

Human Research Protection Program Overview

MUSC Human Research Protection Program

Overview

The mission of the Medical University of South Carolina (MUSC) is to achieve excellence in patient care, education, and research, in an environment that is respectful of others, adaptive to change and accountable for outcomes. Human subjects research is an important element in meeting this mission. The University has established policies, procedures, and programs for the review of human subject research to promote the ethical conduct of research, safeguard the integrity of and protect human subjects and maintain strict compliance with regulatory standards. MUSC investigators are granted the privilege of using human subjects under assurance to the government that research conducted at MUSC complied with all federal and local regulations protecting individuals involved in human subjects research.

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 Biomedical and Behavioral Research, the Declaration of Helsinki, the Nuremberg Code, and the VA Handbook 1200.5. 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.

MUSC has a long-standing human research protection program and human subjects research program that includes our General Clinical Research Center (GCRC) first funded by the National Institutes of Health in 1977. The GCRC has long been a focal point for stimulating, facilitating and conducting multidisciplinary clinical and translational research.

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 Associate Provost and the Vice President for Academic Affairs/Provost 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;
- 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 the HRPP Program Guide Section 6.4 - Subject Complaints, Issues, Concerns and Suggestions Policy and Procedures and Section 9.3 - Quality Improvement Initiatives).

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 programs 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.

TYPES OF HUMAN SUBJECTS RESEARCH CONDUCTED AT MUSC

MUSC has 1060 active research projects involving human subjects in the biomedical, behavioral sciences, social sciences and medical economics and may encompass Phase 1 through Phase IV Medication Trials. These studies are conducted by one of approximately 456 active principal investigators (MD, Ph.D., PharmD, DDS and/or RN). Surgical studies involving innovative therapies, device trials, and organ transplantation are also conducted at MUSC. The MUSC Tissue Bank also serves as a repository for human samples for various research projects.

In FY08, MUSC achieved new benchmarks for total extramural research funding (\$202M) and NIH funding (\$101M). Of the \$202M, ~72% is federal funding and ~16% is corporate funding. ~25% of federal funding and ~87% of corporate funding involves human research protocols submitted to the IRB. The majority of human research studies operate under the oversight of the Department of Health and Human Services and the Food and Drug Administration.

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 Institutions' employees or agents intervene or interact with human subjects for purposes of federally-conducted or -supported research; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects for purposes of federally-conducted or - sponsored research; 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 21 Code of Federal Regulations (CFR) Parts 45, 46, 50 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 1200.5) 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 17 and VHA Handbook 1200.5) 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 (CITI). All individuals involved in human research must complete the initial 17 basic modules focus on biomedical research when commencing such research. Beginning in 2008, all individuals involved in humans 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 VA Handbook 1200.5.

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 reporting structure for these offices is indicated in the organization charts linked below.

President Ray Greenberg is recorded as the Institutional Official on the FWA and he has appointed the Associate Provost (Stephen M. Lanier, Ph.D.) and the Vice President for Academic Affairs/Provost (John R. Raymond, M.D.) as the responsible organizational officials for the operation of the MUSC HRPP. These three individuals form the leadership core for the University and have offices adjacent to each other facilitating communication. The active involvement of senior administration ensures that adequate resources are provided to operate an effective HRPP.

MUSC has a longstanding, close 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 John Barilich, MSW, MBA (Institutional Official for the VAMC FWA) and the Associate Chief of Staff/Research and Development M. Rita I. Young, Ph.D.

The current Vice President for Academic Affairs/Provost at MUSC is the former Associate Chief of Staff/Research and Development at the VAMC. The Associate Provost for Research at MUSC also serves on the board of the VAMC non-profit entity Charleston Research Institute and regularly interacts with Dr. Young for program development. MUSC is the University Affiliate IRB for the Ralph H. Johnson Veterans Affairs Medical Center (VAMC) and the two institutions run a joint Animal Laboratory Program. Additional connectivity within the context of the HRPP is also present through cross-training of staff in compliance and review at the two institutions.

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 directed by Robert Malcolm, M.D., whom reports to the Associate Provost for research. The Office of Research Integrity includes the Institutional Animal Care and Use Committee (IACUC), the Institutional Biosafety Committee (IBC) and the Research Integrity Committee (RIC). Additional internal review mechanisms are provided through Department Chairs, various mentoring groups, the Hollings Cancer Center Clinical Trials Office, our NIH-Supported General Clinical Research Center and the South Carolina Clinical and Translational Research Institute.

The IRB(s) review, and have the authority to approve, require modification, 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.

There are currently three IRBs, each under the direction of a Chair and Vice-Chair, that focus on different areas of research and consists of faculty with appropriate expertise, community representative and staff support as detailed in our governance document (see HRPP Program Guide Section 1.6 - IRB Governance and Operating Procedures Policy and Procedures). It is the responsibility of the IRB 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, external peer review and various internal review mechanisms offered through individual units such as the General Clinical Research Center, the Hollings Cancer Center and the Clinical and Translational Research Program.

In addition to MUSC IRB committees, the MUSC FWA includes the use of the National Cancer Institute Central IRB #2 (IRB00004296) for pediatric protocols and Western Institutional Review Board for selected multi-site clinical trials as needed or defined for specific studies. We currently have 39 protocols approved and 5 under review by the National Cancer Institute Central IRB #2. We will be implementing the use of the NCI Central IRB for adult Phase III clinical trials in the fall of 2008. VA studies reviewed by the MUSC IRBs cannot use a central IRB, although a central VA IRB is currently being developed.

The Policy and Procedures for Governance of the Institutional Review Board (IRB) (see HRPP Program Guide Section 1.6) detail operational elements so 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 4.1 - Principal Investigator

Responsibilities - Supervision of Staff and Protection of Subjects). The PI 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 PI 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 PI 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 and report their results 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.

PROGRAM REVIEW AND QUALITY IMPROVEMENT

The MUSC Institutional Review Board was most recently a component of the accreditation process through the National Committee for Quality Assurance (NCQA) in July 2005 as the University Affiliate of the Ralph H. Johnson Veterans Administration Medical Center (VAMC). The IRB Structure and Operations Category of the NCQA review received a score of 95.9%.

In 2007, MUSC's Accreditation by the Southern Association of Colleges and Schools was reaffirmed with an exemplary recommendation that cited many achievements and the creativity of initiatives in inter-professional education.

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. While the Associate Chief of Staff/Research and Development at the VAMC, the current Vice President for Academic Affairs/Provost at MUSC appointed to monitor for post-approval review of all human subjects research, which made the Ralph H. Johnson VAMC among the first in the country to do so. 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. A similar office was established at MUSC in 2002 under the Office of Compliance. This concept was expanded in 2007 to include post-approval review of animal research protocols and in 2008 for work involving recombinant DNA and infectious materials as reviewed by the Institutional Biosafety Committee.

An important indicator of the quality of our operations and the MUSC/VAMC partnership as well as our commitment to compliance and oversight is provided by the recent review of our Division of Laboratory Animal Resources by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC). In July 2008, AAALAC granted MUSC/Ralph H. Johnson VA medical Center full accreditation for three years. The site visit team and the AAALAC Council described our program as "exemplary", a description used for very few academic laboratory animal programs. This is the eighth consecutive "full accreditation" for our animal program since 1987, a record that may be unprecedented for academic institutions.

The ongoing improvement and quality of our HRPP is initiated through multiple mechanisms including post-review monitoring, education, quarterly visits from external advisors and consultants, ongoing monitoring by the Office of Compliance, ongoing review of best practices, regularly scheduled review of the IRB operations and weekly discussions among the multiple offices involved in our HRPP (see HRPP Program Guide Section 9.1 - Human Research Audit Policy and Procedures and Section 9.3 - 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 our General Clinical Research Center 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.

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 will be posted on the MUSC web site and freely available to guide both investigators and human research participants.