB approval is required relative to the specific protocol, and
 - (2) a HIPAA authorization or a waiver of authorization is required.

Federal guidance regarding the HIPAA regulations states:

“When a (research) database is maintained, any use of the database for a particular research purpose will require a new, protocol-specific authorization or waiver of authorization as well as a research protocol specifically describing the new study which must be approved by the IRB.”

* A HIPAA waiver can only be approved if the IRB assesses the PHI to be used as presenting no more than minimal risk to the privacy of participants. A HIPAA waiver may limit use of the available data; the IRB decides which of the available data elements may be used.

F. Security Considerations in an Electronic Data Protection Plan. A research study using identifiable protected health information must specify an Electronic Data Protection Plan and contain the following elements.

1. Determination of where the data will be stored
 - a) Desktop Computer - computer- security issues must be addressed
 - b) Network Drive - Downloaded/downloadable data

- (1) Frequency and timing of downloads
- (2) Purpose for Downloads
- c) Mobile Media - security issues for each type of mobile media must be addressed
 - (1) Laptop computer
 - (2) PDA
 - (3) Thumb Drive
 - (4) Portable hard drive
- d) Permanent Media- security issues for each type of media must be addressed
 - (1) CD
 - (2) DVD

G. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

VA investigators must follow the procedures established in VHA Handbook 1200.12 "Use of Data and Data Repositories in VHA Research" for the use of data for VHA research purposes, the storage of VHA research data and the development of VHA research data repositories.

H. National Institute of Justice (NIJ) Protocol

1. All projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer.
2. All researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.

I. Bureau of Prisons Protocols

1. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
2. Except as noted in the consent statement to the subject, the researcher must not provide research information that identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
3. Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
4. If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

IV. REFERENCES

- A. [U.S. DHHS Certificates of Confidentiality Kiosk](#)
- B. HIPAA - <http://www.hhs.gov/ocr/privacy/>
- C. <http://www.charleston.va.gov/research/Research.asp>
- D. MUSC OCIO - <http://www.musc.edu/security/policy/data-protection.shtml>



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|---|-------------|--------------------|
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| Replaces Policy: 11/01/2010 | | |

I. INTRODUCTION

Federal regulations require the IRB to review proposed changes in any research activity and to ensure that the investigator does not initiate such changes in approved research without IRB review and approval except when necessary to eliminate apparent immediate hazards/risks to the subject. Research activity includes all aspects of the conduct of the research study (e.g., recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc.) and all of the information outlined in the IRB application/protocol reviewed and approved by the IRB. Most of these changes are submitted as amendments which undergo expedited or full committee review.

II. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

III. DEFINITIONS

A protocol deviation is any variance from the protocol involving a subject or subjects that is not approved by the IRB prior to its initiation or implementation, and occurs when a member of the study team departs from the IRB-approved protocol in any way **without the investigator first obtaining IRB approval**.

Deviations range in seriousness according to how the changes may impact subject safety, the degree of noncompliance with federal and state regulations, and the degree of foreknowledge of the event. Anticipated changes to a protocol should always be reported before the event occurrence unless an immediate change is necessary to protect subject safety. Note that repeated deviations of the same type may be an indication that an amendment is needed to permanently change study criteria.

Examples of deviations may include, but are not limited to:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures;

- Enrollment of a subject who did not meet all inclusion/exclusion criteria;
- Performing study procedure not approved by the IRB;
- Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable) the sponsor;
- Failure to perform a required lab;
- Drug/study medication dispensing or dosing error regardless of whether a subject was negatively impacted;
- Study visit conducted outside of the time frame listed in the IRB-approved protocol;
- Failure to follow data and safety monitoring plan;
- Implementation of unapproved recruitment procedures; individual obtaining informed consent not listed on IRB approved study personnel list;
- Missing original signed and dated consent form (only a photocopy available);
- Missing pages of executed consent form;
- Inappropriate documentation of informed consent, including:
 - missing investigator signature;
 - copy not given to the person signing the form;
 - someone other than the subject dated the consent form;
 - initial's missing from each page – or from HIPAA privacy notice;
- Use of invalid consent form, i.e., approved consent form without IRB approval stamp or outdated/expired consent form;

What are NOT considered to be protocol deviations?

Changes or departures from the study design or procedures that are due to a study participant's non-adherence are not considered to be protocol deviations and should not be submitted to the IRB. However, study participant non-adherence to the study design and/or procedures should be documented in the research records and should be reported to the IRB as an incident if the event adversely impacts the study participant's safety or well-being, or if a pattern of protocol departures indicate a need for changes in the protocol or informed consent document(s).

Examples:

- Study participant did not return for a scheduled study visit
- Participant refused a blood draw

A Single Patient /Subject Exception is when an investigator anticipates a one time, significant, time-sensitive intentional action or process that departs from an IRB approved protocol. In this situation he or she may request that a one time exception be granted by the IRB. The Principal Investigator may submit an amendment request for a one-time enrollment exception as a protocol modification request to the IRB. Obtaining prior approval for an enrollment

exception modification avoids a protocol deviation. An enrollment exception request applies only to a single individual. Such a request should be rare and justified in terms of serving the best interests of the potential study participant. The enrollment exception amendment request will be referred to the appropriate Chair who will evaluate the level of IRB review required. An enrollment exception usually requires the additional approval of the study sponsor.

The IRB approval should note that this modification applies to one subject only and not to the study as a whole.

IV. IRB NOTIFICATION OF PROTOCOL DEVIATIONS

The Principal Investigator submits all protocol deviations that occur during the course of a study to the IRB immediately upon discovering them and no later than 10 working days following the discovery. A corrective action plan must be submitted with the protocol deviation. For protocols in the ERMA system (HR#), the Principal Investigator completes and submits the IRB Protocol Deviation Report Form. For protocols in the eIRB system (PRO#), the Principal Investigator completes and submits a reportable event.

The Principal Investigator also reports all protocol deviations to the sponsor, if applicable, following the sponsor's requirements. *Note:* The above definitions may not match the Sponsor's definition.

With one exception, regulations require prior IRB approval for proposed changes in the ongoing conduct of research studies. The one exception is when changes to the protocol are necessary to eliminate or reduce an apparent immediate hazard to the safety of research participants. Under this one exception, regulations allow changes to be initiated without prior IRB approval. However, please note that such changes must be reported to the IRB as an incident within 5 working days of initiating the changes in the study procedure(s). The incident report should consider whether an appropriate modification to the study application/protocol and/or consent document(s) is necessary.

V. IRB AND OTHER INSTITUTIONAL RESPONSIBILITIES

IRB staff member screens the IRB Protocol Deviation Report Form for completeness and accuracy. If the submission is incomplete, IRB staff member requests additional information from the Principal Investigator, which is returned to the IRB upon completion.

The IRB staff member sends the completed IRB Protocol Deviation Report Form with any applicable attachments to the IRB Chair or his/her designee.

The IRB Chair makes a determination regarding whether the deviation appears to meet the institutional definition of an Unanticipated Problem involving risk to

participants or others and/or an instance of Serious or Continuing Noncompliance. If the deviation is minor, the IRB Chair or his/her designee conducts review using expedited procedures.

If the protocol deviation report undergoes Full Board review, the IRB Chair has the option to invite the investigator to attend the meeting to answer any questions or concerns that the IRB may have concerning the protocol deviation.

If the IRB determines that the deviation is reportable to external agencies, the IRB Chair will promptly notify the Institutional Official (IO) and submit a written report to the IO within 10 working days after review of the event by the convened Board. The Institutional Official will review the event and discuss the report with the IRB. The Institutional Official will notify OHRP, the FDA (if appropriate), the sponsor, and other agency officials as appropriate with 10 working days of receiving the Chair's report.

If the research study is a VA protocol, and the IRB determines the deviation is reportable to external agencies, the following will be notified: 1) The Associate Chief of Staff/Research & Development: 2) the VA Privacy Office (when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information). VA policy for reporting to the VA Office of Research Oversight will be followed.

VI. REFERENCES

- [45CFR46.103\(b\)\(4\)\(iii\)](#)
- [21CFR56.108\(a\)\(4\)](#)
- IRB Protocol Deviation Report Form



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|--|--------------------|---------------------------|
| Policy Name: Application of Industry E6 Good Clinical Practice Requirements | | |
| Approved | | |
| Effective Date: 01/31/2012 | Page 1 of 2 | Section: HRPP 4.15 |
| Replaces Policy: | | |

I. POLICY

A. Introduction

In 1996, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) developed “Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance” [ICH GCP guidance (E6)]. This document provides a unified standard for the European Union (EU), Japan, and the United States to comply with the regulatory authorities in these countries.

B. Assessment

The MUSC IRBs comply with ICH GCP guidance (E6) only to the extent that it is compatible with FDA and DHHS regulations. GCP standards contained in the ICH GCP guidance (E6) document are not regulatory requirements in the United States.

However, selected industry-sponsored studies may require institutional adherence to ICH GCP guidance (E6) *beyond that required by FDA and DHHS.*

If the contract requirement for ICH GCP guidance (E6) is confirmed, the Associate Provost for Research and the Director of the Office of Research Integrity are notified for further review.

If the PI and sponsor attest to the requirement for ICH standards, the APR will consider approval for IRB review in compliance with the ICH-GCP guidance (E6).

II. DEFINITIONS

Definitions for the following terms used in this section may be found in HRPP Program Guide Section 1.3 Definitions of Terms:

A. Good Clinical Practice (GCP)

III. PROCEDURES

A. Investigator Responsibilities

1. Before the contract is finalized, the Principal Investigator will meet with the Associate Provost for Research in order to appreciate fully the additional requirements that adherence to ICH GCP (E6) will entail.
2. All study team members must complete the CITI module for ICH GCP (must be current within 3 years).
3. The PI must confirm that all ICH GCP standards will be followed during the research.
4. The PI must submit to the IRB any additional materials required by ICH GCP (e.g., CV).
5. The PI will assume responsibility for reporting requirements, including termination or suspension of the research study by the PI, sponsor, or IRB (see 4.12 of ICH GCP guidance E6).
6. Additional elements will be included in the informed consent document (see 4.8 of ICH GCP guidance E6).

The ICH GCP guidance E6 lists 20 required elements for consent forms used in studies of investigational pharmaceutical agents.

Note: The ICH GCP guidance E6 required elements for consent are not a regulatory requirement in the United States. FDA regulations on consent do not require all consent elements recommended by GCP guidance.

B. IRB Responsibilities

1. When evaluating study materials, IRB reviewers will take into account the additional requirements of ICH GCP.
2. The IRB will not release approval of documents until investigators have complied with the above procedures.

C. University Compliance Responsibilities

When auditing studies that require adherence to ICH GCP, University Compliance will follow a separate IRB approved checklist for ICH GCP requirements.

IV. REFERENCES

- A. [Guidance for Industry E6 Good Clinical Practice \(ICH GCP guidance \(E6\)\)](#)



| | | |
|---|-------------|--------------------------|
| Policy Name: Principal Investigator Responsibilities – Supervision of Staff and Protection of Subjects | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 3 | Section: HRPP 5.1 |
| Replaces Policy: Effective 01/27/2012 | | |

I. POLICY

A. Introduction

MUSC investigators are granted the privilege of conducting studies in human subjects under assurance to the government that research conducted at MUSC complies with regulations protecting human subjects. Therefore, the Principal Investigator (PI) is fully responsible for the human-subjects research under his/her direction. This responsibility includes the protection of human subjects and ensuring the research is conducted in an ethical manner and in accordance with all federal, state, and local laws and regulations, institutional policies, and requirements or determinations of the MUSC IRB. The Principal Investigator may delegate study tasks to other research team members but still maintains ultimate responsibility for the conduct of the study

Additional requirements of sponsors including Veterans Administration, Department of Energy, Department of Education, Department of Defense, Department of Justice may also apply.

All Principal Investigators and their staff involved with the human research protection program are expected to understand and apply their obligation to protect the rights and welfare of research participants.

B. PI Responsibilities for Supervision

When supervising the conduct of human subjects research, the PI is responsible for ensuring the following points:

1. Study personnel will have completed the mandatory educational compliance training on human research.
2. Study personnel have been appropriately trained to fulfill their role on the study including but not limited to obtaining informed consent, and conducting study procedures.
3. Study personnel follow the IRB-approved protocol.
4. A plan is developed and implemented for supervision and oversight of the research ensuring that there are sufficient study personnel and

resources for the study and that the degree of supervision is commensurate with the subject population and the type of research. Research should not begin unless adequate resources are in place to protect research subjects and should stop if the resources necessary to protect subjects become unavailable.

5. The protection of the rights, safety, and welfare of research subjects are addressed. Special attention must be given to vulnerable populations. Such protection includes the following:
 - a) The Principal Investigator must assure reasonable medical care is provided to a subject for any adverse event(s) that occur during the trial or within 30 days of the subject's completion of the trail if the adverse event is thought to be related to study participation.
 - b) The Principal Investigator must provide a plan for data and safety monitoring for any study that is greater than minimal risk.
 - c) Depending upon the type of research and the risk involved, the Principal Investigator should inform, (if agreed to by the participant) the subject's primary care physician about the subject's participation in the study.
 - d) Research subjects have access to qualified individuals to answer questions or provide care during the conduct of the research.
 - e) All members of the research team conducting the study adhere to the IRB-approved research plan.

C. Qualifications for Principal Investigator and/or Mentor designation

1. Full time faculty may serve as Principal Investigators and mentors.
2. Faculty, who do not meet the qualifications stated above, may 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.
3. MUSC trainees in good academic standing may function as Principal Investigators with the inclusion of a faculty mentor.
4. Non-faculty MUSC employees may function as Principal Investigators with the inclusion of a faculty mentor.

5. A Principal Investigator and the mentor are both responsible for the conduct of the human research. For studies in the ERMA system (HR#), these responsibilities are outlined in the IRB documents signed by the Principal Investigator and mentor. For studies in the eIRB system (PRO#), these responsibilities are on the Principal Investigator Assurance SmartForm page electronically signed by the Principal Investigator.

MENTOR RESPONSIBILITIES

1. The Mentor will review the study protocol prior to submission to the IRB to ensure that the study has a valid research question and the research procedures are sufficient to answer the research question.
2. The Mentor will meet with the Principal Investigator on a regular basis to monitor study progress.
3. If the Mentor will be unavailable for an extended period of time (e.g. on sabbatical or extended leave), s/he will arrange for an alternate faculty Mentor to assume responsibility during the absence. The Mentor will advise the MUSC IRB in advance by letter and change in personnel amendment of such arrangements.

D. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Researchers are responsible for communicating with the Program Officer of the Federal Funding Agency to ensure that all requirements of the Federal Funding Agency are met prior to starting an IRB approved study. Information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)) includes links to the regulations for the Federal Funding Agencies.

E. ICH – Good Clinical Practice (GCP)

The MUSC IRBs operate in accord with ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. GCP

standards contained in the ICH document are not regulatory requirements in the United States and vary from FDA and DHHS regulations. As such, the MUSC IRBs do not voluntarily agree to comply with all of the GCP statements unless requested to do so by sponsors as documented in contractual agreements. The MUSC IRBs comply with most aspects of ICH-GCP, and the MUSC policies, procedures and forms require investigators to comply with most ICH-GCP guidance. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage](http://research.musc.edu/ori/irb/resources.html) (<http://research.musc.edu/ori/irb/resources.html>).

II. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

III. PROCEDURES

- A. No research will be initiated without prospective IRB review and approval.
- B. The study protocol conforms to DHHS and where applicable, FDA regulations ([\[21 CFR 312\]](#) and [\[21 CFR 812\]](#)) and institutional policy for investigational drugs, biologics and devices.
- C. Principal Investigators must certify to the IRB that any changes in the approved research will not be initiated until the IRB has reviewed and approved these changes.
- D. Informed consent is obtained, when applicable, in accordance with IRB-approval.
- E. Promptly report to the IRB any serious or recurring problems, unanticipated problems involving risk to participants or others, or adverse reactions experienced by a subject.
- F. Promptly report to the IRB any problems related to the conduct of a study or subject participation (including those in the recruitment or consent process).
- G. Data and Safety Monitoring Board/Data Monitoring Committee or other monitoring group reports are submitted promptly to the IRB for review.
- H. The Principal Investigator must submit a continuing review application 30 days prior to expiration of IRB approval in accordance with IRB Policy.

- I. The Principal Investigator will report premature completion of a study to the IRB.
- J. A final continuing review report is submitted to the IRB when the research is completed or terminated prior to completion.
- K. The Principal Investigator must maintain an accurate and complete accounting of all investigational drug/device records, and clinical study materials received, dispensed, and returned to the Sponsor as required by the IRB, and when applicable, the sponsor or FDA. These records must be maintained in the study site regulatory binder for the required retention time.
- L. All records must be accessible for inspection and copying by authorized MUSC officials and federal representatives (including HHS, FDA, and VA) upon request.

IV. REFERENCES

- A. Guidance based on United States. U.S. Dept. of Health and Human Services, Food and Drug Administration, et al. [Guidance for Industry: Protecting the Rights, Safety, and Welfare of Study Subjects – Supervisory Responsibilities of Investigators](#). Draft Guidance May 2007



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|---|-------------|--------------------------|
| Policy Name: Principal Investigator Responsibilities - Recordkeeping and Record Retention Requirements | | |
| Approved | | |
| Effective Date: 12/01/2016 | Page 1 of 5 | Section: HRPP 5.2 |
| Replaces Policy: 01/27/2011 | | |

I. POLICY

A. Introduction

Principal Investigators are required to maintain complete and accurate regulatory documentation for clinical studies.

B. Guidance

This policy provides guidance to meet FDA federal regulations, and good clinical practice for appropriate documentation for human research studies.

In general, investigators should establish three sets of files for each study.

1. Regulatory documents
2. IRB Records and Correspondence
3. Individual subject files

C. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

II. PROCEDURES

The Principal Investigator's site file (regulatory binder) contains all required documentation to meet GCP compliance and regulations. The Principal Investigator is required to obtain and maintain these documents in a safe and secure place during the study and for the required retention period.

A. Regulatory Documents

The study regulatory binder must contain specific documents as noted below. Some documents that may be common to more than one study, such

as CVs and professional licenses, may be filed centrally; others may be stored electronically, and the location noted

1. Protocol: original version and all amended versions; all versions should be numbered and dated.
2. Signed and dated CVs for co-investigators documenting qualifications and eligibility to conduct the study and provide clinical management of research subjects.
3. Current licensure/certification for all professional study staff.
4. Study logs.
 - a) Screening log: captures all potential subjects who have been pre- screened for the study.
 - b) Enrollment log: captures all subjects who have signed an MUSC IRB approved consent form or, with IRB approval, have given verbal consent or had informed consent waived and whether the subject meets inclusion/exclusion criteria for the study.
 - c) Staff Signature/Delegation of Responsibility log: documents the signature and initials of all staff that collects and record study data, and lists the study-related procedures each has been delegated by the Principal Investigator.
 - d) Monitoring log: documents any study-related activity performed to monitor study progress or the accuracy and completeness of study records.
 - e) Adverse Event log: documents all adverse events that may be reported to the IRB, sponsor, and/or regulatory groups, indicating their seriousness, expectedness, and relationship to the study.
5. Copy of all IRB-approved versions of the consent form.
6. Laboratory documents (if applicable): Updated copies of Lab certification and normal lab/reference values. These materials document the competency of all lab facilities being used in the study and support the reliability of test results.
7. CRFs (or other data collection forms)
8. NIH grant applications and progress reports (if applicable).

9. Correspondence with study sponsor/funding agency (if applicable).
10. Data/Safety Monitoring Board reports (if applicable).

The Principal Investigator must maintain an accurate and complete accounting of all clinical study materials (investigational drug/device records) received, dispensed, and returned to the Sponsor. These records must be maintained in the study site regulatory binder for the same retention time.

11. Copies of all Form FDA 1572s (Statement of Investigator) and Form FDA 1571s (Investigational New Drug Application), if applicable.
12. Drug/device shipment and receipt records [may be maintained by the Research Pharmacy or Investigational Drug Service (IDS)].
13. Drug/device accountability log (drug accountability log may be maintained by the Research Pharmacy or IDS).
14. Signed/dated copies of financial disclosure for all investigators listed on Form FDA 1572

B. IRB Records and Correspondence

IRB records must include the following:

1. Scientific evaluations.
2. Progress reports submitted by investigators.
3. Records of continuing review activities.
4. Statements of significant new findings provided to participants.
5. For initial and continuing review of research by the expedited procedure:
 - a) The specific permissible category.
 - b) Description of action taken by the reviewer.
 - c) Any findings required under the regulations.
6. For exemption determinations, the specific category of exemption.
7. Unless documented in the IRB minutes, determinations required by the regulation and protocol-specific findings supporting those determinations for:

- a) Waiver or alteration of the consent process.
 - b) Research involving pregnant women, fetuses, and neonates.
 - c) Research involving prisoners.
 - d) Research involving children.
8. For each protocol's initial and continuing review, the frequency for the next continuing review.
9. Copies of IRB Approved Documents.
10. For VA research – in addition to any other requirements noted in this policy
- a) Correspondence between the IRB and the VA Research and Development Committee.
 - b) Correspondence between the IRB and researchers.
 - c) Internal serious adverse events.
 - d) Documentation of Protocol violations..
 - e) A resume for each IRB member.
 - f) All previous membership rosters.
11. All study-related correspondence with the IRB should be maintained in a separate file for each study. These documents include copies of all
- a) Submissions, signed and dated.
 - b) Approval letters or notifications of IRB decisions.
 - c) Investigator responses to IRB notifications (if applicable).
 - d) Approved recruitment materials

C. Individual Subject Files

Regulations and GCP guidelines require the PI to maintain adequate and accurate records of each study subject in a study. These records include the following documents but are not limited to

- 1. CRFs (or other data collection forms)

2. Appropriate source documents where applicable, such as:
 - a) Medical history records
 - b) Physical exam results
 - c) Laboratory results
 - d) Documentation of the informed consent process
 - e) Progress notes including study subject clinical management and documenting study visits.

D. Retention of Records

1. HHS regulations at 45 CFR 46.115(b) require that IRB records be retained for at least 3 years, At the end of three years, records are boxed, labeled and sent to central storage for another 3 years.
2. Research records should be retained for a sufficient minimum period to allow evaluation and repetition by others of the results and to investigate an allegation of research misconduct. Usually [unless granted an exception by the Department of Health and Human Services (HHS) or the Office of Research Integrity (ORI)], this minimum period is six years.
3. For VAMC studies,
 - a) all records, including the investigator's research records and codes/keys linking subject data to identifiers, must be retained in accordance with VHA's Records Control Schedule (RCS 10-1), applicable FDA and DHHS regulations, or as required by outside sponsors. If a VA protocol is cancelled without participant enrollment, IRB records will be maintained in accordance with VHA's Records Control Schedule (RCS 10-1). The local VA Research and Development Committee will have access to all IRB records related to VA Research.
4. All records must be accessible for inspection and copying by authorized representatives of HHS and FDA at reasonable times and in a reasonable manner. A log of stored records is maintained in the IRB office for retrieval if files are needed for audit purposes.

III. REFERENCES

- A. [45 CFR 46.115](#)



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|--|-------------|--------------------------|--------------------|
| Policy Name: Education and Training Requirements for Individuals Involved in Human Research | | | |
| Approved | | | Date: 09/15/2011 |
| Effective Date: 01/31/2013 | Page 1 of 3 | Section: HRPP 5.3 | Policy Number: N/A |
| Replaces Policy: 08/01/2012 | | | Dated: N/A |

I. POLICY

A. Introduction

Specific regulations and requirements have been issued by the Office for Human Research Protection OHRP in the United States Public Health Service regarding the responsibilities of individuals and institutions for compliance with the ethical conduct of research. As recipients of federal funding, MUSC has responsibility to ensure that individuals performing or overseeing research on human subjects are educated on the ethical conduct of research.

All individuals involved in human research must complete the initial 17 basic modules focused on biomedical or behavioral/social research when commencing such research. Beginning in Fall of 2008, all individuals involved in human research must complete the MIAMI CITI COURSE REFRESHER MODULE 101 every three years providing a mechanism of continuing education. Individuals with a Ralph H. Johnson VAMC appointment are required to complete similar continuing education modules at the CITI site every two years and this will satisfy the MUSC requirement for Continuing Education in Human Research Protection.

When the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

B. CITI

MUSC is registered for training of individuals involved in human research through the Miami Collaborative Institutional Training Initiative or CITI <http://www.musc.edu/citi>. Training completion is document through CATTS (Computerized Annual Training and Tracking System).

C. Background

The ethical conduct of research on human subjects is an essential component of our research mission. The principles of the ethical conduct of research are delineated in the following documents

1. [Declaration of Helsinki](#)
2. [Nuremberg Code](#)
3. [Belmont Report](#)
4. [Code of Federal Regulations-PHS \(45 CFR Part 46\)](#)
5. Code of Federal Regulations-FDA (21 CFR Parts 50 and 56)
 - a) [Web-Based](#)
 - b) [PDF Part 50](#)
 - c) [PDF Part 56](#)
 - d) [VA handbook 1200.5](#)

D. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage](http://research.musc.edu/ori/irb/resources.html) <<http://research.musc.edu/ori/irb/resources.html>>

E. International Committee on Harmonisation – Good Clinical Practices (ICHG-GCP)

For an industry-sponsored study where the contract requires adherence to ICH-GCP beyond FDA and DHHS regulations, information on additional training requirements can be found in HRPP 4.15 “Application of Industry E6 Good Clinical Practice Requirements.”

II. PROCEDURES

A. WHO MUST COMPLETE THE EDUCATION REQUIREMENT?

All individuals involved in human research. Exempt protocols do not mean exempt from IRB review and educational requirements.

B. INDIVIDUALS INVOLVED IN HUMAN RESEARCH

1. [Definitions from 45 CFR Part 46](#)

2. In order to help you assess whether participation in the educational activity is required, below are definitions from the Code of Federal Regulations. Additional information is available at http://grants.nih.gov/grants/policy/hs_educ_faq.htm.

- a) “**Research** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.”

MUSC/VA comment: In practical terms, if publication, presentation at a scientific meeting, or other scholarly purpose of the work is intended, it is probably research. If unsure, consult the Director of the Office of Research Integrity.

- b) “**Human subject** means a living individual about whom an investigator (whether professional or student) conducting research obtains:

- (1) data through intervention or interaction with the individual, or
- (2) identifiable private information.”

MUSC/VA comment: This means that use of tissues from living patients or examination of their medical records for the purpose of research qualifies as research on a human subject. If unsure, consult the Director of the Office of Research Integrity.

C. VERIFICATION OF THE COMPLETION OF EDUCATION AND TRAINING REQUIREMENTS

1. The MUSC Compliance office maintains the records of education and other courses completed by MUSC personnel.
2. Prior to release of a new study or continuing renewal of an existing study, the IRB Staff accesses the records maintained by University Compliance and verifies that the education requirements for all personnel on the study are current.

III. REFERENCES



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|---|--------------|--------------------------|
| Policy Name: Informed Consent to Participate in Research Policy and Procedures | | |
| Approved | | |
| Effective Date: 02/17/2017 | Page 1 of 11 | Section: HRPP 6.1 |
| Replaces Policy: Effective 12/01/2016 | | |

I. POLICY

A. Introduction

The purpose of this policy is to detail MUSC expectations for appropriate informed consent to participate in research.

B. Requirement to Obtain Informed Consent

1. Informed consent must be obtained and documented prior to involving any individual in research including invasive screening for eligibility to participate and recording identifiable information unless a waiver of consent is approved by the IRB.
2. Informed consent must be obtained from the individual participating in the research who is 18+ years of age and from the parent(s) of a child less than 18 years of age (see MUSC policy and procedure, Children as Research Subjects). Children between the ages of 12-18 years must give documented "assent".
3. Only those individuals approved by name by the IRB may obtain informed consent.
4. Every informed consent document must be signed and dated by the subject and the individual who obtained the consent.

C. Vulnerable Populations

Special protections are required when obtaining informed consent from vulnerable populations

1. When the study population includes individuals who are possibly cognitively impaired, the IRB must evaluate the proposed plan for assessing that the capacity to consent is adequate and the use of legally authorized representative consent must be approved by the IRB. The IRB must also decide if the assent of the participants is a requirement, and, if so, whether the plan for assent is adequate.
2. When the study population includes pregnant women, the purpose of the research is to improve the mother's health, and the risks to the fetus are minimal, informed consent of both the mother and father is

required unless: 1) the purpose of the research is to meet the health needs of the mother; 2) the father's identity or whereabouts cannot reasonably be ascertained; 3) he is not reasonably available; or 4) the pregnancy resulted from rape (45 CFR 46.204)

D. Emancipated Minor

An "emancipated minor" may only give informed consent when there is documentation that the minor is "emancipated", i.e. a marriage certificate, a rental lease signed by the minor, etc.

E. Legally authorized representative Consent

The IRB must specifically approve informed consent being obtained from a legally authorized representative who must be specifically named rather than from the individual who will be the research participant

F. Required Elements of the Informed Consent

The informed consent must include the following required elements (45 CFR 46.116(a)(1) and 21 CFR 50.25) and must be written in lay language (see MUSC Informed Consent Guidelines):

1. A statement that the study involves research;
2. An explanation of the purpose of the study;
3. A description of the procedures to be followed;
4. Identification of any procedures that are experimental;
5. The expected duration of the subject's participation;
6. A description of any reasonably foreseeable risks or discomforts to the subject;
7. The amount and schedule of payments;
8. A description of any benefits to the subject or to others which may reasonably be expected from the research;

For VA Research

- a) A statement that in the event of a research-related injury, the VA will provide necessary medical treatment to a participant injured by participation.
- b) A statement that a veteran-participant does not have to pay for care received as a participant in a VA research project

except in accordance with federal law and that certain veterans have to pay co-payments for medical care and services provided by VA.

- c) When a VA study involves “usual or standard of care” in the protocol or a separate document in the IRB application the researcher must clearly designate the individual or entity (e.g., the appropriate research personnel versus the subject’s health care provider) responsible for relevant aspects of both the research and the usual care.
9. A disclosure of alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
10. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained (For FDA-regulated Research, the FDA may inspect the records);
11. 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;
12. 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
13. 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 will be provided when appropriate under [45 CFR 46 116 and 21 CFR 50.25]:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
6. The approximate number of subjects involved in the study.
7. For applicable clinical trials, a statement notifying the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank. The statement is: "A description of this clinical trial will be available on <http://ClinicalTrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time."

G. Exclusion of Exculpatory Language

Informed consent documents may not include exculpatory language (45 CFR 46.116 and 21 CFR 50.20)

H. Genetic Research

Any genetic research study will include the MUSC genetic research required paragraphs in the informed consent documents as appropriate for:

1. Human Biological Material (HBM) linked to the subject with the potential for recontact,
2. HBM linked to the subject with no intent to recontact, and
3. HBM that is not linked to the subject with no recontact possible (see MUSC Standard Genetic Research Paragraphs)

I. MUSC Standard Paragraphs

Every informed consent will include the appropriate MUSC standard paragraphs regarding the institution's commitment, the sponsor's commitment, and the potential termination of the research by the investigator, and the "volunteer's agreement" (see MUSC Informed Consent Guidelines).

J. English Literacy

Subjects who do not speak/read English will be given an informed consent document understandable to them. (45 CFR 46.116, 46.117 and 21 CFR 50.20)

K. IRB Observation of the Informed Consent Process

The IRB may observe the process of informed consent at any time. For example, observation of the consent process might provide additional protections when research involves adults with diminished decision-making capacity. Observation of the consent process might be performed by the IRB, IRB staff, other individuals in the organization, or by a third party hired by the organization, investigator, or sponsor.

L. NIH Supported Clinical Trials

If a research study is a NIH supported clinical trial with an NIH approved sample informed consent document, any deletion or substantive modification of information concerning risks or alternative procedures contained in the NIH approved sample consent must be justified in writing by the investigator, approved by the IRB and reflected in the IRB minutes.

M. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

If a research is a VA study, the informed consent will incorporate requirements of VHA 1200.05.

N. Long form of Consent Documentation

For the long form of consent documentation, the IRB will determine that the regulatory criteria for the long form of consent documentation are met:

1. The consent document embodies the basic and appropriate additional elements of disclosure.
2. The participant or the participant's legally authorized representative has signed and dated the consent document.
3. A copy of the signed and dated consent document is given to the person signing the consent document.

4. The investigator will give either the participant or the participant's legally authorized representative adequate opportunity to read the consent document before signing and dating the document.
5. For VA research, the consent document is on VA Form 10-1086

O. Short Form of Consent Document

For the short form of consent documentation, the IRB will determine that the regulatory criteria for the short form of consent documentation are met:

1. The consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant's legally authorized representative.
2. A written summary embodies the basic and appropriate additional elements of disclosure.
3. There was a witness to the oral presentation.
4. For participants who did not speak English, the witness was conversant in both English and the language of the participant.
5. The participant or the participant's legally authorized representative signed the consent document. If the research is FDA-regulated or VA research, the participant or the participant's legally authorized representative signed and dated the consent document.
6. A copy of the summary has been given to the participant or the participant's legally authorized representative

P. Consent Process

The following information will be provided to the IRB in order to determine whether the consent process can be approved. This information can be collected as part of the application or be included in the protocol:

1. The person who will conduct the consent interview.
2. The person who will provide consent or permission.
3. Any waiting period between informing the prospective participant and obtaining consent.
4. Steps taken to minimize the possibility of coercion or undue influence.
5. The language to be used by those obtaining consent.

6. The language understood by the prospective participant or the legally authorized representative.
7. The information to be communicated to the prospective participant or the legally authorized representative

NOTE: These policies do not apply to research determined to be “exempt”.

Q. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

II. DEFINITIONS

Definitions for the following terms used in this section may be found in the HRPP Program Guide Section 1.3 – Definitions of terms

- A. Informed consent**
- B. Legal guardian**
- C. Legal representative**
- D. Children**
- E. Exculpatory language**
- F. Witness**

III. PROCEDURES

- A.** The principal investigator will submit a description of the informed consent process and the informed consent document when submitting an application packet to the IRB either for full Board (see MUSC Policy and

Procedure, Full Board Initial Review) or expedited review (see MUSC Policy and Procedure, Expedited Review).

- B.** The designated IRB reviewer(s) will assess the process and document for appropriateness, completeness, and understandability.
- C.** The IRB reviewer(s) will assess the qualifications of those individuals the principal investigator has requested be allowed to obtain informed consent and to give informed consent. The IRB reviewer(s) may request additional documentation of described qualifications. If required by the convened IRB as part of the protocol approval, a witness to the participant's signature or the legally authorized representative's signature sign and date the consent document. This will be communicated to the investigator upon review of the protocol.
- D.** The following must occur when using the short form consent documentation:
 - 1. The witness will sign and date both the short form and a copy of the summary.
 - 2. The person actually obtaining consent will sign and date a copy of the summary.
 - 3. A copy of the signed and dated short form will be given to the participant or the legally authorized representative.
 - 4. A copy of the signed summary will be given to the subject or the legally authorized representative.
- E.** Informed consents must be translated into a foreign language by a translator certified by the American Translators Association. The principal investigator will submit documentation that any foreign language informed consent has been translated by a certified translator.
- F.** If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion.
 - 1. After the written consent document and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the consent document, the witness should sign and personally date the consent document.

2. By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that consent was freely given by the subject or the subject's legally acceptable representative.
- G.** For corporate sponsored studies, ORSP will verify the consistency between the contract agreement and the informed consent. Any discrepancies noted are then addressed with the IRB Administrator or Program Manager.
- H.** When the informed consent document and process have 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 provided 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.
- I. VA Protocols:**
1. Unless otherwise requested and approved, all VA research subjects medical records will be flagged in the VA electronic medical record (CPRS) per VA regulations. The flag will contain the name of the study, the study investigator, and study contact information. The flag is activated by the RHJVAMC staff after being contacted regarding the subject's enrollment by the investigator/study team.

The flag will be required for all studies involving investigational medications, devices and/or interventions. Some studies may not require a flag and will be determined on a case by case bases after a request not to flag has been submitted to the IRB by the PI. Examples of studies that may not require a flag include:
 - a) Retrospective chart audit studies
 - b) Studies involving only one encounter
 - c) Participation in the study involves the use of a questionnaire or previously collected biological specimens; and/or
 - d) Studies where identification of the patient as a subject in the study would place the subject at greater than minimal risk.
 2. In the event of a research-related injury, the VA has to provide necessary medical treatment to a participant injured by participation. Except in limited circumstances, the necessary care will be provided in VA medical facilities. Exceptions to the above include;
 - a) Situations where VA facilities are not capable of furnishing economical care; and/or

- b) Situations where VA facilities are not capable of furnishing the care or services required.
- 3. A veteran-participant will not be required to pay for care received as a participant in a VA research project except in accordance with Title 38 United States Code USC 1710(f) and 1710(g). Certain veterans will be required to pay co-payments for medical care and services provided by the VA.
- 4. All regulations pertaining to the participation of veterans as participants including requirements for indemnification in cases of research-related injury pertain to non-veteran participants enrolled in VA-approved research.
- 5. The Consent Process
 - a) If someone other than the investigator conducts the interview and obtains consent, the investigator formally delegates this responsibility and the person so delegated has received the appropriate training to perform this activity.
 - b) The participant or the participant's legally authorized representative will sign and date the consent document.
 - c) A copy of the signed and dated consent document is given to the person signing the consent document.
 - d) IRB approval of the working of the consent document will be documented through a stamp on each page of VA Form 10-1086, indicating the date of most recent IRB approval.
 - e) If the consent document is amended during the protocol approval period, the consent document must bear the approval date of the amendment rather than the date of the approved protocol.
 - f) Investigator must include a progress note in the participant's medical record of the consent. This note should include:
 - (1) The name of the study;
 - (2) The person obtaining the participant's consent;
 - (3) A statement that the participant or the participant's legally authorized representative is capable of understanding the consent process;

- (4) A statement that the study was explained to the participant; and
 - (5) A statement that the participant was given the opportunity to ask questions.
- g) The investigator will place additional progress notes in the participant's medical record when;
- (1) The participant is entered into the study; and
 - (2) The participant's participation is terminated

J. Subject Withdrawal

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access, for purposes related to the study, the subject's medical record or other confidential records requiring the subject's consent. However, a research may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

For FDA regulated studies, when participants withdraw from a clinical trial, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.

A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequently to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such a medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

The researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.

IV. REFERENCES

- A. [DHHS Title 45 Subpart 46 \(45 CFR 46\)](#)
- B. [FDA 20 CFR 50](#)



| | | |
|---|-------------|--------------------------|
| Policy Name: Waiver or Alteration of the Consent Process and Waiver of Consent Documentation – Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 4 | Section: HRPP 6.2 |
| Replaces Policy: HRPP 6.3 01/27/2012 | | |

I. INTRODUCTION

This purpose of this policy is to detail the procedure for approving a Waiver or alteration of the consent process and the waiver of consent documentation.

II. PROCEDURES

- A. A Principal Investigator may request a waiver or alteration of the required elements of the informed consent process by completing the appropriate questions in the eIRB system.
- B. The request is reviewed by the IRB, the IRB Chair or the IRB Chair's designee.
 - 1. The proposed consent procedure which does not include, or which alters some or all of the requirements of informed consent process set forth in the federal regulations [45 CFR 46.116 (a) and (b)] may be approved or the requirement to obtain informed consent or parental permission may be waived provided the IRB finds and documents that:
 - a) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine [45 CFR 46.116(c)]:
 - (1) Public benefit or service programs;
 - (2) Procedures for obtaining benefits or services under those programs;
 - (3) Possible changes in or alternatives to those programs or procedures; or
 - (4) Possible changes in methods or levels of payment for benefits or services under those programs;
 - b) The research could not practicably be carried out without the waiver or alteration;
 - c) The research is not subject to FDA regulation; and

- d) The research is not subject to DoD regulation or the Secretary of the Department of Defense has approved a waiver.
2. The consent procedure which does not include, or which alters, some or all of the elements of informed consent may be approved or the requirements to obtain informed consent waived provided the IRB finds and documents that [45 CFR 46.116(d)]:
- a) The research involves no more than minimal risk to the participants;
 - b) The waiver or alteration will not adversely affect the rights and welfare of the participants;
 - c) The research could not practicably be carried out without the waiver or alteration;
 - d) Whenever appropriate, the participants will be provided with additional pertinent information after participation;
 - e) The research is not subject to FDA regulation; and
 - f) The research is not subject to DoD regulation or the Secretary of the Department of Defense has approved a waiver.
3. Waiver of Documentation of the Informed Consent Process
- a) The following stipulations must be true before waiving the requirement for the investigator to obtain a signed informed consent document for some or all of the participants ([45 CFR 46.117(c)(1)].
 - (1) The only record linking the participant and the research would be the consent document.
 - (2) The principal risk would be potential harm resulting from a breach of confidentiality.
 - (3) Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern; or a written statement describing the research will be provided to participants (e.g., copy of consent document, study information sheet);
 - 4) The research is not subject to FDA regulations.

- b) The following stipulations must be true before waiving the requirement for the investigator to obtain a signed informed consent document for some or all of the participants true [45 CFR 46.117(c)(2)] [21 CFR 56.109(c)(1)]
 - (1) The research presents no more than minimal risk of harm to participants.
 - (2) The research involves no procedures for which written consent is normally required outside of the research context.
- c) The IRB, the IRB Chair or the IRB Chair's designee reviews:
 - a) a copy of the consent document or written statement of information for inclusion of all required and appropriate additional elements of disclosure and b) considers whether to require the investigator to provide subjects with a written statement regarding the research.

4. Waiver of Consent Process – Permission is not a reasonable requirement

- a) The research is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects.
- b) An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted.
- c) The research is not FDA-regulated.

III. FDA Regulations

- A.** FDA regulations do not allow waiver of any informed consent requirements except in emergency use situations.
- B.** When following FDA regulations, the IRB is allowed to waive the requirement to document the consent process by determining that the regulatory criteria for waivers are met as follows.
 - 1. The IRB reviews a written description of the information that will be provided to subjects.
 - 2. The IRB considers requiring the researcher to provide subjects with a written statement regarding the research.

IV. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

V. ADDITIONAL IRB RESPONSIBILITIES

A. If waiver or alteration of informed consent, signed informed consent, or elements of informed consent is requested, the reviewer(s) will document if the proposed research study meets the requirements for waiver approval. If not, the reviewer or IRB administrator will communicate this denial of waiver to the principal investigator and ask for necessary revisions to the informed consent process/document.

B. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html))

C. VA Research

For VA research, the IRB will document the reason for waiver when it waives the requirement to obtain written documentation of the consent process.



| | | |
|---|-------------|--------------------------|
| Policy Name: Equitable Selection of Subjects | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 7.1 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

The Belmont Report's principle of justice requires the fair distribution of the overall benefits and burdens of research. One of the federally required criteria that the IRB must assess when determining whether research may be approved is that the selection of subjects is fair and equitable. (45 CFR 46.111).

B. Research Obligations

In making this assessment, the IRB must take into account the purposes of the research and the setting in which the research will be conducted. Particular attention must be given to vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. When research does not involve a therapeutic component, the IRB will consider who should participate and accept the risks of the research and will assess whether overburdened classes of subjects are being included solely for reasons such as easy availability or their economic status.

II. PROCEDURES

During review and assessment of subject selection, the IRB must determine the procedures outlined by the investigator reflect a fair distribution of the risks and benefits of research among the populations. In making this assessment, the following items are considered:

- A. The purpose of the research and its target population.
- B. Methods of recruitment, including the screening procedures and the settings for recruitment and conduction of the research.
- C. The inclusion/exclusion criteria to be used and how it relates to the representative population that potentially stands to potentially benefit from the research.
- D. Justification for exclusion of certain populations.

E. The amount and timing of payments to participants.

F. **MEMORANDUM OF UNDERSTANDING**

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

Studies should permit entry of non-veterans only when there are insufficient veterans available to complete the study.

III. REFERENCES

A. [45 CFR 46.111 Criteria for IRB Approval of Research](#)



| | | |
|--|-------------|--------------------------|
| Policy Name: Advertisements for Research Participants Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 3 | Section: HRPP 7.2 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

A. Introduction

Advertisements designed to recruit participants into human research must be fair and equitable.

B. Requirements

The MUSC IRB considers advertising to be part of the recruitment and consent process. Therefore, the MUSC IRB requires that all means of advertising, recruiting and notifying individuals of a study for enrollment be submitted for review and approval.

II. PROCEDURES

A. Generally, advertisements should be submitted with the initial proposal review but can be submitted at any time for review. The review of advertisements is generally considered a minor change to approved research and may be reviewed under the expedited review procedure.

B. When reviewing advertisements and recruitment the MUSC IRB will consider:

1. The information presented within the advertisement.
2. The mode of its communication.
3. The final copy of printed advertisements as they will be displayed.
4. The final audio/video taped advertisements as they will be broadcast.

C. Advertisements may not:

1. State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
2. Include exculpatory language.
3. Promise "free treatment" when the intent is only to say participants will not be charged for taking part in the investigation.

4. Make claims, either explicitly or implicitly, about the drug, biologic or device under investigation that are inconsistent with FDA labeling.
 5. Use terms, such as “new treatment,” “new medication” or “new drug” without explaining that the test article is investigational.
 6. Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.
 7. Place emphasis on the payment or the amount to be paid using large or bold type.
- D. Advertisements are limited to the information prospective participants need to determine their eligibility and interest, such as:
1. The name of the investigator or research facility.
 2. The purpose of the research or the condition under study.
 3. In summary form, the criteria that will be used to determine eligibility for the study.
 4. A brief list of participation benefits, if any.
 5. The time or other commitment required of the participants.
 6. The location of the research and the person or office to contact for further information.

All advertisements should include the following statement: “A research study at the Medical University of South Carolina.”

- E. IRB review and approval of listings of clinical trials on the internet would provide no additional safeguard and is not required when the system format limits the information provided to basic trial information, such as:
1. the title;
 2. purpose of the study;
 3. protocol summary;
 4. basic eligibility criteria;
 5. study site location(s); and
 6. how to contact the site for further information.

Examples of clinical trial listing services that do not require prospective IRB approval include:

1. The National Cancer Institute's cancer clinical trial listing (PDQ) and
2. The government-sponsored AIDS Clinical Trials Information Service (ACTIS).

However, when the opportunity to add additional descriptive information is not precluded by the database system, IRB review and approval may assure that the additional information does not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document.

III. REFERENCES

- A. [NIH Clinical Trials](#)



| | | |
|--|-------------|--------------------------|
| Policy Name: Payments for Participation Policy and Procedures | | |
| Approved | | |
| Effective Date: 04/01/2013 | Page 1 of 3 | Section: HRPP 7.3 |
| Replaces Policy: Effective 01/27/2012 | | |

I. POLICY

A. Introduction

Payment of human subjects for participation in research must be fair and equitable.

B. Requirements

Any and all payments made to research participants in MUSC studies must be reviewed by IRB and monitored for fairness and equity.

C. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

II. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage](http://research.musc.edu/ori/irb/resources.html) (<http://research.musc.edu/ori/irb/resources.html>)

III. PROCEDURES

A. Criteria for IRB Review of Payments for Participation

1. The amount of payment and the proposed method and timing of disbursement is neither coercive nor presents undue influence.
2. Credit for payment accrues as the study progresses and not be contingent upon the participant completing the entire study.
3. Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
4. All information concerning payment, including the amount and schedule of payments, is set forth in the consent document. Disclosure regarding IRS reporting regulations shall be included in the Payment to Participants section of the Informed Consent Document. The Research Study Payment Information Document may be used when a Waiver of Signed Consent is approved by the IRB.
5. In the case of VA research, payment to research participants is prohibited when the research is integrated with a patient's medical care and when the research makes no special demands on the patient beyond those of usual medical care.

B. Allowable Criteria for Payment to Participants

1. The research is not directly intended to enhance the diagnosis or treatment of the medical condition for which the participant is being treated, and when the standard of practice in affiliated non-VA institutions is to pay participants in this situation.
2. The research is a multi-institutional study and participants at collaborating non-VA institutions are paid for the same participation in the same study at the same rate proposed.
3. In the opinion of the IRB, payment of participants is appropriate in other comparable situations.
4. The participant will incur transportation expenses that would not be incurred in the normal course of receiving treatment and are not reimbursed by another mechanism.
5. The IRB allows non-veterans to be entered into VA-approved research studies only when there are insufficient veterans available to complete the study or when the researcher can present a

compelling argument to the IRB for the inclusion of non-veterans (e.g., survey of VA employees; study of active duty military; study involving veterans' family members), and the research is relevant to the care of veterans or active duty military personnel.

III. REFERENCES

MUSC Finance & Administration Policies:

Section: 6-Purchasing & Accounts Payable

[Policy Procedure: 6-13.0](#)

[Subject: Remuneration for Research Trial Participants](#)

Established Date: 06/01/2010



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|--|-------------|-------------------|--------------------|
| Policy Name: Recruitment Incentives Policy and Procedures | | | |
| Approved | | | Date: 11/01/08 |
| Effective Date: 02/20/09 | Page 1 of 3 | Section: HRPP 7.4 | Policy Number: N/A |
| Replaces Policy: N/A | | | Dated: N/A |

I. POLICY

A. Introduction

Recruitment incentives paid to Institutions or individuals to boost recruitment into a study takes many forms. This policy primarily deals with personal incentives that are given to individual Investigators, Co-Investigators, research staff members or Clinicians who may or may not be affiliated with the research study. Incentives are defined as any monetary payment, gift or gift certificate that may be given to the individual by the study sponsor or by the research sponsoring Institution. Federal statute does not cover this area in sufficient detail for firm guidance to Researches, Institutions and Sponsors. See “Recruiting Human Subjects, Sample Guidelines for Practice”, Office of the Inspector General, Department of Health & Human Services – June 2000, (OEI01-97-00196). This is an area where ethical principals must guide Investigators, Sponsors, Institutions and IRB members. The Belmont principals of justice, beneficence and equality must be guided by truthfulness, moderation and wisdom.

In principal, the Office of Research Integrity (ORI) of MUSC discourages and disapproves of recruitment incentives to boost subject numbers participating in all forms of human research. Such recruitment incentives give the appearance of conflict of interest, raising questions of coercion of subjects for personal gain. Several medical associations, including the AMA have prohibited fees paid either to or by consultants for referrals and have branded them as unethical. Many states and some countries also have laws prohibiting this practice in the clinical setting. However, in the spirit of moderation and wisdom, the ORI of MUSC recognizes there may be some circumstances in which incentives for recruitment may serve the public interest, benefit individual subjects and the acquisition of scientific knowledge for possible future gain to humanity.

B. Payment to Clinicians, Investigators, Co-Investigators, Study Staff and Other Personnel Directly Involved in the Research Study

The ORI of MUSC does not condone the routine payment of incentives to individuals connected or not connected to a particular study. These

incentives give the appearance of conflict and could lead to adverse consequences for individual subjects, study personnel and the Institution.

If an Investigator and or Sponsor wish to provide financial or non-financial incentives for recruitment the following steps must be taken and reviewed and approved by the IRB of jurisdiction. This will require full board approval by majority vote. The IRB members with a conflict in this area will recuse themselves.

The Investigator will provide evidence that the sponsor approves of the practices and will give justification for the incentive, will specifically identify the incentive and its cash value. The Principal Investigator will identify how this incentive may be used by the recipient. Example: the recipient may receive a cash amount which will be spent at their discretion, receive income into an account that will provide for travel, books, educational materials, etc. or some other purpose. The incentive amount, source and its purpose must be clearly stated in the informed consent agreement in plain language for the subject to understand. This information must also be contained in the protocol. The full board of the IRB will determine whether to allow this practice for any particular study.

C. Incentives Paid to Research Subjects, Patients to Boost Enrollment

Word of mouth recruitment by present or former research subjects in a study is often one of the most effective methods of recruiting new subjects into a study. Some forms of this type recruitment are often called “snowball” recruiting. It is permissible to allow this form of recruitment for studies by providing cash, gift certificates or other incentives to subjects to promote their aid in recruiting new individual subjects into studies. Such practices are allowable. The incentive to any subject should be picked with moderation, with justice and autonomy being considered. The level or amount of the incentive should be based on current local norms and must be reviewed by an IRB Chair, Vice Chair or full board depending on the type of application.

II. CONCLUSIONS

Incentives are not advised. The investigator may wish to seek further guidance on the matter of incentives from the IRB Manager, ORI Director, individual Chairs of IRB's, the Director of the Office of Research and Sponsored Programs and/or the Office of General Counsel of the University. Other useful resources may be the Office of Public Relations at the University and the Office of Risk Management. **Caution:** discretion and consultation with incentives is always prudent.

III. REFERENCES

- A. [“Recruiting Human Subjects, Sample Guidelines for Practice”](#), Office of the Inspector General, Department of Health & Human Services – June 2000, (OEI01-97-00196).



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| Policy Name: Research Involving Non-English-Speaking Subjects Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/30/2015 | Page 1 of 7 | Section: HRPP 7.5 |
| Replaces Policy: 01/27/2012 | | |

I. POLICY

A. Introduction

An increasing number of research studies include subjects who may not understand the English language. It is imperative that all subjects, irrespective of their knowledge of English, have an understanding of the study and the elements of consent that is sufficient for deciding whether or not they participate in the research. This means that consent must be obtained using language that non-English-speaking subjects understand. To implement this requires either written translation or oral presentation in the relevant non-English language by a person who is fluent in both English and the other language, and who understands both cultures. The basic requirements are stated in the federal regulations (45CFR46), but specific rules for implementation are determined by the MUSC IRB.

B. Federal Regulations on Informed Consent

1. **45CFR46.116 “General Requirements for Informed Consent”**
“...The information that is given to the subject or the [legal] representative shall be in language understandable to the subject or representative...”
2. **45CFR46.117 “Documentation of Informed Consent”**
46.117(a) “Except as provided in paragraph (c) of this section [waiver of documentation], informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject’s legally authorized representative...”

46.117(b) “...the consent form may be either of the following:
 - a) “A written consent document that embodies the elements of informed consent required by 45CFR46.116...” or
 - b) “A short form written consent document stating that the elements of informed consent required by 45CFR46.116 have been presented orally to the subject or the subject’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the

IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.”

C. MUSC IRB Policy on Informed Consent

1. Consent Form Option #1: Long Form Written Consent Document

a) Translation Process for the Long Form:

The consent form for non-English-speaking subjects or legal representatives shall be the same as for English-speaking subjects or legal representatives in content and format, except that the non-English consent form will be translated into the language that is understandable by the subject or legal representative. The translation process is described below:

- (1) Forward translation from English to non-English by American Translators Association (ATA) certified translator or IRB-approved equivalent; and
- (2) Submission of English and non-English consent; and
- (3) Invoice or written statement by the translator for the translation service.

b) Qualifications for Translators

The IRB protocol must contain a description of the qualifications of each translator to verify that he/she is both bilingual and bicultural.

c) Consenting Process When Using the Long Form

A person who knows the study, its procedures and its scientific basis shall be available by telephone or in person to answer questions before the subject signs the translated consent form. If this knowledgeable person is not fluent in both English and the subject’s primary language, a second person who is fluent in both languages shall be present to translate questions and answers for the person.

2. **Consent Form Option #2: Short Form Written Consent Document**

The federal regulations at 45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2) permit the use of a short form consent document stating that the required elements of informed consent have been presented to the subject or the subject's legally authorized representative orally, with a witness present. Within MUSC use of a short form consent document is largely limited to situations where English is not understandable to a potential research subject who is considering whether to participate in a research study, and the investigator does not have an IRB-approved consent document translated into a language understandable to the potential subject.

An IRB-approved short form template is available for use in the above-described instance. Within 30 days of the subject's consent, an amendment translating the long form consent into the subject's language must be submitted to the IRB and the subject must be re-consented using the translated long form at his/her next study visit.

a) **Written Short Form Consent**

- (1) **Content:** A statement that the basic elements of consent (as detailed in 45CFR46.1116) were presented to the subject or legal representative in a language that was understandable to him or her.
- (2) **Language:** Understandable to the subject or legal representative. The translation process shall be as outlined in I.C.i.a above.
- (3) **Approval:** By the MUSC IRB.
- (4) **Witness:** Required.
- (5) **Signed by:** Subject or legal representative, Witness, and Oral Presented. (Note: Although the signature of the Oral Presenter is not specifically required on the Written Short Form by the federal regulations, this requirement is determined by the MUSC IRB as a method to document the name of the Oral Presenter for the subject or legal representative.)
- (6) **Copy:** To the subject or legal representative.

b) **Written Summary of the oral consent presentation**

- (1) Content: The basic elements of consent (as detailed in 45CFR46.116) to be presented orally to the subject or legal representative. In studies where there is a consent form for English speaking subjects or legal representatives, the content of the Written Summary shall be the same as that of the consent form.
 - (2) Language: English.
 - (3) Approval: By the MUSC IRB.
 - (4) Signed by: Witness and Oral Presenter.
 - (5) Copy: To the subject or legal representative.
- c) Translator
- (1) Language: Bilingual so that the presentation is understandable to the subject or legal representative.
 - (2) Relationship: Not related to, or a close associate of, the subject or legal representative.
 - (3) Function: Gives an oral presentation to the subject or legal representative in the language that is understandable to him or her that describes the content of the Written Summary. The Translator also may serve as the Person Obtaining Consent, provided that he/she meets the IRB requirements for Person Obtaining Consent, as described in I.c.2.e) below, but may not serve as the Witness. (Note: Although not specified by federal regulations, these dual roles have been determined by the MUSC IRB.)
 - (4) Signatures: Signs the Written Summary and the Written Short Form. (Note: Although the signature of the Translator is not specifically required on the Written Short Form by the federal regulations, this requirement has been determined by the MSUC IRB as a method to document the name of the Translator for the subject or legal representative.)
- d) Witness to the Oral Presentation
- (1) Language: Bilingual so that the presentation is understandable to the subject or legal representative. (Note: Although it is not specified by the federal regulations that the witness be bilingual, this

requirement has been determined by the MUSC IRB. Otherwise, the Witness would not be a witness to the fact that understandable consent content was being presented to the subject or legal representative, but rather, the Witness would be only a witness to the fact that an interaction occurred and that the subject or legal representative signed the document.)

- (2) Relationship: The Witness can be related to, or a close associate of the subject or legal representative if the Witness meets the other requirements described in this section, and also is acceptable to the subject or legal representative.
- (3) Function: Certifies that an oral presentation was made to the subject or legally authorized representative in the language that is understandable to him or her that describes the content of the Written Summary, which contains the basic elements of consent. The Witness also may serve as the Person Obtaining Consent, but may not serve as the Oral Presenter. (Note: Although not specified by federal regulations, these dual roles have been determined by the MUSC IRB.)
- (4) Signatures: Signs the Written Summary and the Written Short Form.

e) Person Obtaining Consent

- (1) Language: English, if the Person Obtaining Consent is neither the Translator nor the Witness. If the Person Obtaining Consent is serving also as either the Translator or the Witness, then he/she must be both bilingual.
- (2) Relationship: Not related to, or a close associate of, the subject or legal representative.
- (3) Function: Supervises the process of obtaining consent, and must be knowledgeable about the research study, so as to be able to answer questions about the study that may be asked by the subject. The Person Obtaining Consent also may serve as either the Translator or the Witness but not both, provided that he/she meets the IRB requirements for those positions (as outlined in I.C.2.c and I.C.2.d, respectively). (Note: Although not specified by federal

regulations, these dual roles have been determined by the MUSC IRB.)

- (4) Signatures: Signs the written Summary and the Written Short Form. (Note: Although the signature of the person Obtaining Consent is not required specifically on the Written Short Form by the federal regulations, this requirement has been determined by the MSUC IRB as a method to document the name of the person obtaining consent for the subject or legal representative.)

D. Questionnaires for Non-English-Speaking Subjects

1. Introduction

When subjects who do not understand the English language are involved in research studies that require responding to questionnaires, it is important that those questionnaires are translated into a language that the subjects understand. Also, it is important that the questionnaires convey the same meaning as the original English version. Otherwise, responses of non-English-speaking subjects will not be comparable to responses of those who speak English.

2. MUSC IRB Policy on Self-Administered Questionnaires

Self-administered questionnaires for non-English-speaking subjects shall be the same as for English-speaking subjects in content and format, except that the non-English questionnaires will be translated into the language that is understandable by the subject. The translation process is described below:

- a) Forward translation from English to non-English by American Translators Association (ATA) certified translator or IRB-approved equivalent; and
- b) Submission of English and non-English consents; and
- c) Invoice or written statement by the translator for the translation service.

3. MUSC IRB Policy on Verbally Administered Questionnaires

- a) Verbal Questionnaire Option #1: Translation of the Questionnaire

The verbal questionnaire will be translated into the language that is understandable to the subject. This translated questionnaire can be administered to the subject by a person who is fluent in the subject's language, but not necessarily fluent in English. The translation process shall be as outlined in Section B2 above

b) Verbal Questionnaire Option #2: Verbal Administration of the Questionnaire

The verbal questionnaire does not require a written translation into the language that is understandable to the subject. However, verbal administration shall be done by a bilingual and bicultural person, and a second bilingual and bicultural person must witness the verbal administration to ensure that the meaning of the original English is being translated accurately.

E. Other Documents for Non-English-Speaking Subjects

If the research involving non-English-speaking subjects includes the use of verbal scripts or documents other than the consent form and questionnaires, then the investigators must describe the measures they will take to ensure that the information in these scripts or documents will be conveyed to the subjects accordingly and in an understandable way.



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| Policy Name: Research Subject Advocacy Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 3 | Section: HRPP 7.6 |
| Replaces Policy: 09/17/2012 | | |

I. POLICY

A. Introduction

Federal regulations require that IRBs give special consideration to protecting the welfare of special research participant groups that are more vulnerable than general participants. These research participant groups include, but are not limited to: pregnant women, children, cognitively impaired persons, prisoners, comatose patients, terminally ill patients, elderly/aged persons, minorities, students, and employees.

Human research participant advocates are part of the overall human research risk protection program. They can enhance the protection of special vulnerable groups as noted above and serve as liaisons to the IRB on behalf of research participants. Research participant advocacy encompasses a variety of roles which may be provided by a number of individuals trained to serve in this capacity. Research participant advocates at MUSC may come from many backgrounds and perspectives and may include: faculty or staff volunteers who have special expertise with the vulnerable population of a study; community members who have a background in working with vulnerable populations, and single providers who serve as the research participant advocate for research requiring such services.

B. Responsibilities of the Research Participant Advocate

The primary responsibilities of research participant advocates are to provide assurance to institutional officials, our community, the IRBs, the principal investigators, and other officials that appropriate efforts are being made to protect vulnerable populations and to ensure that safety receives the highest priority. Duties of a research participant advocate are diverse and may vary according to the request of the IRB, University officials, principal investigator, or the unit conducting the research. Research participant advocates may serve as educators to participants and researchers. They may participate as observers of the consent process and may monitor specific research procedures. Research participant advocates may assist potential research participants in their understanding of research participation as well as research staff with the resolution of questions regarding selection of human subjects in research. Other duties may be

specified by the IRB, Director of the Office of Research Integrity, or other officials as needed. IRBs occasionally request that the Principal Investigator of a particular study find a research participant advocate to observe, monitor, and report to the board on various aspects of research studies. The MUSC Conflict of Interest Committee may request the provision of a research participant advocate as part of a comprehensive management program of perceived conflict of interest.

II. PROCEDURES

A. Sources of Research Participant Advocates

Advocates may be selected from the community, faculty, and staff of the Medical University and its affiliates. Those selecting a research participant advocate for any particular human research study should keep in mind that the advocate should have some background knowledge in working with the particular vulnerable population; have knowledge of the bioethical foundations, federal regulations, and University policies regarding human subjects research and the special needs of vulnerable populations and have the time commitment available to participate with the research participants on an on-going basis for the duration of the research endeavor. If requested either by the IRB or investigator, SCTR will facilitate the selection of research participant advocates.

B. Institutional Responsibilities

The research advocate program and all research advocates have direct access to the Director of the Office of Research Integrity and other organizational officials. Advocates may also report to the IRBs. It is the responsibility of the University to create an atmosphere of advocacy for special populations and to ensure that principal investigators, centers, departments, and special research units all support the use of research participant advocates.

C. IRB Responsibilities

Each of the Institutional Review Boards, Chairs, Vice Chairs, and staff will be responsible for assessing the types of participants being selected for studies. The IRB may suggest or require that studies have a research participant advocate. The IRB will review the research participant advocate nominated by the Principal Investigator to ensure that the advocate is appropriate and not conflicted. When a Research Participant Advocate is required to be present during the consent process, the IRB approved informed consent document will include a signature line for the Advocate to sign and date.

III. REFERENCES

- A. [45CFR 46 Sub Part B, C, D.](#)
- B. [OHRP Policies, Chapter 6, Special Classes of Subjects; Institutional Review Board Guidebook](#)



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|--|-------------|--------------------------|
| Policy Name: Subject Complaints, Issues, Concerns and Suggestions Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 7.7 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

All significant subject complaints, issues and concerns are to be reported by the Principal Investigator to the IRB within five working days of becoming aware of a subject's complaint, issue or concern.

B. IRB Obligations

The IRB is obligated to receive and respond to all human research related complaints, issues, and concerns regardless of the source. In addition to any complaints or concerns, any suggestions for improvement or compliments should be noted and communicated to the Director of the Office of Research Integrity for incorporation into our quality improvement operation.

II. DEFINITIONS

Definition of the following terms used in the Section may be found in the HRPP Program Guide Section 1.3 – Definitions of terms:

A. Significant complaints, issues or concerns

III. PROCEDURES

A. The Principal Investigator should report any complaint/issue/concern about the conduct of human research in writing. This report should include:

1. The name and the HR / PRO number of the protocol;
2. A complete description of the complaint/issue/concern;
3. Actions taken to resolve the complaint/issue/concern; and
4. Actions requested by the individual sharing the complaint, issue/concern.

- B.** Complaints/issues/concerns may be communicated directly to the IRB by telephone, US mail, e-mail, or the MUSC Compliance Hotline. The IRB Program Manager or Administrators will initially process all complaints.
- C.** The IRB chairs in consultation with the IRB Administrators and MUSC Legal Counsel and MUSC Risk Management Office, as appropriate, will determine what actions will be taken to investigate the complaint/concern/issue in preparation for review by the convened Board. If the report of the complaint/issue/concern is made to the IRB by a person other than the Principal Investigator, the Principal Investigator will be notified of the complaint/issue/concern and asked to submit a written report regarding the incident when appropriate. The name of the individual reporting the complaint/issue/concern will not be released unless the individual has given permission and it is pertinent to the investigation and resolution.
- D.** The Board will work with the Principal Investigator to determine the resolution of the complaint/issue/concern and the actions to be implemented to prevent similar incidents. The Board will determine if the complaint/concern/issue represents an unanticipated problem, a protocol violation or investigator noncompliance. The Board's discussion and decisions will be recorded in the meeting's Minutes.
- E.** Upon resolution, as expeditiously as possible, the IRB Chair or senior IRB administrator to the specific IRB will contact (by phone or email) the subject to discuss the resolution of the concern and elicit any additional relevant information the subject may have to offer. This will be followed by a formal communication to the subject and, if appropriate, a follow-up phone call.
- F.** If appropriate, a copy of the formal communication will be filed in the research folder.

III. REFERENCES



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|--|-------------|--------------------------|
| Policy Name: Recruitment of Research Participants | | |
| Approved | | |
| Effective Date: 07/01/2016 | Page 1 of 4 | Section: HRPP 7.8 |
| Replaces Policy: | | |

I. INTRODUCTION

The policy applies to all research recruitment activities by MUSC researchers. The IRB will evaluate the selection and recruitment of research participants in accordance with all relevant laws and regulations.

Recruitment is considered the start of the participant selection process and is a prelude to the informed consent/assent process. Investigators and the IRB must respect an individual's reasonable expectation for privacy when considering how information is gathered about a potential participant and who will invite the individual to participate in the research. Investigators and the IRB must also ensure that recruitment activities are free of bias, do not exert undue influence on or coerce a potential participant to volunteer, or imply a guarantee of benefits beyond what is outlined in the protocol and consent form approved by the IRB.

II. POLICY

Recruitment methods used to solicit volunteers into human research must be equitable and free of bias, undue influence and coercion and must respect the privacy of potential research participants. The IRB must review and approve the methods, materials, procedures, and tools used to recruit potential research participants before they are implemented.

A. Contacting Prospective Participants Who Were Identified From Medical Records

In general, the IRB does not approve of "cold calling" patients about potential research opportunities. Cold calling is when an individual is contacted by someone they do not know and the contact is unexpected.

When the participant's clinician is also the Principal Investigator for a study, the PI may approach a patient directly about participation in any of the PI's IRB approved research trials. The PI's personnel may also approach the patient and provide information about the research study.

PIs or research staff, who are not directly involved in a patient's clinical care, may NOT contact that patient regarding research participation without the patient's permission.

The research team may request that a clinician present his/her patient with information about the opportunity to participate in research. The clinician may directly (e.g. during an office visit) or indirectly (e.g. by letter, email, flyer) provide information about the research study, and/or provide a contact number for the PI or research staff to the patient. Study information provided by a clinician should not include any language or information that may be perceived as unduly influencing or coercive, or imply that medical care could be influenced by choice to participate or not. If the patient is interested in the research study, then he/she contacts the research team for more information. Patient information may be released to the PI or research staff only if a potential participant gives permission for his/her identifying information to be shared.

One way in which a patient may give permission to be contacted about a research study would be by agreeing to be contacted for research through the MUSC electronic health record (e.g. via MyChart). In this instance the PI/research team may directly contact patients who have agreed to be contacted for research. This method must be discussed in IRB application and must be approved by the IRB.

B. Opting In Versus Opting Out of Research

Opt-in: Researchers using this method contact potential subjects, usually with a recruitment letter, and ask them to get in touch with study staff if they wish to learn more about a research study. The investigators must then wait for subjects to contact them. The Opt-in method is more respectful and presents less risk of annoying potential subjects because they only contact the researchers if they are interested in the study. Opt-in recruitment is less popular with investigators since they must passively wait to be contacted by potential subjects, who might not initiate contact even though they might be interested in participating.

Opt-out: Researchers using this method contact potential subjects with a recruitment letter informing them about the existence of a research study. Individuals are told that they will be contacted by the researchers *unless* they call or mail back a card indicating that they are not interested (opt-out). Potential subjects could potentially be annoyed or offended by this approach since they have less choice in deciding whether or not to learn more about the research because they must make an effort to opt out. At the same time, this method is more feasible for investigators, particularly if subjects are difficult to contact or belong to a group that typically does not actively volunteer for research studies. As a rule, many subjects who might be willing to participate don't make the effort to opt-in so by using the opt-out approach these subjects may be contacted and may agree to participate.

The IRB may approve opt-out methods of recruitment if:

- The researchers provide justification in the IRB application as to why this strategy is appropriate
- The research does not involve very sensitive information (e.g., questions about illicit drug use, sexually transmitted diseases, alcohol abuse, emotional and/or mental disorders) – if it does the investigator must explain in the IRB application how this can be done without offending potential subjects
- The recruitment letter gives the potential participant clear instructions about how to opt out and offers **preferably two ways of opting out** (e.g., mail, phone, email)
- When individuals who did not opt out are contacted, they are reminded that they were sent a letter and are told at the start of the call that they can still “opt out now”
- The number of times the investigator will attempt to contact subjects who do NOT opt-out is limited (usually to three attempts). Making a large number of attempts to contact subjects trying to get them to participate could be viewed by the general public as harassment.

C. Secondary Recruitment

Secondary recruitment methods are used when investigators wish to recruit specific groups of participants through friends and family of existing participants. Some forms of this type recruitment are often called "snowball" recruiting. To protect the privacy of those being recruited, the IRB carefully considers whether these methods are appropriate for a given study.

Participant-initiated Secondary Recruitment is when the researcher asks current subjects to pass along recruitment materials or information to friends and family. The participant initiates the contact with family and friends, and these people must then contact the researcher if they wish to learn more about the study. This method is generally acceptable to the IRB.

Payment for Secondary Recruitment. It is permissible to allow this form of recruitment for studies by providing cash, gift certificates or other incentives to subjects to promote their aid in recruiting new individual subjects into studies. Such practices are allowable. The incentive to any subject should be picked with moderation, with justice and autonomy being considered. The level or amount of the incentive should be based on current local norms and must be approved by the IRB.

Modified Snowball Recruitment is when investigators ask participants if they have family and friends who might be eligible and interested in

participating in the research. The investigators only get in touch with these secondary contacts AFTER the subject has confirmed that he/she has obtained permission from the family members/friends to have the researchers contact them.

D. Future Recontact

During the consent process, investigators may ask potential participants if they would be willing to be recontacted for future research studies. The response to this should be documented in the informed consent. It is then permissible for the investigator to include the name and contact information of that individual for future studies. This list of individuals who are willing to be contacted for research purposes should not be stored with health information.

E. Research Involving MUSC Employees or MUSC Students

For specific guidance see HRPP 8.6 Research Involving MUSC Employees and Students

F. Recruitment Materials

For specific guidance see HRPP 7.2 - Advertisements for Research Participants Policy and Procedures

G. Finders Fees

The MUSC IRB does not allow the use of finders' fees in research. For specific guidance see HRPP 7.4 – Recruitment Incentives Policy and Procedures



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|---|-------------|-------------------|
| Policy Name: Vulnerable Populations – General Guidelines | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 8.1 |
| Replaces Policy: 03/03/2010 | | |

I. POLICY

A. Introduction

When some or all of the subjects in a protocol are likely to be vulnerable to coercion or undue influence, the IRB will include additional safeguards to protect the rights and welfare of these subjects. The review process will include one or more individuals who are knowledgeable about or experienced in working with the population involved in the research project.

B. Federal Regulations

45 CFR 46 has additional subparts which require extra protection for vulnerable populations and have additional requirements for IRBs.

1. Subpart B – Additional Protection for Pregnant Women, Human Fetuses and Neonates
2. Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
3. Subpart D – Additional Protections for Children Involved as Subjects in Research

C. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

D. ICH – Good Clinical Practice (GCP)

The MUSC IRBs operate in accord with ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. CGP standards contained in the ICH document are not regulatory requirements in the United States and vary from FDA and DHHS regulations. As such, the MUSC IRBs do not voluntarily agree to comply with all of the GCP statements unless requested to do so by sponsors as documented in contractual agreements. The MUSC IRBs comply with most aspects of ICH-GCP, and the MUC polices, procedures and forms require investigators to comply with most ICH-GCP guidance. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

E. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

Restrictions on Vulnerable Populations Specific to VA Research Studies

The following are prohibited as VA research study protocols:

1. Research involving fetuses
2. Research involving neonates
3. Research involving *in vitro* fertilization
4. Research involving prisoners unless a waiver has been granted by the VACO Chief Research and Development Officer
5. Research involving children unless
 - a) A waiver has been granted by the VACO Chief Research and Development Officer
 - b) The study presents no greater than minimal risk
 - c) The study meets all requirements of Subpart D of the DHHS or RDA regulations

- d) The Ralph H. Johnson VAMC Medical Center Director certifies that the facility is able to respond to pediatric emergencies
- e) The research is conducted by a contractor or non-VA employee and the individual or entity performing the research has appropriate liability insurance.

6. Research involving pregnant women unless

- a) The research includes adequate provisions to monitor the risks to the participant and the fetus.
- b) Adequate consideration is given to the manner in which prospective participants are going to be selected
- c) Adequate provisions are made to monitor the actual consent process by procedures such as:
 - (1) Overseeing the process by which individual consents are secured either by:
 - (a) Approving enrollment of each individual
 - (b) Verifying, perhaps through sampling, that approved procedures for enrollment of individuals into the activity were being followed
 - (c) Monitoring the progress of the activity and intervening, as necessary, through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen.

F. EPA Research

- 1. EPA policy requires submission of IRB determinations and approval to the EPA human subjects research review official for final review and approval before the research can begin.
- 2. For research not conducted or supported by any federal agency that has regulations for protecting human research subjects and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research subjects apply as the EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.



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|---|-------------|--------------------------|
| Policy Name: Research Involving Persons with Impaired Decision Making Capacity | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 5 | Section: HRPP 8.2 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

Research involving cognitively impaired individuals may only be approved by the IRB when the following conditions apply:

1. Only cognitively impaired persons are suitable as research subjects and competent persons are not suitable for the proposed research. Subjects with impaired decision making capability may not be included in research because they are readily available.
2. The research entails no significant risk or if the research presents some probability of harm, there must be greater probability of direct benefit to the subjects.

B. Assessment

Decision-making capacity/competency assessment of a potential subject who can reasonably be expected to be cognitively impaired must be assessed by a qualified professional independent of the research team. The frequency of this assessment will be appropriate to the population involved in a longitudinal study. It is the responsibility of the investigators to determine and monitor the decision-making capacity of subjects enrolled in research studies. This includes the event when a subject's decision-making capacity changes during the course of the study. The investigator should consider whether consent should be re-obtained from the subject's legal representative. For studies where it is anticipated that subjects may experience diminished decision making capacity, procedures for re-consenting should be detailed in the initial application. Only a legal representative may consent, .i.e. give permission, for a cognitively impaired individual to be enrolled in a research study. If a cognitively impaired adult subject objects to or resists participation in any way at any time, the subject must be immediately withdrawn from the study

C. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

VA Policy places additional requirements/limitations on research with this population. Details may be found in Appendix D of VHA Handbook 1200.5.

D. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

E. ICH – Good Clinical Practice (GCP)

The MUSC IRBs operate in accord with ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. CGP standards contained in the ICH document are not regulatory requirements in the United States and vary from FDA and DHHS regulations. As such, the MUSC IRBs do not voluntarily agree to comply with all of the GCP statements unless requested to do so by sponsors as documented in contractual agreements. The MUSC IRBs comply with most aspects of ICH-GCP, and the MUC polices, procedures and forms require investigators to com ploy with most ICH-GCP guidance. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html))

II. DEFINITIONS

Definitions for the following terms used in this section may be found in HRPP Program Guide Section 1.3 Definitions of Terms:

A. Cognitively Impaired

B. Competence

C. Legally Authorized Representative or Legal Representative

1. **VA Policy:** Legally Authorized Representative. A legally authorized representative is an individual or body authorized under applicable law to provide permission on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. For the purposes of VHA 1200.05, a legally authorized representative includes not only a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC), a court appointed guardian of the person, but also next-of-kin in the following order of priority unless otherwise specified by applicable state law:
 - a) spouse,
 - b) adult child (18 years of age or older),
 - c) parent,
 - d) adult sibling (18 years of age or older),
 - e) grandparent, or
 - f) adult grandchild (18 years of age or older)
 - g) close friend
2. **South Carolina Law:** per § 44-66-30 "The Adult Health Care Consent Act", the following, in priority order, may make health care decisions for individuals unable to give consent:
 - a) Court appointed guardian
 - b) Attorney-in-fact with durable power of attorney related to health care decision
 - c) Individual authorized by another statute
 - d) Spouse – unless legally separated, with provisions
 - e) Parent or adult child

- f) Adult sibling, grandparent, adult grandchild
- g) Other relative (by blood or marriage) believed by health care professional, to have close personal relationship

III. PROCEDURES

A. Standard

1. The Principal Investigator will describe the rationale for including this vulnerable population in the research, the method to be used to assess decision-making capacity including the name and qualifications of individual performing the assessment, and the frequency of this assessment in the human subject protections section of the protocol.
2. The Principal Investigator will describe the process of informed consent including who will be asked for consent, i.e. permission, to enroll the subject if the subject is assessed as cognitively impaired.
3. Using the “Special Subject Populations – Cognitively Impaired or Persons Unable to Consent” checklist, the IRB will determine:
 - a) if the risk level of participation is reasonable given the intended benefit and possible alternatives,
 - b) the appropriateness of the decision-making capacity assessment,
 - c) the appropriateness of obtaining surrogate informed consent from a legal representative,
 - d) if the available compensation might provide undue influence, and
 - e) if any additional protections are required such as the presence of a subject advocate during the consenting process, documented assent of the subject even when lacking decision making capacity, and/or excluding subjects without decision-making capacity from selected procedures of the research protocol.

These IRB discussions and decisions will be documented in the IRB minutes and communicated to the Principal Investigator.

B. VA Studies

1. An individual is presumed to have decision-making capacity unless any one or more of the following apply:
 - a) It has been documented by a qualified practitioner in the individual's medical record in a signed and dated progress note that the individual lacks capacity to make the decision to participate in the proposed study. **NOTE:** *The qualified practitioner may be a member of the research team.*
 - b) The individual has been ruled incompetent by a court of law.
2. If there is any question as to whether or not a potential adult subject has decision-making capacity, and there is no documentation in the medical record that the individual lacks decision-making capacity, and the individual has not been ruled incompetent by a court of law, the investigator must consult with a qualified practitioner (who may be a member of the research team) about the individual's decision-making capacity before proceeding with the informed consent process.
3. **Temporary or Fluctuating Lack of Decision-Making Capacity.** Individuals, who because of a known condition, are at high risk for temporary (e.g., head trauma) or fluctuating (e.g., schizophrenia) lack of decision-making capacity must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual's ability to provide informed consent. This evaluation must be performed as described in the IRB-approved protocol. If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a LAR must provide informed consent. If the subject regains decision-making capacity, the investigator or designee must repeat the informed consent process with the subject, and obtain the subject's permission to continue with the study.
4. The practitioner will explain the proposed research to the prospective participant when feasible.
5. The participant will not be forced or coerced to participate in the research study.
6. The IRB will find and document in the minutes or IRB records that:
 - a) Only incompetent persons or persons with impaired decision making capacity are suitable as participants.
 - b) Competent persons are not suitable for the proposed research.

- c) The investigator has demonstrated to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as participants.
 - (1) Incompetent persons or persons with impaired decision-making capacity are not being proposed as participants simply because they are readily available.
 - (2) The proposed research entails no significant risks, tangible or intangible, or if the research presented some probability of harm, there has to be at least a greater probability of direct benefit to the participant.
 - (3) The research does not impose a risk of injury, unless the research is intended to benefit that participant and the probability of benefit is greater than the probability of harm.
 - (4) Procedures are devised to ensure that participants' legally authority representatives are well informed regarding their roles and obligations to protect incompetent participants or persons with impaired decision making capacity.
 - (1) (5) Legally authorized representatives are told that their obligation is to try to determine what the prospective participant would do if competent, or if the prospective participant's wishes could not be determined, what they think is in the incompetent person's best interest.

IV. REFERENCES

- A. [Special Subject Populations Checklist - Cognitively Impaired or Persons Unable to Consent](#)



| | | |
|--|-------------|--------------------------|
| Policy Name: Research Involving Prisoners | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 4 | Section: HRPP 8.3 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Introduction

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

1. The majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.
2. At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

B. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

C. ICH – Good Clinical Practice (GCP)

The MUSC IRBs operate in accord with ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. CGP standards contained in the ICH document are not regulatory requirements

in the United States and vary from FDA and DHHS regulations. As such, the MUSC IRBs do not voluntarily agree to comply with all of the GCP statements unless requested to do so by sponsors as documented in contractual agreements. The MUSC IRBs comply with most aspects of ICH-GCP, and the MUC policies, procedures and forms require investigators to comply with most ICH-GCP guidance. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GCP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

D. Incarceration of a Research Subject

If during the course of the research, an individual subject becomes a “prisoner” as defined above, the investigator is required to notify the IRB promptly. At that point the investigator must discontinue all research activities with the subject unless the investigator asserts in writing and the reviewing Chair agree in writing that it is in the best interests of the subject to continue to participate in the research while the research is being re-reviewed by the IRB in accordance with the additional protections for research involving prisoners.

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

E. Prisoner Representative

A qualified “prisoner representative” must review all research proposing inclusion of a prisoner population and be a voting Board member at the convened meeting when a protocol including prisoners is discussed. The prisoner representative must be involved in the initial review, continuing review, review of protocol amendments, and review of unanticipated problems associated with a protocol involving a prisoner population.

F. IRB Deliberation and Documentation

When reviewing a protocol involving prisoners, the IRB must make and document the following findings (45 CFR 46.305(a)) that are in addition to those decisions required of all human research studies:

1. The research represents one of the categories of research permissible under 45 CFR 46.306(a)(2);

2. Any possible advantages gained by the prisoner by participating, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that the individual's ability to weigh the risks of the research against the value of such advantages in the limited choice environment is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Control subjects must be selected randomly from the group of available prisoners who meet the required characteristics unless the Principal Investigator provides rationale for varying the selection process acceptable to the IRB;
5. The information is presented in language which is understandable to the prisoner population of interest;
6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly told in advance that participation in the research will have no effect on parole decisions;
7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision have been made for this examination or care, taking in account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

Note: "Certification", i.e. documentation, of these findings must be sent to OHRP; the research cannot proceed until OHRP notifies the IRB in writing of their approval (45 CFR 46.306(a)(2)).

G. Categories of Research Involving Prisoners Allowable under 45 CFR 46.306(a)(2)

1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than an inconvenience to the subjects;
2. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than an inconvenience to the subjects;

3. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary, HHS, (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research; or
4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health and well being of the subject. When those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary, HHS, (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research (OHRP Guidance on the Involvement of Prisoners in Research, 2003).
5. Epidemiological Research addressing the prevalence, incidence, or risk factors for diseases that might affect prisoners (waiver published in the Federal Register on June 20, 2003 as 68 FR 36929). The research must pose no more than a minimal risk and present no more than an inconvenience to the prisoner participant.

H. Research conducted within the Bureau of Prisons - The Medical University of South Carolina, IRB and researchers and research staff must follow the requirements of 28 CFR 512 including,

1. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
2. The research design must be compatible with both the operation of prison facilities and protection of human subjects. The researcher must observe the rules of the institution or office in which the research is conducted.
3. Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.
4. All research proposals will be reviewed by the Bureau of Prisons Research Review Board.

II. DEFINITIONS

Definitions for the following terms used in this section may be found in HRPP Program Guide Section 1.3 Definitions of Terms:

A. Minimal Risk

B. Prisoner

III. PROCEDURES

A. The Principal Investigator will describe the rationale for including this vulnerable population in the research and specify the applicable permissible category of research involving prisoners, in the human subjects section of the protocol.

B. The IRB administrator and chair will assign the protocol to the primary reviewers; one of the reviewers must be the prisoner representative.

C. Using the “Special Subject Populations – Prisoners” checklist, the Board will determine if the research fits one of the allowed categories, the Board will specifically address the federally mandated issues described under 45 CFR Part 46, subpart C.

D. The Board’s discussion and decisions will be documented in the meeting minutes.

E. If the Board approves the research, the IRB Administrator will prepare the federally required “certification” letter to be sent to OHRP; the letter will be signed by the chair. OHRP also requires a copy of the approved research protocol, any HHS grant application or proposal, the IRB application form, and all other materials submitted to the IRB as requested. The IRB Administrator will notify the Principal Investigator of the status of the approval and will upload the letters to and from OHRP to the eIRB study workarea.

IV. REFERENCES

A. [Special Subject Populations Checklist - Prisoners](#)



| | | |
|--|-------------|--------------------------|
| Policy Name: Research Involving Pregnant Women, Fetuses, and Neonates | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 6 | Section: HRPP 8.4 |
| Replaces Policy: 02/20/2009 | | |

I. POLICY

A. Procedures When Pregnancy is Coincidental to Subject Selection

1. Women of childbearing potential will be included in all study populations unless the investigator provides clear, sound rationale for excluding this population group. If exclusion of pregnant women, nursing women, or women who wish to start a pregnancy is justified, the protocol and informed consent document should explain the reasons for the exclusion.
2. If the research study poses known risks and/or lack of knowledge relative to the risks to a pregnant woman and/or fetus, the eligibility screening will include a pregnancy test; pregnancy tests will be performed throughout the woman's participation as appropriate.
3. As appropriate, the informed consent will include statements regarding:
 - a) the need for pregnancy testing before and during the study,
 - b) the recommended contraceptive methods based on the known risks,
 - c) the need to notify the Principal Investigator immediately if pregnancy occurs and
 - d) the possibility of unforeseen risks to the subject and/or fetus.

B. Procedures for Studies Directed Primarily Toward the Mother's and/or Fetus's Health

1. The "Special Subject Populations – Pregnant Women, Fetuses, Neonates" checklist will be used as a guide for IRB evaluation and will be completed by the primary reviewer.
2. If the research holds the prospect of direct benefit to the mother or to the mother and the fetus, a greater than minimal risk to the fetus is acceptable if:

- a) where appropriate, data are available from prior animal studies and nonpregnant women clinical studies to assess potential risks to pregnant women and fetuses;
- b) the risk to the fetus is caused solely by interventions or procedures that hold the prospect of direct benefit for the woman or the woman and fetus; and,
- c) 3) the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.

The pregnant woman's consent is sufficient to enroll in the study. The informed consent document will fully describe the reasonably foreseeable impact of the research on the fetus or neonate [45 CFR 46.204]

- 3. If the research holds the prospect of direct benefit solely to the fetus, a greater than minimal risk to the fetus is acceptable if:
 - a) where appropriate, data are available from prior animal studies and nonpregnant women clinical studies to assess potential risks to pregnant women and fetuses;
 - b) the risk to the fetus is caused solely by interventions or procedures that hold the prospect of direct benefit for the fetus; and
 - c) any risk is the least possible for achieving the research objectives.

Informed consent must be obtained both from the mother and the father unless he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest. The reason for not obtaining the father's informed consent must be documented in the research record. The informed consent document will fully describe the reasonably foreseeable impact of the research on the fetus or neonate (45 CFR 46.204).

- 4. If the research does not hold the prospect of direct benefit to the woman or fetus, the research is acceptable if the risk to the fetus is not greater than minimal and:
 - a) where appropriate, data are available from prior animal studies and nonpregnant women clinical studies to assess potential risks to pregnant women and fetuses,

- b) the study intends to develop important biomedical knowledge that cannot be obtained by any other means, and
- c) any risk is the least possible for achieving the research objectives.

The pregnant woman's consent is sufficient to enroll in the study. The informed consent document will fully describe the reasonably foreseeable impact of the research on the fetus or neonate (45 CFR 46.204)

- 5. Research involving pregnant women and fetuses can only be conducted if:
 - a) no inducements, monetary or otherwise, will be offered to terminate a pregnancy;
 - b) individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
 - c) individuals engaged in the research will no part in determining the viability of a neonate [45 CFR 46.204].
- 6. For children who are pregnant, assent and permission will be obtained in accordance with regulations.

C. Procedures for Research Involving nonviable Neonates

- 1. The "Special Subject Populations – Pregnant Women, Fetuses, Neonates" checklist will be used as a guide for IRB evaluation and will be completed by the primary reviewer.
- 2. A "nonviable neonate" means a neonate after delivery that, although living is not viable (45 CFR 46.202). Nonviable neonates may be involved in research if: 1) where appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; 2) individuals engaged in the research will have no part in determining the viability of the neonate; 3) vital functions of the neonate will not be artificially maintained; 4) the research will not terminate the heartbeat or respirations of the neonate; 5) there will be no added risk to the neonate resulting from the research; and, 6) the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means [45 CFR 46.205].
- 3. The informed consent of both parents is required. The informed consent of one parent is acceptable if either parent is unable to

consent because of unavailability, incompetence, or temporary incapacity. The consent of the father is not required if the pregnancy resulted from rape or incest. The consent of a legal representative of either parent is not acceptable. The reason for not obtaining both parents' informed consent must be documented in the research record. The informed consent document will fully describe the reasonably foreseeable impact of the research on the neonate [45 CFR 46.205].

D. Procedures for Research Involving Neonates of Uncertain Viability

1. The "Special Subject Populations – Pregnant Women, Fetuses, Neonates" checklist will be used as a guide for IRB evaluation and will be completed by the primary reviewer.
2. Neonates of uncertain viability may be involved in research if:
 - a) where appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
 - b) individuals engaged in the research will have no part in determining the viability of the neonate; and
 - c) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability and any risk is the least possible for achieving that objective **or** the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means and there will be no added risk to the neonate resulting from the research [45 CFR 46.205].
3. The informed consent of either parent is required. The informed consent of one parent is acceptable if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity. The consent of the father is not required if the pregnancy resulted from rape or incest. The consent of a legal representative of either parent is not acceptable. The reason for not obtaining both parents' informed consent must be documented in the research record. The informed consent document will fully describe the reasonably foreseeable impact of the research on the neonate [45 CFR 46.205].

E. Research Involving Pregnant Women as Participants is Not Approved Unless All of the Following Conditions are Met:

1. Appropriate studies on animals and non-pregnant individuals have been completed, and for data assessing risks to pregnant women and fetuses are provided.
2. The purpose of the activity is to meet the health needs of the mother or the particular fetus.
3. The risk to the fetus is minimal.
4. The risk to the fetus is the least possible risk for achieving the objectives of the activity.
5. Individuals engaged in the activity have no part in:
 - a) Any decisions as to the timing, method, and procedures used to terminate the pregnancy.
 - b) Determining the viability of the fetus at the termination of the pregnancy.
 - c) Introducing any procedural changes, for research purposes, into the procedures for terminating the pregnancy.
6. No inducements, monetary or otherwise, are offered to terminate pregnancy for purposes of research.
7. One of the following is true:
 - a) The fetus is placed at risk only to the minimum extent necessary to meet the health care needs of the mother.
 - b) The risk to the fetus is minimal.
8. Consent is obtained from the mother and father, except that the father's consent need not be secured if:
 - a) The purpose of the activity is to meet the health needs of the mother.
 - b) His identity or whereabouts cannot reasonably be ascertained.
 - c) He is not reasonably available.
9. The pregnancy resulted from rape

F. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

G. ICH – Good Clinical Practice (GCP)

The MUSC IRBs operate in accord with ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. CGP standards contained in the ICH document are not regulatory requirements in the United States and vary from FDA and DHHS regulations. As such, the MUSC IRBs do not voluntarily agree to comply with all of the GCP statements unless requested to do so by sponsors as documented in contractual agreements. The MUSC IRBs comply with most aspects of ICH-GCP, and the MUSC policies, procedures and forms require investigators to comply with most ICH-GCP guidance. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

II. REFERENCES

- A. [Special Subject Populations Checklist – Pregnant Women, Fetuses, and Neonates](#)



| | | |
|---|-------------|--------------------------|
| Policy Name: Research Involving Children | | |
| Approved | | |
| Effective Date: 01/30/2015 | Page 1 of 5 | Section: HRPP 8.5 |
| Replaces Policy: 05/15/2012 | | |

I. POLICY

- A. The IRB will consider the potential benefits, risks, and discomforts of research involving children within the context of the justification for inclusion of children in the research. The IRB will consider the circumstances of the children to be enrolled in a study, e.g. their health status, age, and ability to understand their involvement, as well as potential benefit to the subjects, other children with the same disease/condition, or society as a whole. (OHRP Guidance, 2005).
- B. The IRB will decide which of four risk categories defined by federal regulations [45CFR 46(d) and 21CFR 50.51-50.54] apply to any study enrolling children other than exempt research.
- C. Minimally, an adult parent with legal custody of a child or an adult awarded legal custody of a child must give informed consent for a child to be enrolled in research. A child 12 years of age or older must give documented "assent" to be enrolled in research unless the IRB provides a waiver of assent. The assent will be documented on the informed consent document. An "emancipated minor" must provide documentation of his/her financial independence such as a rental lease, marriage certificate or court document in his/her name proving emancipation before consenting as an adult to participate in research [45 CFR 46 Subpart D Additional DHHS Protections for Children Involved as Subjects in Research]
- D. The IRB may decide that both parents must give informed consent for a child to be enrolled in research. The IRB will require that both parents must give informed consent for a child to enroll in research if the research is assessed by the IRB to be category 3 or category 4 unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal custody of a child [45CFR 46.408(c)]. The regulations make two parents the default and one is appropriate if the IRB determines it is so and the research falls into the first two "categories".
- E. Under certain circumstances, to protect the welfare of the minor, the convened IRB board may chose to waive parental consent. An example would be a study involving child abuse in which parental consent would be ill-advised. In circumstances where parental consent is waived, a child subject advocate must be assigned to protect the children who would participate as participants in the research.

F. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html))

G. ICH – Good Clinical Practice (GCP)

The MUSC IRBs operate in accord with ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. CGP standards contained in the ICH document are not regulatory requirements in the United States and vary from FDA and DHHS regulations. As such, the MUSC IRBs do not voluntarily agree to comply with all of the GCP statements unless requested to do so by sponsors as documented in contractual agreements. The MUSC IRBs comply with most aspects of ICH-GCP, and the MUSC policies, procedures and forms require investigators to comply with most ICH-GCP guidance. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

II. DEFINITIONS

Definitions for the following terms used in this section may be found in HRPP Guide Section 1.3 Definitions Terms:

A. Children

III. CHILDRENS RESEARCH CATEGORIES

- A. Category I [45 CFR 46.404 and 21 CFR 50.51] = research not involving greater than minimal risk to the children.** To approve this category, the IRB must make the following determinations: 1) the research presents no more than minimal risk to the children; and 2) adequate provisions are

made for soliciting the assent of the children and permission of their parents or guardians.

- B. Category II [CFR 46.405 and 21 CFR 50.52] = research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research.** To approve this category, the IRB must make the following determinations: 1) the risk is justified by the anticipated benefits to the subjects; 2) the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; and 3) adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
- C. Category III [45 CFR 46.406 and 21 CFR 50.53] = research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition.** To approve this category, the IRB must make the following determinations: 1) risk of the research presents a minor increase over minimal risk; 2) the intervention or procedure presents experiences to the child subjects that are reasonable commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations; 3) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and 4) adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
- D. Category IV [45 CFR 46.407 and 21 CFR 50.54] = research that the IRB believes does not meet the conditions of the other categories but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.** This category of research requires a federal level of review by the Secretary, Health and Human Services, or designee and the Commissioner of FDA who will request the review by a panel of experts in pertinent disciplines and call for public review and comment.

IV. PROCEDURES

- A.** The "Special Subject Populations - Children" checklist will be used as a guide for IRB evaluation and will be completed by the primary reviewer.
- B.** During the initial review of a protocol involving children, the IRB assigned primary reviewers will designate the appropriate risk category as defined above and give a brief rationale for the category selected.

- C. The Board will determine the appropriate research category as part of the motion relative to approval of a protocol involving children; the rationale for this categorization will be documented in the Board meeting minutes.
- D. If the research is determined to fit category I or II, the IRB will decide if the consent of one parent is adequate or if the consent of both parents is required. This decision will be documented in the IRB meeting minutes.
- E. If the research is determined to fit category III or IV, the documented consent of both parents will be required unless the Board stipulates documented consent from one parent is acceptable; the rationale for this decision will be documented in the IRB meeting minutes.
- F. The IRB will make protocol-specific determinations regarding whether adequate provisions should be made for soliciting the assent of the children younger than 12-years old, when in the judgment of the IRB members, the children are capable of providing assent. This determination will be documented in the IRB minutes.

For expedited protocols, the IRB chair or chair's designee will make this determination. This determination will be documented in the IRB expedited protocol checklist.

- G. Family Educational Rights and Privacy Act (FERPA) and Protection of Pupil Rights Amendment (PPRA)
 1. Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99) is a Federal law that protects the privacy of student education records. The law applied to all schools that receive funds under an applicable program of the U.S. Department of Education (ED). FERPA regulates the disclosure of Personally Identifiable Information from youth Education Records in all public elementary and secondary schools, school districts, intermediate education agencies, state education agencies, and any public or private agency or institution that uses funds from ED. The purpose of FERPA is to protect all student and parent information maintained in an Education Record.
 2. The protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h; 34 CFR Part 98), a.k.a. "Student Rights in Research, Experimental Programs, and Testing", applies to programs and institutions that receive funding from the U.S. Department of education (ED). PPRA is intended to protect the rights of parents and students.
 3. When reviewing research involving students, the convened IRB or the reviewer for expedited procedure will determine and document that the regulatory criteria allowing approval under 34 CFR 98

“Protection of Pupil Rights Amendment (PPRA)” or 34 CFR 99
“Family Educational Rights Protection Act (FERPA)” have been
met.

II. REFERENCES

- A. [Special Subject Populations Checklist – Children](#)



| | | | |
|--|-------------|--------------------------|--------------------|
| Policy Name: Research Involving MUSC Employees or MUSC Students | | | |
| Approved | | | Date: 11/01/08 |
| Effective Date: 02/20/09 | Page 1 of 1 | Section: HRPP 8.6 | Policy Number: N/A |
| Replaces Policy: N/A | | | Dated: N/A |

I. POLICY

- A.** MUSC employees may not participate in the research of an immediate supervisor if that research presents greater than minimal risk. The IRB may approve an exception to this policy if an employee may derive direct health benefits from participation, e.g. cancer research. Consideration will be on a case-by-case basis.

- B.** MUSC students may not participate in the research of a mentor if that research presents greater than minimal risk. The IRB may approve an exception to this policy if a student may derive direct health benefits from participation, e.g. cancer research. Consideration will be on a case-by-case basis. If approved, the student will receive an annual renewal notice with an option to terminate participation by completion of a closeout form.



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|--|-------------|-------------------|
| Policy Name: Off-Campus Research Studies | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 7 | Section: HRPP 9.1 |
| Replaces Policy: Effective 01/27/2012 | | |

I. POLICY

A. Purpose

This policy applies to research studies in which research activities are conducted at sites that are not owned or operated by the Medical University of South Carolina and do not fall under the MUSC IRB's authority.

B. Policy

Off-campus research that is conducted by an agent of MUSC must be reviewed and approved by the MUSC IRB. The off campus site(s) may require its/their own review. If this is the case, approval from both sites would be required before the investigator initiated research. With an appropriate reliance agreement, single review by one IRB may occur.

C. Introduction

Off-campus research is defined as research conducted at a site that is external from MUSC (i.e. a non-MUSC site). An off-campus site may be domestic or international and may or may not have its own IRB.

Off-campus research may involve more than one institutional review board responsible for research oversight. In these cases, MUSC has established additional procedures to define the responsibilities of each IRB, coordinate communication among responsible IRBs, and manage information obtained in off-campus site research to ensure protection of human subjects.

A determination must be made as to whether the non-MUSC institution is "engaged" in the human subjects research activity. Research procedures should not be initiated at an off-campus site location prior to MUSC IRB's review of the appropriate documentation for that site.

If the off-campus/non-MUSC site(s) has its own IRB, the research may either be reviewed by that institution or a reliance agreement may be established between MUSC-IRB and the off-campus site's IRB. If the off-campus site(s) does not have its own IRB, the MUSC IRB may serve as the relied-upon IRB for the non-MUSC institution if that institution is considered engaged in research per OHRP guidance.

D. Memorandum Of Understanding

In situations where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards". For some multi-center studies, the use of the VA Central IRB may be required.

II. PROCEDURES

A. Investigator Responsibilities

1. In either the human research review application on-line form for an initial study or in an amendment to an existing study include:
 - a) That the research will be conducted at a site or multiple sites not affiliated with MUSC (non-MUSC site);
 - b) A description of the specific research activities to be conducted at the site;
 - c) For each non-MUSC site that is not engaged in research, submit a letter of support (on letterhead stationery) from the appropriate administrator of the non-MUSC site stating that the study may occur at the location in question. There may be exceptions to this requirement (e.g. interviews in public restaurants or parks).
 - d) For each non-MUSC site that is engaged in research, approval to conduct the study at that site will be documented by either the off-campus site's IRB or through a reliance agreement with MUSC IRB.
 - (1) The MUSC PI should provide written confirmation that facility personnel have the appropriate expertise to carry out the research procedures and assurance that personnel from the facility who are engaged in the research have appropriate training in human subject research protections (CITI)
2. Complete the "Off-Campus Study Site Form" for each site non-MUSC site indicating the following:
 - a) A determination of whether the site is "engaged" in research using the OHRP Guidance Document, "Engagement of Institutions in Research".

The IRB Staff may assist the PI in determining whether the non-MUSC employees are actively participating in the implementation of research procedures or are obtaining individually identifiable private data about human subjects for research purposes. If the non-MUSC employees are engaged in the research, then the non-MUSC site must also have IRB approval before the study may be conducted there.

- b) Documentation of whether the non-MUSC site has an IRB and if so, whether it has approved the research or will request reliance upon the MUSC IRB.
 - c) If the off-campus site has an approved FWA, provide the off-campus site's FWA number.
3. If the off-campus site has an IRB and does not plan to request reliance on the MUSC IRB, the MUSC investigator is responsible for providing documentation of that off-campus site's IRB approval of the investigator's research at that site if requested by the MUSC IRB. In addition, the investigator is responsible for ensuring that the off-campus site's IRB approval is current for the duration of that site's involvement.

B. MUSC IRB Responsibilities

1. Review initial, continuing, and amended applications to the IRB to determine if the research is being conducted at other sites.
2. Make preliminary determination if the off-campus site(s) is "engaged in research" based on OHRP guidance.
3. For off-campus sites that are engaged, determine if the off-campus site has an IRB with a Federal Wide Assurance (FWA) and, if so, check for documentation of IRB approval.

C. VA Research - When following VA regulations and guidance:

1. The principal researcher, and also the VA PI (if different), must obtain written approvals from the relevant local VA facilities' IRBs of record and all other local committees, subcommittees, and other approvals according to the respective applicable local, VA and other federal requirements.
2. Research cannot be initiated at any given VA site until the local researcher has obtained written notification that the research can be initiated from the local Research and Development committee.

- D. Institutional Officials Responsibilities** – When the off-campus site is engaged in the MUSC PI's research, the Institutional Official is responsible for making the final determination as to whether MUSC will serve as the relied-upon IRB or whether the MUSC IRB will defer review to another IRB (see policies 9.4 and 9.5).
- E. Guidance on Additional Requirements of Federal Funding Agencies**
Regardless of where research is conducted, research sponsored by any of the following may have additional regulations that must be followed:
- * Department of Defense (DOD),
 - * Department of Education,
 - * Department of Energy,
 - * Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
 - * Environmental Protection Agency (EPA)
- Specific sponsors may have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation - Good Clinical Practices (ICH-GCP) have additional requirements. Further information available on the MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>)

III. REFERENCES

- A. OHRP Guidance Document:** "[Engagement of Institutions in Human Subjects Research](#)"
- B. HRPP Policy Guide Section 9.4** –"MUSC as Single IRB of Record"
- C. HRPP Policy Guide Section 9.5** - "Relying on an External IRB"



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|---|-------------|--------------------------|
| Policy Name: Management of Reporting Events in Multi-Site Research Studies Policy and Procedures | | |
| Approved | | |
| Effective Date: 01/27/2012 | Page 1 of 2 | Section: HRPP 9.2 |
| Replaces Policy: 02/20/09 | | |

I. POLICY

A. Introduction

The guidance for this policy is based on guidance on continuing review from OHRP dated January 15, 2007, in particular on item 2, "Additional considerations for continuing review of multi-center trials.....". In this guidance, OHRP acknowledges that local investigators participating in multi-center trials often are not able to prepare a meaningful summary of adverse events or may not have access to other communications from other sites. However, OHRP recommends that at the time of continuing review local investigators send their IRB a current report from the monitoring entity. This could include information from the research sponsor, a coordinating or statistical center or as data safety monitoring board or data safety monitoring committee.

B. OHRP Recommendations

OHRP recommends the report include, but may not be limited to the following:

1. A statement of what type of information was reviewed by the monitoring entity (e.g., recent published literature, interim findings, study-wide adverse events with aggregate data analysis blinded or un-blinded);
2. The date of this review;
3. The monitoring entity's assessment of the information reviewed; and
4. The local principal investigator should make judgment as to whether or not this information warrants changes in the local informed consent document and/or the research protocol.

Information obtained from multi-center trials by the local investigator should be reviewed for its relevance on the basis of safety, ethics and clinical implications. Any information that is received that is felt to be of a vital, timely or urgent nature should be forwarded to the appropriate IRB administrator without delay and without waiting for the next continuing

review. This information should be sent electronically by the principal investigator or his/her designee regarding this particular multi-center trial.

C. IRB Responsibilities

The report will be forwarded to the appropriate IRB administrator for initial review and then forwarded to the appropriate chair person, vice chair person or their designee. This IRB official may request further information from the local investigator, the originator of the communication or from the research sponsor. A host of actions or no action could be anticipated based on the nature of the information received in the report. The information could be passed to the next IRB meeting for further discussion and actions. The IRB chair person or vice chair could request the investigator provide a detailed report from the monitoring entity, a request for cessation of study recruitment could be requested at the local site, and reports to OHRP and/or the FDA could be applicable.



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|---|-------------|-------------------|
| Policy Name: Transnational Studies Policy and Procedures | | |
| Approved | | |
| Effective Date: 08/01/2012 | Page 1 of 5 | Section: HRPP 9.3 |
| Replaces Policy: 05/15/2012 | | |

I. POLICY

A. Introduction

In reviewing research protocols that will be conducted at international or other non-MUSC University sites, the MUSC IRB must obtain sufficient knowledge of the local Research context in order to fulfill its responsibilities under its FWA and to comply with all applicable required standards. In particular, the IRB must be sensitive to community attitudes and be able to ascertain the acceptability of the proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. All policies and procedures that are applied to research conducted domestically will be applied to research conducted in other countries, as appropriate, including oversight of the following: initial review, continuing review, and review of modifications; post-approval monitoring; and handling of complaints, noncompliance, and UPIRSOs.

B. Regulations

1. In accordance with federal regulations, the MUSC IRB, in reviewing research protocols that will be conducted at a non-MUSC foreign site, must obtain sufficient knowledge about the local research context to ensure that adequate protections are in place for the conduct of the research in that geographic location. Federal Regulations require that IRBs be knowledgeable about the local research context as demonstrated by fulfillment of the following criteria:
 - a) The IRB's composition must be adequate in light of the scope of the institution's research activities, types of subject populations, appropriateness of proposed review procedures in light of probable risks, and the size and complexity of the institution. [45 CFR §46.103(d)]
 - b) The IRB's members must be sufficiently qualified through experience, expertise, diversity (including race, gender, cultural background), and sensitivity to such issues as

community attitudes to promote respect for the IRB's advice and counsel. [45 CFR §46.107(a)]

- c) The IRB must be able to evaluate research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. [45 CFR §46.107(a)]
- d) The IRB must also be capable of ensuring that the selection of subjects is equitable, privacy and confidentiality of subjects is maintained, informed consent is sought in language understandable to the subject and in circumstances that minimize the possibility of coercion, and that there are appropriate safeguards protecting vulnerable subjects. [45 CFR §46.111(a)(3),(a)(4),(a)(7),(b) and 46.116]

- 2. For the purposes of research that may be subject to regulation by the FDA, the FDA Regulations contain essentially the same requirements as those set forth above. [21 CFR 561.07, 56.111(a)(3),(a)(7) and (b)]. Both HHS and FDA Regulations, as well as other Federal regulations, may apply to the same research protocol.

C. Guidance on Additional Requirements of Federal Funding Agencies

Please note that protocols conducted by MUSC and sponsored by any of the following federal agencies

- the Department of Defense (DOD),
- Department of Education,
- Department of Energy,
- Department of Justice (DOJ) / National Institute of Justice (NIJ) and Bureau of Prisons (BOP) or
- Environmental Protection Agency (EPA)

have additional operational and review requirements. In addition, protocols following the International Committee on Harmonisation – Good Clinical Practices (ICH-GHP) have additional requirements. Further information available on the [MUSC IRB Resources & Guidance Webpage <http://research.musc.edu/ori/irb/resources.html>](http://research.musc.edu/ori/irb/resources.html)).

II. Definitions

Definitions of the following terms used in this section may be found in HRPP Guide Section 1.3 - Definition of terms

- A. Transnational Research** (Research conducted outside of the United States of America.)

III. Procedures

- A.** Knowledge of the local research context is essential for the IRB reviewing and overseeing non-exempt research conducted at an external location/site or for determining that the research is exempt. Sufficient information to assess the local context may be obtained in various ways, depending on the distance and differences between the IRB and the research site, previous experience with the location/site, presence of local collaborators, etc. The information that should be obtained also depends on the nature and scope of the research to be conducted at the site.

- B.** For research conducted off-site, adequate knowledge of the local context may be obtained in various ways, including the following:

Personal knowledge of one or more IRB members or an appropriate consultant, obtained through direct experience with the site, its populations, and the surrounding community;

Written materials submitted by the investigator or local site contact;

Site visit or conversation with the local site contact or other individual identified by the investigator as being knowledgeable about the research site.

- C.** For collaborating external investigators engaged in research, documentation of appropriate credentials to perform the proposed research and completion of training in human subjects' protection will be obtained.

- D.** For research conducted outside of the United States, the following information should be described in the research protocol:

- a. Scope and nature of the research activities to be performed at the external location/site;
- b. Relevance of the research to the local population's needs and interests;
- c. Community in which the research will take place, including any customs or practices (e.g., cultural, political, or religious) unique to the location/population;
- d. Characteristics of the site that may affect selection and/or privacy of participants;

- e. Influence of local officials on the population;
 - f. Literacy rate and language(s) understood by potential participants;
 - g. Local legal rights of the population (including relevant sub-populations such as women in general, unmarried v. married women, children, etc.);
 - h. Appropriateness of proposed compensation (if any) at the external location;
 - i. Facilities/equipment at the external site relevant to research performance and protection of participants;
 - j. Methods for maintaining confidentiality of data stored and transferred between sites;
 - k. Communication and oversight plans between MUSC and the external site;
 - l. How complaints will be reported and to whom;
 - m. The possibility of including officials from the area in the monitoring of the research;
 - n. Local standards of care for relevant medical conditions;
 - o. Applicable laws, site policies, and requirements relevant to the research and how the research team will comply with such.
- E.** The MUSC IRB must also assure that adequate provisions are made for data and safety monitoring, and take into consideration that some foreign IRBs or Ethics Committees may not require Continuing Review of approved research.
- F.** The informed consent documents must be in a language understandable to the proposed participants. The IRB encourages investigators to obtain back translations of the foreign language informed consent document(s) to verify translation accuracy. The translator's credentials should be provided in the IRB application. In some circumstances it may be inappropriate to document consent by using the standard written and signed informed consent document. The IRB must take also into account that there may be different laws regarding determination of who may serve as a Legally Authorized Representative (LAR).
- G.** Documentation Required from PI: The MUSC IRB also requires that the PI provide the following documentation before research that takes place at an international site is approved: an OHRP-approved FWA for the international site, if federally funded; a letter of cooperation showing that the appropriate

institutional or oversight officials are permitting the research to be conducted at the site; an OHRP-registered local IRB (Ethics Committee) approval letter for the proposed research if an IRB (or Ethics Committee) exists, or documentation that the IRB (Ethics Committee) has determined that approval is not necessary.

- H. The investigator is responsible for completing the amendments, continuing reviews, and reportable events, and for following all IRB policies and procedures. The investigator is responsible for notifying the MUSC IRB promptly if a change in research activities alters the international site's engagement in the research (e.g., an international site previously determined to be "not engaged" begins consenting research participants). The IRB is responsible for monitoring the research as with all other human subjects research under its purview.
- I. The Investigator is responsible for providing to the MUSC IRB any reports of correspondence with the foreign institution or site and appropriate documentation of data and safety measures throughout the course of the study, including serious and unexpected adverse events and unanticipated problems to participants or others (e.g., a breach of participant confidentiality resulting in local ramifications). Any problems encountered with the research should be reported to the study sponsor, relevant regulatory bodies, and all reviewing IRBs or ECs as appropriate.
- J. When necessary, the MUSC IRB will communicate with the host country's IRB or EC, should any of these exist.
- K. MUSC General Council is available for consultation regarding questions about the laws of other countries where the research is conducted, particularly biomedical research.

IV. HIPAA Considerations

- A. The extent to which HIPAA applies to international research is currently a matter of discussion; however, once individually identifiable health information is received by MUSC (a covered entity), that information becomes protected health information (PHI) (with a narrow exception for overseas foreign nationals receiving health care from US agencies). This means that when a researcher sends individually identifiable health information collected internationally across a MUSC network or stores such information on a MUSC computer or server, the information becomes PHI.
- B. Because HIPAA concepts can be difficult to translate in international studies, researchers may request a "Waiver or Alteration of HIPAA Authorization", to ask the IRB to approve altered language or a simplified form of the required authorization language, and/or to approve an oral authorization process.

Another option, where cultural barriers are significant, is for the IRB to waive the requirement of HIPAA Authorization entirely. To grant any of these requests, the IRB must determine that the request meets all of the waiver criteria in the HIPAA Privacy Rule. Or the investigator can avoid HIPAA considerations altogether by not bringing PHI to MUSC, and instead bringing only coded de-identified health information, or by bringing only a limited data set with an established data use agreement in place.

V. MEMORANDUM OF UNDERSTANDING

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current “Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina’s Institutional Review Boards”.

Transnational human subjects research conducted at the VA requires that the following requirements be met:

1. Permission must be obtained from the chief research and development officer, or designee, prior to initiating any VA-approved international research.
2. The VA facility director must approve any request for permission to conduct international research prior to forwarding it to the chief research and development officer.
3. The researcher must conduct the research in accordance with VA requirements and all other applicable federal requirements for protecting human subjects, tissue banking, use of databases, federal criminal laws, and the standards of ethical conduct for employees of the executive branch.

VI. REFERENCES

- A. [DHHS Title 45 Part 46](#)
 1. 45 CFR §§ 46.103(d);
 2. 46.107(a);
 3. 46.111(a)(3), (a)(4), (a)(7), (b)
 4. 46.116
- B. [FDA Title 21 Part 56](#)
 1. 21 CFR §56.111(a)(3),(a)(7) and (b)
- C. [OHRP Guidance Document: Knowledge of Local Research Context](#), July 21, 2000



| | | |
|---|-------------|-------------------|
| Policy Name: MUSC as Single IRB of Record | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 2 | Section: HRPP 9.4 |
| Replaces Policy: n/a | | |

I. POLICY

The policy describes how the MUSC IRB may serve as the Single IRB of Record for a nonexempt multi-site study in which an MUSC investigator will serve as the Lead PI. In this situation, the MUSC IRB is the *IRB of Record*, and the non-MUSC (remote) sites' IRB is/are the *Relying IRBs*.

II. INTRODUCTION

MUSC will typically only serve as the Single IRB of Record for a multi-site trial if the MUSC PI is either the Lead Investigator or serves as the Coordinating Center for the multi-site trial. There may be other circumstances for which MUSC IRB would serve as the Single IRB or Record, which will be determined on a case-by-case basis.

Criteria for Relying Institutions to use MUSC as the Single IRB of Record:

MUSC will apply the following criteria when deciding whether MUSC IRB will serve as Single IRB for a given site:

- The remote site currently has a valid FWA.
- The remote site has the ability to perform post-approval monitoring of the research.
- The remote site is located within the U.S.

III. IRB Authorization Agreement/Reliance Agreement

In accordance with OHRP Guidance, when a remote site requests to rely on MUSC IRB for review and approval of human research, the relationship will be documented with an IRB Authorization Agreement (IAA) or other formal reliance agreement. This formal agreement requires each institution to have an FWA and

- Identifies MUSC's IRB as the IRB of record, specifies which institution's IRB will review which components of a study, and includes a description of the regulatory requirements for which each party will assume responsibility.
- The MUSC Institutional Official (IO) or designee has the ultimate authority regarding whether or not MUSC will serve as the Single IRB of Record. The

IO is authorized to execute IAAs / Reliance Agreements on MUSC's behalf and may delegate this authority.

IV. MUSC PI Responsibilities

1. The MUSC PI will serve as either the Lead Investigator of the multi-site trial or as the Coordinating Center (unless as determined different on a case by case basis as stipulated in agreement).
2. The PI will work with the MUSC IRB to get Reliance Agreements out to the Remote Sites interested in relying on MUSC IRB.
3. The PI will submit appropriate documents for MUSC IRB approval including protocol, consent form for local site, as well as consent template for the Remote Sites.
4. Once the PI has initial approval, the PI will be responsible for adding each Remote site in the MUSC eIRB system. This will include adding remote site staff, local context information, and appropriate site-specific documents.
5. The MUSC PI is responsible for ensuring appropriate communication regarding MUSC IRB approvals/requirements with the Remote Sites (e.g. IRB approved documents).
6. After Remote Site approval, the MUSC PI is responsible for:
 - submitting any amendments for Remote Sites
 - obtaining information necessary for continuing review from each site and collating it into a single continuing review application for review and approval by MUSC IRB
 - reviewing all Remote Site regulatory documents/reports and submitting them for IRB review on behalf of the remote site

V. Responsibilities of Remote Sites

1. The Remote Site is responsible for ensuring compliance with the MUSC IRB's requirements at the research site.
2. Prior to review, provide the MUSC IRB with any local context issues relevant to the research protocol.
3. Research may be further reviewed and approved or disapproved by officials of the Remote Site as the relying institution, but the Remote Site IRB may not approve the research if it has not been approved by the MUSC IRB.
4. Educate and train its investigators to perform research in compliance with human research protection regulations. If Remote Site does not have a human subjects' protection educational requirement, the Remote Site research staff must follow MUSC training requirements (CITI course)
5. The Remote Site and its researchers acknowledge and agree to cooperate in MUSC IRB's responsibility for initial and continuing review, record keeping and reporting. All information requested by the MUSC IRB will be provided in a timely manner.
6. Researchers will not enroll individuals in research prior to review and approval by the MUSC IRB.

7. The researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative as stipulated by the MUSC IRB.
8. The Remote Site must have the capacity to conduct post-approval monitoring in addition to, or in cooperation with, the MUSC IRB.
9. The Remote Site will identify local Conflict of Interest and provide management plan to MUSC IRB.
10. Researchers will report to the MUSC IRB any unanticipated problems involving risks to participants or others according to the MUSC IRB's reporting policy.
11. Researchers will report to the MUSC IRB any non-compliance or protocol deviations according to MUSC IRB's reporting policy.
12. Researchers will report to the MUSC IRB any complaints from a subject or other person regarding the research.
13. The Remote site PI will also need to provide any necessary documents or reports that the remote site IRB deems necessary to be in compliance with remote site policies.

VI. Responsibilities of the MUSC IRB of Record

1. Conduct review of research according to all applicable regulations and laws, including initial review, continuing review, and review of modification to previously approved research.
2. Suspend or terminate IRB approval when determined necessary.
3. Review unanticipated problems involving risks to subjects or others.
4. Review incidents of serious or continuing non-compliance.
5. Notify the researchers and Remote Site IRB in writing of any determinations.
6. Make available relevant IRB minutes to the Remote Site IRB upon request.
7. When appropriate, request post approval monitoring or audits, by the Remote Site's institution.
8. Specify the contact person and provide contact information to the Remote Site IRB.
9. Report to Remote Site IRB, regulatory agencies, and sponsors of serious or continuing non-compliance, unanticipated problems involving risks to subjects or others, suspensions or terminations of IRB approval (unless other provisions have been stipulated in the Reliance agreement).
10. Review and approve Conflict of Interest management plans for Remote Sites.

VII. Roles that may be delegated to either the Remote Site IRB or MUSC IRB or Record:

The above roles and responsibilities represent what would typically be in a standard reliance agreement between MUSC and another institution. However, there may be different arrangements on which institution will be responsible for what part of study oversight as long as it is stipulated in the Reliance Agreement and both parties agree.



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|--|-------------|--------------------------|
| Policy Name: Relying on an External IRB | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 2 | Section: HRPP 9.5 |
| Replaces Policy: n/a | | |

I. POLICY

The policy describes how the MUSC IRB may rely on an external IRB to serve as the IRB of Record for a nonexempt study in which an MUSC investigator is deemed to be engaged (Per OHRP Guidelines on Engagement in Research). In this situation, the External IRB is the *IRB of Record*, and the MUSC IRB is the *Relying IRB*.

II. INTRODUCTION

MUSC may rely on an external IRB, including the IRB of another institution or organization, or an independent (Commercial) IRB, for review and approval of human research if such reliance is a requirement of the research, or if it benefits MUSC, its investigators and/or its research participants.

III. CRITERIA FOR SELECTING AN EXTERNAL IRB

MUSC will apply the following criteria in selecting an external IRB to conduct the review of MUSC protocols:

- The external IRB is currently registered with ORHP/FDA
- The IRB is AAHRPP-accredited
- The external IRB is located within the U.S.

IV. IRB AUTHORIZATION AGREEMENT/RELIANCE AGREEMENT

In accordance with OHRP Guidance, when MUSC relies on an external IRB for review and approval of human research, the relationship is documented with an IRB Authorization Agreement (IAA) or other formal reliance agreement. This formal agreement requires each institution to have an FWA and

- Identifies one institution's IRB as the IRB of record, or specifies which institution's IRB will review which components of a study, and includes a description of the regulatory requirements for which each party will assume responsibility.
- The MUSC Institutional Official (IO) or designee has the ultimate authority regarding whether or not to rely on an external IRB. The IO is authorized to execute IAAs / Reliance Agreements on MUSC's behalf and may delegate this authority

V. MUSC PI Responsibilities

1. Submit an abbreviated application through the MUSC eIRB system.
2. Meet MUSC education requirements (e.g. CITI training).
3. Researchers must comply with the determinations and requirements of the IRB of Record.
4. Researchers and research staff agree to disclose financial conflicts of interest according to the agreed upon process and comply with any conflict management plans that may result.
5. Researchers will report promptly to the IRB of Record any proposed changes in the research. The investigator will not initiate changes in the research (including changes in the consent document) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
6. Researchers will report to the IRB of Record any unanticipated problems involving risks to participants or others according to the IRB's reporting policy.
7. Researchers will report to the IRB of Record any non-compliance or protocol deviations according to the IRB's reporting policy.
8. Researchers will report to the IRB of Record as well as the MUSC IRB any complaints from a subject or other person regarding the research

VI. Responsibilities MUSC

1. The organization is responsible for ensuring compliance with the IRB of Record's requirements at the research site.
2. Prior to review, provide the IRB of Record with any local context issues relevant to the research protocol.
3. Research may be further reviewed and approved or disapproved by officials of MUSC as the relying institution, but MUSC may not approve the research if it has not been approved by the reviewing IRB.
4. Educate and train its investigators to perform research in compliance with human research protection regulations.
5. MUSC and its researchers acknowledge and agree to cooperate in the IRB or Record's responsibility for initial and continuing review, record keeping and reporting. All information requested by the IRB of Record will be provided in a timely manner.
6. Researchers will not enroll individuals in research prior to review and approval by the IRB of Record.
7. The researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative as stipulated by the IRB of Record.
8. MUSC may conduct post-approval monitoring in addition to, or in cooperation with, the reviewing IRB.

VII. RESPONSIBILITIES OF THE External IRB of Record

1. Conduct review of research according to all applicable regulations and laws, including initial review, continuing review, and review of modification to previously approved research.
2. Suspend or terminate IRB approval when determined necessary.
3. Review unanticipated problems involving risks to subjects or others.
4. Review incidents of serious or continuing non-compliance.
5. Notify the researchers and MUSC IRB in writing of its decision.
6. Make available recent IRB minutes to the MUSC IRB upon request.
7. When appropriate, conduct on-site or remote post approval monitoring or audits, unless delegated to MUSC.
8. Specify the contact person and provide contact information to the MUSC IRB.
9. Report to MUSC IRB, regulatory agencies, and sponsors of serious or continuing non-compliance, unanticipated problems involving risks to subjects or others, suspensions or terminations of IRB approval (unless other provisions have been stipulated in the Reliance agreement).

VIII. Roles that may be delegated to either the IRB of Record or MUSC IRB:

1. The IRB Authorization Agreement/Reliance Agreement should stipulate whether the relying organization or IRB of Record performs these responsibilities:
 - a. Reporting to organizational officials, regulatory agencies, and sponsors of serious or continuing non-compliance, unanticipated problems involving risks to participants or others, suspension or termination of IRB approval.
 - b. Education and continuing education of researcher and research staff. The education requirements followed should be specified in the agreement
 - c. Obtaining disclosure and management of financial conflict of interest, although if MUSC maintains responsibility for this issue, any disclosure of management plan(s) will be provided to the IRB of Record in a timely manner prior to the decision by the IRB of Record.
 - d. Management of organizational conflict of interest related to the research.



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|--|-------------|---------------------------|
| Policy Name: Human Research Audit Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 4 | Section: HRPP 10.1 |
| Replaces Policy: 01/27/2011 | | |

I. POLICY

A. Introduction

The MUSC University Compliance Office conducts audits on research projects involving human participants.

B. MUSC Policy

Audits are a tool to assist the Medical University in achieving compliance with applicable federal regulations and laws and MUSC policy and procedures during the conduct of research involving human participants. This mechanism of post-review monitoring also serves as a vehicle for continuing education, increased operational awareness and quality improvement. Audits consist of record review of both the Institutional Review Board (IRB) and the applicable Principal Investigator's HR study files.

II. PROCEDURES

A. The University Compliance Office initiates audits based on the following criteria:

1. Priority 1: For-Cause-Audit: Study where allegations of human participants' violations have been lodged against a Principal Investigator.
2. Priority 2: Administrative Audit: Study where the IRB Chair has identified a potential administrative problem with study documentation.
3. Priority 3: Random Audit: Study randomly selected. Each study has an equal chance of selection.

B. The University Compliance Office maintains files to document the selection of studies involving human participants for audit.

C. Once a study has been selected for audit, the University Compliance Officer will assign the audit to the appropriate Compliance Auditor with the Compliance Auditor conducting the highest priority audit first.

- D.** Compliance Auditors will use IRB approved checklists as guidance to conduct the audit.
- E.** Once a study is assigned for audit, the Compliance Auditor will prepare a written audit report and forward to the IRB Program Manager for a response. The IRB Program Manager will provide a written response on audit findings within a timely manner and forward to the University Compliance Officer who will review the audit report and response. The University Compliance Officer will approve and/or return the report to the IRB Manager if any additional action or information is needed to resolve any finding(s). Upon approved by the University Compliance Officer, a copy of the audit report and response will be filed in the University Compliance Office.
- F.** The Compliance Auditor will contact the Principal Investigator by phone or e-mail to schedule the audit. Once the audit is scheduled, the Compliance Auditor will confirm the time, date, and place of the audit and provide the Principal Investigator a copy of the checklist used to conduct the audit.
- G.** The Principal Investigator and/or the Study Coordinator will:
 - 1. Provide the following study files for the auditor's review.
 - a) All study related regulatory documents
 - b) Research Participant Screening/Enrollment log (as appropriate)
 - c) Case Report Forms
 - d) Case Report Forms source documents
 - e) Informed Consents and HIPAA for all enrolled/screened subjects
 - f) Study drug and drug accountability logs (as applicable)
 - g) Device accountability logs (as applicable)
 - h) Lab logs (as applicable)
 - i) Other documents/files supporting the conduct of the study.
 - 2. The Principal Investigator and/or Study Coordinator will arrange for a private work area for the conduct of the audit.
- H.** The Compliance Auditor reviews all pertinent study documents and records and completes the checklist to document the audit finding(s).

- I. The Compliance Auditor keeps the Principal Investigator and/or Study Coordinator informed of the progress of the audit. The Compliance Auditor *informally* debriefs the Principal Investigator and/or Study Coordinator at the completion of the audit.
- J. After completion of the audit, the Compliance Auditor prepares a final audit report that is forwarded directly to the University Compliance Officer.
- K. The University Compliance Officer reviews the audit report and adds comments as appropriate. The approved audit report is then forwarded to the Principal Investigator for a response. The Principal Investigator's response includes a correction action plan to reflect the audit findings. Once the Principal Investigator has completed the response, the report should be uploaded into the eIRB system for review by the IRB. The Compliance Auditor will review the Principal Investigator's response and communicate any concerns or correction, if needed, with the IRB Administrator. Once the audit report and response have been appropriately reviewed the audit response is forwarded to the appropriate IRB Chair for information and/or action. A copy of the audit report, Principal Investigator's response, and IRB determination is stored in the eIRB system under Reportable Events.
- L. If so warranted, the IRB Chair/IRB Office may take immediate action to prevent any further enrollment in the study until the audit report is reviewed by the full IRB.
- M. The IRB Chair will present the audit report and Principal Investigator response at the next scheduled IRB meeting.
 - 1. The eIRB system will send reportable event notifications for Principal Investigator submissions and IRB acknowledgments of internal audits to the Compliance Auditor. The IRB Office will keep the University Compliance Office informed regarding the progress of all assigned action(s) until all action(s) are resolved to the satisfaction of the IRB.
- N. The University Compliance Office will document the conduct of audits from initiation to resolution of audit finding(s) on the Audit Status Report.

III. REFERENCES



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|--|-------------|---------------------------|
| Policy Name: Research Data Ownership and Record Retention Policy and Procedures | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 4 | Section: HRPP 10.2 |
| Replaces Policy: 01/27/2011 | | |

I. POLICY

A. Introduction

Each department chairman or center director is ultimately responsible for the review and scientific integrity of any proposal that will be sent to the IRB. In the case of most centers, such as the Hollings Cancer Center, there are standing committees of scientists, physicians, statisticians, and other health professionals that review protocols for scientific integrity prior to review by the director or chairman's office.

B. Federal Regulations

Federal Regulations for record retention and access to records for awards to recipients are set forth in OMB Circular A-110, (Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations), and specifies that financial records, supporting documents, statistical records and all other pertinent records shall be retained by the institution. Research records are pertinent to the award and therefore, must be retained. In addition, 42 Code of Federal Regulations (CFR) Part 93 (Public Health Service Policies on Research Misconduct) specifies evidentiary retention requirements for research records.

C. MUSC Agents and Affiliates

The record retention and access to records requirements specified in this policy apply to research conducted by the Medical University of South Carolina, its agents or affiliates.

II. PROCEDURES

A. Record Retention

1. Research records should be retained for a sufficient minimum period to allow evaluation and repetition by others of the results and to investigate an allegation of research misconduct. Usually [unless granted an exception by the Department of Health and Human Services (HHS) or the Office of Research Integrity (ORI)], this minimum period is six years.

2. For research involving children, this minimum period for research to keep research records is six years or until the child reaches the age of eighteen, whichever is later.

B. Definition of Research Record

Research record means the record of data or results that embody the facts resulting from scientific inquiry, including but not limited to, research proposals, laboratory records, both physical and electronic, progress reports, abstracts, clinical trial records, theses, oral presentations, internal reports, journal articles, and any documents and materials provided to the Department of Health and Human Services (HHS) or an institutional official by a respondent in the course of a research misconduct proceeding

C. Ownership

1. MUSC assumes legal and financial accountability for awarded funds and owns the rights in data resulting from a grant-supported project. Therefore, MUSC retains ownership rights to research records generated by MUSC faculty, scholars, staff, post-doctoral fellows, students and visiting scientists whether generated during scholarly activities or in conducting sponsored activities funded by external agencies.
2. MUSC may choose not to claim ownership rights if there is a term or condition of the award, an agreement or in law or regulation. In addition, MUSC supports the National Institutes of Health (NIH) Data Sharing Policy as defined in NIH Notice: NOT-OD-03-032. However, MUSC retains the right to use research records for its own educational, research and non-commercial purposes

D. Management of Data

1. Data management, including the decision to publish, is the responsibility of the principal investigator. Research data, including detailed experimental protocols, all primary data, and procedures of reduction and analysis are the essential components of scientific progress. Scientific integrity is inseparable from meticulous attention to the acquisition and maintenance of these research data.
2. The results of research should be carefully recorded in a form that will allow continuous access for analysis and review. Attention should be given to annotating and indexing notebooks and documenting computerized information to facilitate detailed review of data. All data, even from observations and experiments not directly leading to publication, should be treated comparably. Investigators should be aware that research data are legal documents for purposes such as establishing patient rights or when the veracity of

published results is challenged and the data are subject to subpoena by congressional committees and the courts.

E. Access to Research Records

1. Since MUSC is responsible for managing and monitoring each project, program, sub award, function or activity for awarded research, MUSC retains the right of access and to make copies of records for all research performed at MUSC or supported by MUSC sponsored funds. Where feasible, appropriate notice will be given of the need to review, copy or duplicate records while being sensitive to causing the least inconvenience or disruption of on-going work. Examples of MUSC's right of access are to conduct compliance audits, investigate allegations of research misconduct, etc.
2. All research data should be available to scientific collaborators and supervisors for immediate review, consistent with requirements of confidentiality.
3. Either before or when MUSC notifies the respondent of an allegation, inquiry or investigation, MUSC shall promptly take all reasonable and practical steps to obtain custody of all the research records and evidence needed to conduct the research misconduct proceeding, inventory the records and evidence, and sequester them in a secure manner, except that where the research records or evidence encompass scientific instruments shared by a number of users, custody may be limited to copies of the data or evidence on such instruments, so long as those copies are substantially equivalent to the evidentiary value of the instruments.
4. The PI maintains the right to either retain or obtain copies of research records to use for their defense.

F. Health Insurance Portability and Accountability Act (HIPAA)

HIPAA prohibits removing research-related identifiable protected health information (PHI) from MUSC unless:

1. The removal is authorized by the patient/research subject;
2. The PHI is de-identified;
3. The PHI is part of a Limited Data Set with an approved Data Use Agreement;
4. The Institutional Review Board (IRB) grants a waiver of authorization; or

5. The removal is required by law.

G. Transfer of Research Records

1. In the event the Principal Investigator (PI) transfers or leaves MUSC, the PI and the Vice President for Research will negotiate an agreement on the disposition of research records. This agreement will specify MUSC's right of access to research records for reasonable cause after reasonable notice regardless of the location of the records.
2. The HIPAA Privacy Rule does not permit a PI to transfer control of subject identifiable research records to another institution unless the original permission under which the PI obtained or created the data in the record (such as the individual's authorization or approved by the Institutional Review Board) was granted explicitly for the PI, rather than solely for MUSC. Otherwise, any transfer of PHI from MUSC to another institution for research purposes must be done according to a new permission (authorization, waiver, etc.).
3. As authorized by the PI, when individuals (i.e. students, post-doc fellows, etc.) involved in a research project leave MUSC, they may take copies of research records which they generated unless restricted by the terms of the applicable contract, other contractual agreements, and/or law (i.e. HIPAA) or regulations.

H. Resolution of Disputes Involving Research Records

1. The Provost or designee shall arbitrate all disputes involving the ownership, retention and access to research records.

III. REFERENCES



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|---|-------------|---------------------------|
| Quality Improvement Initiatives within the Human Research Protection Program of MUSC | | |
| Approved | | |
| Effective Date: 09/15/2016 | Page 1 of 6 | Section: HRPP 10.3 |
| Replaces Policy: 01/27/2012 | | |

I. BACKGROUND

In February 2016, Dr. Kathleen Brady was named Vice President for Research (VPR) at the Medical University of South Carolina to lead a newly reorganized structure to lead the Human Research Protection Program at MUSC. Dr. Brady established a new position and named Dr. Patrick Flume the Assistant Provost for Research Compliance and Regulatory Affairs. More recently, Dr. Aimee McRae was named as the Director of the Office of Research Integrity. Under this leadership, there has been a close working relationship between the Office of Research Development, the Office of Research Integrity, the S.C. Clinical and Translational Research (SCTR) Institute, the Office of Research and Sponsored Programs, and the Office of Compliance.

Important milestones in the Quality Improvement Program in research include initial AAHRPP accreditation in 2009, renewal of the AAHRPP accreditation in 2012, the renewal of the Clinical and Translational Sciences Award in 2014, and the renewal of the National Cancer Institute designation of the Hollings Cancer Center in 2012. These signature accomplishments allowed for continued support for overall operational quality improvement.

Dr. Flume had led College of Medicine initiative, the Clinical Research Task Force, which ultimately led to the establishment of a standing committee, the Clinical and Translational Research Action Committee (CTRAC), which reports to the VPR and the University Research Council (URC). The charge of this committee is to identify opportunities for improvement in clinical and translational research. Included on this committee are representatives from all six colleges, investigators, research coordinators and administrators. Once the committee identifies a project of interest, a working group is established to develop a plan for improvement by identifying best practices as well as unique solutions for MUSC. These working groups include key stakeholders and ambassadors for change representing the IRB, SCTR, the Office of Compliance, and the MUSC legal office, among others.

SPECIFIC QUALITY IMPROVEMENT PROJECTS

Annually, leadership meets to evaluate the effectiveness of compliance and quality improvement activities, and identifies at least one goal, an objective for meeting that goal, and at least one way of measuring whether the objective is being met. Further information on the Program Review and Quality Improvements can be found in Section VI of HRPP 1.1 – Description Principles and Authority for MUSC HRPP. In addition, there are multiple projects, some new while others considered

of utmost importance to warrant continued attention, initiated to improve the quality of the MUSC HRPP with recent examples outlined below.

A. Education Quality Improvement Central to the HRPP is the concept of education, communication and awareness. This theme is nurtured by several mechanisms.

1. **The Core Clinical Research Training (CCRT) Course**, offered through SCTR's Clinical and Translational Research Center (CTRC), was developed by the Office of Research Integrity to train research coordinators and new investigators. The course has now evolved to be an essential component of the clinical investigator and research staff toolkit. In addition to covering basic aspects of the HRPP operations and philosophy, this course is structured to allow the addition of new modules that can address specific evolving issues in the field. One example is provided by the addition of a module to train individuals for roles as research subject advocates. In addition to live training sessions, the CCRT course is now available as an online format, offering more flexibility with course attendance.
2. **Research Orientation** - In 2008, two initiatives were put in place to coordinate research support mechanisms. One is the development of a web portal (<http://research.musc.edu/>) that provides access to all aspects of the research process from idea development to grant development to grant submission to post-award monitoring. The second initiative was the establishment of a Research Orientation Session for new faculty and the broader research community with slides posted on our research web site. In 2009, the Research Toolkit, an online research guide, was developed (http://academicdepartments.musc.edu/sctr/tools_links/toolkit_sitem ap.html). The Toolkit assists MUSC research personnel in navigating the research enterprise, addresses steps involved with submitting, conducting, closing and disseminating results of a research study and includes links to institutional, state and federal resources and regulations. The research orientation is an annual event.
3. **The SUCCESS Center** - While we have several strong research support systems in place, there is often an educational and awareness gap for investigators entering into human subject research or for investigators new to MUSC on how to navigate their way through the various offices. The SUCCESS Center (<http://sctr.musc.edu>) provides support for such investigators through a group of individuals with expertise in a variety of areas related to human subjects research including the following: a) Research navigation to help with research processes and resources including Good Clinical Practice processes for research, study organization and conduct, study documentation, and research tools and

templates; b) Regulatory processes and documentation, including areas such as IRB protocol submissions, IND and IDE applications and study quality improvement reviews; c) Subject recruitment, and d) Grant application process and budget development. The SUCCESS Center works closely with the Offices of Research Integrity and Vice President for Research to identify, develop and disseminate educational resources to the research community. In addition, monthly educational sessions, seminars and webinars for the research community on a variety of research topics are hosted by SCTR and coordinated by the SUCCESS Center.

4. **Post-Audit Targeted Education** - The University Compliance Office conducts an annual review of all human research audits conducted for that particular calendar year and submits a report to the Provost office. This report serves as a guide to initiate focused educational efforts to increase awareness of common audit findings. In addition, a collaboration between the Compliance Office, IRB and the SCTR Regulatory Knowledge and Support () core will review new federal regulations to develop new audit procedures and educational and support mechanisms to help investigators and their staff. For example, NCATS has placed a priority on investigational drug management, and this collaboration is developing the processes for this subject area. Previously, we had identified that documentation errors in the informed consent document and/or HIPAA authorization documents accounted for about 80% of discrepancies. Most of these errors were minor involving signature errors, initialing errors, dating errors or the use of obsolete forms of the informed consent document. A PowerPoint educational module was developed to address this issue and outlined several courses of action including immediate review of HIPAA and informed consent documents by other staff members, verification of the informed consent process documentation by the Principal Investigators or his/her delegate and encouragement of self-study audits.
5. **Networking and Peer Engagement** – We maintain a program for leaders in various aspects of human subject research to network with staff in various offices, IRB Chairs and members, investigators and senior administration. These individuals may visit MUSC and present a seminar for the entire research community. This initiative provides an important mechanism for continuing education, awareness of best practices and connectivity.

B. IRB Performance and Workload Analysis

The Director of the Office of Research Integrity meets regularly with the IRB Chairs and staff to review work distribution. In addition, IRB Performance statistics are monitored through the extensive capabilities of the eIRB

system. We publish our metrics regarding turnaround time for all types of reviews on our institutional website. The reporting capabilities of the eIRB system allow us to identify opportunities for further improvement. Some recent examples are as follows:

1. **Not Ready for Review** – Many protocols submitted to the IRB are severely lacking in essential details that permit review. Rather than committing IRB staff time to the corrections required of the protocol, we have established a NRR category in which the protocol is referred back to the investigator with recommendation for consultation with the SUCCESS Center.

2. **ICF Library** – Consent forms often use the same elements that could be present in other ICFs. For example, study protocols frequently use the same procedures, and so would require explanation of these procedures in the consent forms. Rather than reviewing new language to describe procedures, we have created a library of terminology accepted by the IRB for a growing number of ICF elements that can be copied and pasted into consent forms to reduce review time.

3. **IRB retreats** – we have engaged the IRB leadership and staff to participate in an annual retreat in which key issues important to staff as well as to investigative teams can be discussed and solutions developed. As an example, the previous retreat included a discussion of harmonization of processes and procedures across the three IRBs. These retreats are important for continually driving improvement as well as enhancing the satisfaction of the staff.

C. CTSA Consortium

As a member of the consortium of institutions with NIH-supported Clinical and Translational Science Awards, we have access to a wealth of shared resources for performance statistics and peer networking. NCATS is leading a push for common metrics.

D. Novel Initiatives

We take a proactive approach to evaluating new technologies and services to address the varying needs of investigative teams. Some examples include:

1. **Evaluation of alternative IRB Models** – we previously expanded our use of a central IRB (Western IRB) initially for Phase III and IV trials. We have expanded on this initiative through a willingness to use other central IRBs, as long as they adhere to our institutional policies and procedures. We are currently working on adopting single IRB policies and procedures as mandated by the NIH for future

multisite trials. Our IRB director will be serving on a NIH-sponsored committee to guide successful achievement of these goals.

2. **Electronic consenting** – Through a collaboration between the IRB, the CTRAC, and RKS, a process for capturing an electronic signature for the ICF and HIPAA documents has been developed. SOPs are under review and a pilot study is in process. This will provide for considerable improvements in the consenting process as well as storage of files.
3. **Remote consenting** – To satisfy the unique needs for clinical permissions and for clinical research in which subjects or surrogates are not physically present to sign a consent form. A novel approach (Doxy.me) was developed by our BMIC program to allow for an interaction between the investigator and subject through a Skype-like, secure format. The IRB was instrumental in perfecting the policies and procedures to make this available to investigators.

E. Upgrade of Automated Support Systems

A research informatics team supports current operations of our HRPP program. The goals of this group are to provide seamless electronic, compliant processes for submission, review and monitoring of research involving human subjects to provide mechanisms to communicate among different reporting units in the HRPP program by cross-queries of data sources. We have fully transitioned from our system “Electronic Research Management Applications” (ERMA), which was established in 2004, although there are some legacy protocols that remain open in that system.

The research informatics team continues to work with our partners in Health Sciences South Carolina to support the statewide process for IRB submission and review through the “Click Commerce” management platform. The electronic IRB (eIRB) system was implemented at MUSC in December 2010. Training is available for new users through educational materials (<http://research.musc.edu/ori/irb/eIRB.html>) with instructions on how to submit protocols within the system.

The Offices of Vice President for Research, Research Integrity and SUCCESS Center have staff available to assist users with system navigation. The eIRB system allows a more robust monitoring of operations and oversight that will allow us to make another level of informed decisions for enhancement of our HRPP units. It is also far easier to track adverse events over time and develop new processes for intervening and reducing problems.

The eIRB system has granted significant transparency for those departments, groups and committees needing to provide an ancillary review

of research protocols. The eIRB system is programmed to automatically route the protocol to ancillary review areas such as: Hollings Protocol Review Committee, Departmental Approvers, VAMC, Office of Research and Sponsored Programs, Grants and Accounting, Investigational Drug Services. This ability easily increases awareness of the project as well as streamlines the entire ancillary review process minimizing traditional delays encountered with paper submission.

F. IRB Continuing Education

The IRB staff, chairs and Board members continue to take advantage of educational training opportunities. Regular meetings of staff and chairs cover various aspects of human subjects research protection. PRIM&R-sponsored webinars are accessed by the HRPP personnel. IRB staff and Chairs attend national PRIM&R conferences and/or the AAHRPP annual meeting.

G. Outreach

Over the last couple of years, the IRB has increased the education and training provided to research groups. A big focus of this outreach has centered on students and new investigators. The IRB Administrators developed presentation materials and visited several departments to educate and inform researchers about the IRB process. These sessions have been incredibly popular and the IRB Administrators continue to receive invitations to return. The goals of this outreach are to provide enough information for the researchers and their teams to be aware of how, what and when to submit to the IRB, as well as providing the researcher with a specific individual to call upon when needing IRB assistance.

H. Communication

Communication and connection have become vitally important for the success of a strong human research protection program. Under the direction of the Vice President for Research, a number of groups hold regular meetings and sessions to stay connected and updated on all situations involving the protection of human subjects. These group meetings involve the Vice President for Research and all Directors of research support offices as well as IRB Staff and the SUCCESS Center.