



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 ad 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 Assistant 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.