

March 14, 2017

## HUMAN RESEARCH PROTECTION PROGRAM

**1. PURPOSE:** The purpose of this policy memorandum is to describe the South Texas Veterans Health Care System (STVHCS) Human Research Protection Program (HRPP) as a complete entity. This document describes the varied and diverse components of the STVHCS HRPP. Other documents that provide more detailed description of aspects of the HRPP are referenced in this document.

**2. POLICY:** The STVHCS, as a Department of Veterans Affairs (VA) health care system, will maintain a human research protection program (HRPP) to adhere to all regulations and directives related to the protection of human subjects in research as required by the VA and all other responsible Federal agencies. All individuals involved in the HRPP must understand and apply their obligation to protect the rights and welfare of human research subjects.

**a. Vision for Research:** The STVHCS aspires to discover knowledge, develop VA researchers and health care leaders, and create innovations that advance health care for our veterans and the nation.

**b. Definitions:**

(1) **Adverse Event (AE) in Research.** An AE is any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable and unintended event, including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research

(2) **Federal Wide Assurance (FWA):** An agreement or contract between the institution and Office of Human Research Protections (OHRP), on behalf of the Secretary, Department of Health and Human Services (DHHS), stipulating the method(s) by which the organization will protect the welfare of research subjects in accordance with the regulations (45 Code of Federal Regulations [CFR] 46 and 38 CFR Part 16).

(3) **Good Clinical Practices (GCP):** The international ethical and scientific quality standard for designing, conducting, monitoring, recording, auditing, analyzing and reporting research. Adhering to GCP will ensure that the research data reported will be collected using credible and accurate methods to protect research participants' rights and confidentiality.

(4) **Health Insurance Portability and Accountability Act (HIPAA) Authorization:** Prior written permission for use and disclosure of protected health information (PHI) from the research subject or legally authorized personal representative is required under law, including HIPAA. The written authorization must include all elements of a compliant authorization (see Veterans Health Administration [VHA] Directive 1605.1) prior to any disclosure of information.

(5) **Human Biological Specimen:** Materials derived from human individuals, such as blood, urine, tissue, organs, hair, nail clippings, buccal swabs, or any other materials that are either collected specifically for research purposes or as residual specimens from diagnostic, therapeutic, or surgical procedures. Bacteria, fungi, or viruses obtained from human biological specimens are not considered human biological specimens, as long as the human material has been removed.

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(6) **Human Research Protection Program (HRPP):** The systematic and comprehensive approach by an organization to ensure human subject protection in all research. The implementation of any part of the program may be delegated to specific committees, individuals or entities, by the organization. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

(7) **Human subject:** The STVHCS oversees and conducts research that is covered by the Department of Veterans Affairs, Department of Health and Human Services, and Food and Drug Administration (FDA) regulations, therefore, the definition of human subject (also called a research participant) employed by the STVHCS HRPP includes both DHHS (and VA) and FDA definitions:

(a) DHHS and VA definition: 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.

(b) FDA definition: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. Under 21 CFR 812 this also includes an individual on whose specimen an investigational device is used

(8) **Human subject research:** Human subject research includes all research meeting the definition of "research" (see Paragraph 2.b.(20)) performed with "human subjects" (see Paragraph 2.b.(7)). Human subjects research also includes research involving identifiable human biological specimens. A human specimen with no identifying information, when used in research, does not constitute human subjects research unless FDA-regulated.

(9) **Informed Consent:** Informed consent is a process, not just a form. It is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. Information provided in the informed consent process must be presented in terms that the subject population can understand, to enable persons to voluntarily decide whether or not to participate as a research subject. The written presentation of information is used to document the basis for consent and for the subjects' future reference. The process of obtaining informed consent must comply with the requirements of 45 CFR 46.116 and the documentation of informed consent must comply with 45 CFR 46.117.

(10) **Institutional Review Board (IRB):** An IRB is a board, committee, or other group formally designated by an institution to review, approve, require modification in, disapprove, and conduct continuing oversight of human research in accordance with 38 CFR Part 16 and other applicable VA and Federal requirements.

(11) **Investigational device:** As defined by the FDA, an investigational device is a device that is the object of a clinical study designed to evaluate the safety or effectiveness of the device (21 CFR 812.3(g)). Investigational devices include transitional devices (21 CFR 812.3(r)) that are objects of investigations.

(12) **Investigational drug:** The FDA considers the term "Investigational New Drug (IND)" synonymous with investigational drug (21 CFR 312.3). According to VHA Handbook 1108.04, an investigational drug is a chemical or biological drug that is used in a clinical investigation. An investigational drug can be:

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(a) A new chemical compound, which has not been released by the FDA for general use; or

(b) An approved drug that is being studied for an approved or unapproved use, dose, dosage form, administration schedule, or under an IND application, in a controlled, randomized, or blinded study (see VHA Handbook 1108.04). **NOTE:** *Concurrent medications, comparators, or rescue medications used in the investigational trial that are not the drug(s) being studied are not defined as investigational drugs unless they are not commercially approved or not available through commercial channels. Prescription drugs, over-the-counter drugs, nutritional supplements, herbal preparations, and legend items used for diagnosis or treatment and meeting the definition of “investigational drug” are considered investigational drugs.*

### (13) Investigator:

(a) An investigator is any individual who conducts research involving human subjects including, but not limited to, the Principal Investigator (PI), co-PI, and Local Site Investigator (LSI). The investigator must uphold professional and ethical standards and practices, adhere to all applicable Federal requirements, and comply with applicable local policies and procedures.

(b) VA Investigator. A VA investigator is any individual who conducts research approved by the VA Research & Development (R&D) committee while acting under a VA appointment on VA time, including full and part-time employees, without compensation (WOC) employees, and individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970. In addition, a VA investigator must comply with all applicable VA and VHA requirements, and comply with applicable local VA facility policies and procedures.

(c) Principal Investigator (PI). The PI is a qualified person or persons designated by an applicant institution to direct a research project or program and who usually writes the grant application. The PI oversees scientific, technical, and day-to-day management of the research. In the event of an investigation conducted by a team of individuals, the PI is the responsible leader of that team. **NOTE:** *FDA considers Investigator and PI to be synonymous.*

(d) Co-Principal Investigator (Co-PI). A Co-PI is when one of two or more PIs share equally in the accountability for a study. A Co-PI must meet the same qualifications of a PI.

(e) Site Investigator or Local Site Investigator (LSI). The Site Investigator or LSI is an investigator at a site participating in a multi-site research project. The LSI oversees scientific, technical, and day-to-day management of the research at the local site.

(14) **Legally Authorized Representative (LAR):** A legally authorized representative is 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 (38 CFR 16.102(c)).

(15) **Memorandum of Understanding (MOU):** A written agreement outlining the details of the relationship between organizations, including the responsibilities of each. Such an agreement is used by the STVHCS to delineate the terms and conditions under which the STVHCS utilizes the IRB of the affiliated University of Texas Health Science Center at San Antonio (UTHSCSA) (also called the “affiliate”).

(16) **Non-compliance:** The STVHCS adheres to the definition of research non-compliance found in the UTHSCSA IRB glossary at:

[http://research.uthscsa.edu/irb/glossary/IRB\\_glossary.php](http://research.uthscsa.edu/irb/glossary/IRB_glossary.php)

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(17) **Office for Human Research Protections (OHRP):** The Federal government office responsible for implementing DHHS regulations governing research with human subjects.

(18) **Office of Research Oversight (ORO):** ORO serves as the primary VHA office in advising the Under Secretary for Health on all matters of compliance and assurance regarding human subject protections, animal welfare, research safety and security, research information protection, and research misconduct.

(19) **Protocol:** A plan that includes, at a minimum, the objectives, rationale, design, methods and other conditions for the conduct of a research study.

(20) **Research:** The STVHCS oversees and conducts research that is covered by the Department of Veterans Affairs, Department of Health and Human Services, and the FDA regulations; therefore, the definition of research employed by the STVHCS HRPP includes both DHHS (and VA) and FDA definitions:

(a) DHHS and VA definitions: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The STVHCS adheres to the definition of systematic investigation (use of a clear plan, system or method to conduct a detailed examination or inquiry for facts.) and generalizable knowledge (knowledge that is universally or widely applicable -The Common Rule does not define generalizable in the definition of research). Activities that meet this definition constitute research for purposes of the STVHCS HRPP, even if they are conducted or supported under a program that is not typically considered research. For example, some demonstration and service programs may include research activities.

(b) FDA definition: Clinical investigation (Per FDA Title 21 CFR 50 & 56) means 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 FDA under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

(21) **Research Impropriety:** Research impropriety is any ethical lapse or other impropriety involving or occurring in connection with research other than research misconduct as defined in Paragraph 2.b.(22). Examples of research impropriety include, but are not limited to, conflicts of interest, misallocation of funds, sexual harassment, discrimination, and breaches of human subject's protections and animal welfare requirements. Some instances of research impropriety may also meet the definition of research noncompliance.

(22) **Research misconduct:** Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

(23) **Serious Adverse Event (SAE):** A local SAE in human research is an AE that results in death, a life threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome.

(24) **Sponsor:** For FDA studies, the FDA considers a sponsor to be the person or entity that takes responsibility for and initiates a clinical investigation. The sponsor may be an

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individual, pharmaceutical company, device manufacturer, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A sponsor-investigator is an individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug/device is being administered, used or dispensed. **NOTE:** *The term sponsor may be used outside of the FDA definition to indicate the entity that funds the clinical research.*

(25) **Test article:** A test article is any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act or under §§ 351 and 354-60F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n; 21 CFR 50.3(j)).

(26) **Unanticipated Problems Involving Risk to Subjects and Others (UPIRSO):** The STVHCS adheres to the definition of UPIRSO found in the UTHSCSA IRB glossary at: [http://research.uthscsa.edu/irb/glossary/IRB\\_glossary.php](http://research.uthscsa.edu/irb/glossary/IRB_glossary.php)

(27) **VA Research:** All research and all other activities that in part involve research are considered VA research and subject to evaluation and approval by the VA R&D Committee and other VA regulation, if any of the following conditions are met:

(a) The research is sponsored by the VA. **NOTE:** *VA research may be funded by sponsors other than the VA or be unfunded as well.*

(b) The research is conducted by or under the direction of VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments).

(c) The research is conducted utilizing VA resources (e.g., equipment), or on any property or facility of STVHCS including space leased to, and used by VA.

(d) The research recruits subjects at the STVHCS or uses the STVHCS's nonpublic information to identify or contact human research subjects for research purposes.

(e) The funds for the research activities are managed by the STVHCS or its affiliated non-profit corporation, the Foundation for Advancing Veterans' Health Research (FAVHR)

### 3. ACTION:

a. **Mission of the STVHCS HRPP:** The STVHCS is committed to accomplishing the following mission:

(1) **To advance the protection and well-being of** research subjects by creating a dynamic and collegial environment of respect and understanding of the rights and welfare of human research participants.

(2) **To foster high ethical standards for the conduct of research involving humans.**

(3) **To ensure Investigators use sound scientific design in conduct of research.**

(4) **To continually provide research administrative staff, investigators and their**

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**research staff with** the current up-to-date information on regulations and ethical principles regarding human protection and research.

(5) **To continually assess the effectiveness of the multiple components of the HRPP**, including the IRB and the R&D Committee, in their protection of human subjects, review of research, and compliance with federal regulations.

(6) **To continually review and implement new approaches to** advance the responsible conduct of research and protection of human research subjects.

### **b. Principles Governing the HRPP:**

(1) **Ethical principles:** All activities related to human subject research at the STVHCS, regardless of funding source, will be guided by the ethical principles found in the *Ethical Principles and Guidelines for the Protections of Human Subjects of Research* (the “Belmont Report”) and governed by the Federal policy for the Protection of Human Subjects (Common Rule) codified by the VA at 38 CFR 16 and VHA Handbook 1200.05. The ethical principles defined in the Belmont Report are as follows:

(a) **Beneficence:** The sum of the benefits to the subject and the importance of the knowledge to be gained outweigh the risks to the subjects as to warrant a decision to allow the subject to accept these risks.

(b) **Autonomy:** Legally effective informed consent is obtained, unless the requirements for waiver of informed consent are met by adequate and appropriate methods in accordance with the provisions of applicable regulations.

(c) **Justice:** The selection of subjects is equitable and is representative of the group that will benefit from the research. Because exempt research does not fall under the normal regulatory requirements, review of this research by the R&D Committee, and Privacy Office will include a review to identify any ethical issues that would preclude the conduct of the research at the STVHCS.

(2) **Integration and Cooperation:** In order to fulfill its human research protection obligations, the STVHCS distributes responsibilities to various interdependent entities and individuals, each with its own set of responsibilities, creating an integrated system for protecting human research subjects. The ethical conduct of research is a shared responsibility, requiring cooperation, collaboration, trust, and effective communication. The HRPP includes institutional officials, the Research and Development (R&D) Committee and its subcommittees, the Institutional Review Boards (IRB), R&D office staff, Research Compliance Office, Research Pharmacy, investigators and their research staff, and various other elements and individuals.

(3) **Continuous improvement:** The STVHCS HRPP is a flexible and dynamic program, continually being changed and refined to effectively meet the goals of providing human research protection. All components of the HRPP have the responsibility and capacity to effect change to better provide protection in human subjects research.

### **c. Authority for the HRPP:**

(1) **Assurances:** The STVHCS has given and maintains written assurance in a FWA with the OHRP that it will comply with the DHHS regulations for the protection of human research subjects, 45 CFR Part 46, as amended, to include provisions of the Federal Policy for the

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Protection of Human Subjects. This assurance states that the institution is guided by the ethical principles regarding all research involving human subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled Ethical Principles and Guidelines for the Protection of Human Subjects of Research (The "Belmont Report"). The Assurance sets out the responsibilities for protecting human subjects. The STVHCS operates under Federal Wide Assurance #FWA00001220. The signatory official for the FWA is the Director of the STVHCS.

(2) **Federal regulatory guidelines:** In addition to the FWA, authority and direction for the HRPP comes from a large body of VA and other federal regulations. These are listed as references at the end of this policy.

(3) **State laws and regulations:** Texas State law differs slightly from VA regulations pertaining to the definition of the LAR. As a general rule, the STVHCS follows the more restrictive of the regulations.

(a) In the State of Texas a legally authorized representative of a subject who provides consent for subjects who lack decision-making capacity (surrogate consent) is a health care agent appointed by the person in a Durable Power of Attorney for Health Care (DPAHC); court-appointed guardian of the person, or from next-of-kin in the following order of priority: the patient's spouse, an adult child of the patient who has the waiver and consent of all other qualified adult children of the patient to act as the sole decision-maker; a majority of the patient's reasonably available adult children, patient's parents, the individual clearly identified to act for the patient by the patient before the patient became incapacitated, the patients' nearest living relative, or a member of the clergy.

(b) Texas state law defines an "adult" as someone 18 years of age or older OR someone less than 18 years of age but who has had the disabilities of minority removed by court order, unless the court ordered a limited removal that does not include health care decision-making capacity.

(c) Texas state law also provides additional regulations related to the surrogate consent for foster children.

(d) Where there is a question of interpretation of applicability of State law, the Regional Counsel for the STVHCS is consulted.

(4) **Local Policies and Procedures:** The diverse activities of the HRPP are outlined in various local policies and procedures. These include, but are not limited to, policy memorandums and standard operating procedures from the involved components, such as the R&D office (e.g. training, processing complaints, WOC appointments), Pharmacy Service (Investigational Drugs), and Research Compliance Office (auditing activities, noncompliance reporting).

(5) **Legal counsel:** Where there is a question of applicability of federal and other regulations and guidance, the Regional Counsel for the STVHCS is consulted.

### **d. Conditions Under Which Human Research Becomes Subject to the STVHCS HRPP:**

(1) **Human Research Subjects and the STVHCS HRPP:** When research involving human subjects meets the definition of "VA Research" (Paragraph 2.b.(27)), this research is subject to the STVHCS HRPP. The research may be VA funded, funded from extra-VA sources, or

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conducted without direct funding. Any questions concerning whether an activity is human subject research at the STVHCS should be brought to the IRB or R&D office.

(2) **"Engaged" In Human Subjects Research:** The STVHCS is considered "engaged" in human subjects research under our FWA when the research is subject to our HRPP, has a VA PI or LSI for the study, is approved by the affiliate IRB, and when STVHCS employees or agents (all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility either through salaried full or part-time, or WOC appointments) are involved in the following for research purposes:

(a) Intervening with living individuals by performing invasive or noninvasive procedures for research purposes (e.g., drawing blood; collecting other biological samples; dispensing drugs; administering other treatments; employing medical technologies; utilizing physical sensors; utilizing other measurement procedures);

(b) Manipulating the environment for research purposes (e.g., controlling environmental light, sound, or temperature; presenting sensory stimuli; orchestrating environmental events or social interactions);

(c) Interacting with living individuals for research purposes (e.g., engaging in protocol-dictated communication or interpersonal contact; conducting research interviews; obtaining informed consent);

(d) Obtaining, receiving, or possessing private information that is individually identifiable (either directly or indirectly through coding systems) for research purposes.

**e. Research Conducted at the STVHCS:** Research conducted at the STVHCS has the overall goal to advance health and health care for our veteran population and the nation. The STVHCS HRPP covers all types of human subjects research conducted at the STVHCS, including:

(1) **Biomedical Research.** Biomedical research involves research to:

(a) To increase scientific understanding about normal or abnormal physiology, disease states, or development; and

(b) To evaluate the safety, effectiveness or usefulness of a medical product, procedure, or intervention.

(2) **Social and Behavioral Research.** Social and behavioral research involving human subjects focuses on individual and group behavior, mental processes, or social constructs and usually generates data by means of surveys, interviews, observations, studies of existing records, and experimental designs involving exposure to some type of stimulus or environmental intervention.

(3) **Clinical Research.** Clinical research involves the evaluation of biomedical or behavioral interventions related to disease processes or normal physiological functioning. Clinical research often, but not always, includes drugs, devices, or biological products regulated by the FDA.

(4) **Health Services and Epidemiologic Research.** Health services and epidemiologic research targets specific health outcomes, interventions, or disease states, and attempts to

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reach conclusions about cost-effectiveness, efficacy, interventions, or delivery of services to affected populations. Data may be collected through surveillance, monitoring, and reporting programs or may employ retrospective review of medical, public health, and/or other records or databases. Because this type of research often involves aggregate examination of data, it may not always be necessary for the investigator to collect individually identifiable information. When this is the case, the research may qualify for exemption or expedited review, or may be deemed non-human subjects research. In all cases, the IRB Director or their designated reviewer, not the individual investigator, will determine when IRB review of the activity is required.

(5) **Research Involving a Data Repository or Tissue Bank:** Research utilizing stored data and/or materials (cells, tissues, fluids, and body parts) from individually identifiable living persons qualifies as human subject research, and requires IRB review. When data or materials are stored in a bank or repository for use in future research, the IRB and R&D Committee must review a protocol detailing the repository's policies and procedures for obtaining, storing, and sharing its resources, for verifying informed consent provisions, and for protecting subjects' privacy and maintaining the confidentiality of data. The IRB may then determine the parameters under which the repository may share its data or materials with, or without, IRB review of individual research protocols. VA-sponsored tissue banks must follow the guidance on the Office of Research and Development (ORD) website, [http://www.research.va.gov/programs/tissue\\_banking/default.cfm](http://www.research.va.gov/programs/tissue_banking/default.cfm), and any subsequent handbooks or directives.

(6) **Activities that may or may not be research:** Several activities may or may not constitute research, depending on whether the activity is designed or intended, at least in part, to develop or contribute to generalizable knowledge. A tool for determining when an activity is considered research is found on the UTHSCSA IRB website: <http://research.uthscsa.edu/irb/nonregresearch.shtml>. Investigators should seek input from the IRB Director and/or Associate Chief of Staff (ACOS) for R&D if they have questions on when an activity constitutes research.

(a) **Quality Improvement Activities:** Quality Improvement activities attempt to measure the effectiveness of programs or services and often provide recommendations for improvement. Quality Improvement activities constitute human subject research, and require IRB review, when they involve human subjects and are designed or intended, at least in part, to develop or contribute to generalizable knowledge. On the other hand, Quality Improvement activities that are designed solely for internal program evaluation purposes, with no external application or generalization, usually do not constitute human subject research, and usually do not require IRB and R&D Committee review. In cases where the intent of the activity changes after it has begun (e.g., findings from an activity intended solely for internal STVHCS purposes lead to a desire to generalize and disseminate the results for application outside the STVHCS), the activity may become research at the moment the intent to generalize the findings is formed, and the IRB should be contacted immediately. In all cases, it is the IRB, not the investigator, which will determine when an activity constitutes research and the conditions under which the investigator may pursue the research objectives.

(b) **Innovative Treatments in Medical Practice:** In the course of medical practice, clinical judgment sometimes leads physicians to employ "innovative" or "off-label" treatments when more common treatments appear to be ineffective or otherwise unsuitable in addressing a patient's needs. Such innovative treatments employed on an occasional basis and solely for clinical purposes do not normally constitute human subject research and do not normally require IRB review. However, the use of innovative treatments as part of a systematic investigation

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designed, at least in part; to develop or contribute to generalizable knowledge does constitute human subject research and does require prospective IRB review. In all cases, it is the IRB, not the investigator, which will determine when an activity constitutes research and the conditions under which the investigator may pursue the research objectives.

(c) Medical Case Reports: Generally speaking, a case report is not usually considered research because it is not usually a systematic investigation designed to develop or contribute to generalizable knowledge. A retrospective review of a series of cases with the intent of publishing a generalizable conclusion would be considered research and requires approval by the IRB and R&D Committee.

### **f. Research Not Conducted, or Conducted Under Special Restrictions, at the STVHCS:**

(1) **Research in which the subject is a fetus, in-utero or ex-utero** (including human fetal tissue) will not be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities. Use of stem cells shall be governed by the policy set by National Institutes of Health (NIH) for recipients of NIH research funding.

(2) **Research related to in vitro fertilization** will not be conducted by STVHCS investigators while on official duty, or at VA facilities, or at VA approved off-site facilities. **NOTE:** *Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.*

(3) **VA investigators cannot conduct interventions** in research that enroll neonates while on official duty, or at VA facilities, or at VA-approved off-site facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

(4) **Women who are known to be pregnant and/or their fetuses** may be involved in research if all of the requirements of 45 CFR 46.204 are met including informed consent requirements and the following ethical and scientific criteria:

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

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

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

(d) The VA medical facility Director certifies that the medical facility has sufficient expertise in women's health to conduct the proposed research (see guidance at: <http://www.research.va.gov/resources/policies/default.cfm>)

(5) **Children are defined as persons who** have not attained the legal age for consent to treatment or procedures involved in research, as determined under the applicable law of the jurisdiction in which the research will be conducted.

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(a) VA is authorized to care for Veterans and to conduct research that supports the mission of VHA and that enhances the quality of health care delivery to Veterans. Therefore, research involving children must be reviewed carefully by the IRB for its relevance to VA and must not be greater than minimal risk. The VA medical facility Director must approve participation in the proposed research that includes children (see guidance at:

<http://www.research.va.gov/resources/policies/default.cfm>. **NOTE:** *Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.*

(b) The IRB must have the appropriate expertise to evaluate any VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408. **NOTE:** *A link to these requirements is provided on the ORD Web site at:*

<http://www.research.va.gov/resources/policies/default.cfm>.

(6) **Research involving prisoners as participants will not be conducted at the STVHCS** unless the additional criteria in the VA Handbook 1200.05 are met and a waiver has been granted by the Chief Research and Development Officer. This also applies when a subject becomes incarcerated during the course of a study.

(7) **Research involving subjects who lack decision-making capacity** will not be conducted at the STVHCS unless the additional criteria in the VA Handbook 1200.05 are met. Additional information on temporary or fluctuating lack of decision-making capacity can also be found in VA Handbook 1200.05.

(8) **Planned emergency research will not be conducted at the STVHCS** in accordance with VA Handbook 1200.05.

(9) **Classified research involving human subjects** will not be conducted at the STVHCS in accordance with VA Handbook 1200.05.

(10) **Research involving international sites** may be conducted by STVHCS investigators while on official duty or at VA or approved off-site facilities with a signed approval document by the VA medical facility Director, with the exception of Cooperative Studies Program activities which must be approved by the Chief Research & Development Officer (CRADO) in accordance with VHA Handbook 1200.05.

(a) VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, Collaborative Research & Development Agreements (CRADAs), grants, contracts, or other agreements. **NOTE:** *Research conducted at U.S. military bases, ships, or embassies is not considered international research.*

Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.

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(b) International research includes multi-site trials involving non-U.S. sites where:

1. VA is the study sponsor;
2. A VA investigator is the overall study-wide PI;
3. VA holds the Investigational New Drug (IND); or
4. VA manages the data collection and the data analyses.

(c) International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).

(d) Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. (see OHRP guidance at <http://www.hhs.gov/ohrp/international/index.html>). **NOTE:** *The VA medical facility Director must approve participation in the proposed international research (see guidance at: <http://www.research.va.gov/resources/policies/default.cfm>*

(e) All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.

### **g. Subjects that Participate in Research at the STVHCS:**

(1) **Veterans:** Research subjects that participate in studies at the STVHCS are typically veterans receiving health care from the STVHCS.

(a) Adults with independent decision-making capacity, which may include healthy volunteers and those with conditions that affect the veteran population.

(b) Adults who lack decision-making capacity may also be included as long as the procedures and conditions detailed in VHA Handbook 1200.05, designed to protect these subjects from exploitation and harm, are met.

(2) **STVHCS staff:** The professional and support staff of the STVHCS may be included in a research study; however, a request must be submitted through the STVHCS Office of Labor Relations and the appropriate Union(s). The point of contact for this will be the STVHCS R&D office for further guidance and will provide assistance as needed. **NOTE:** *According to the Master Agreement between the Department of Veteran Affairs and the American Federation of Government Employees, Article 49 section 8.*

(3) **Non-veterans:** Non-veterans may be entered into VA approved research studies when the R&D Committee determines recruitment of non-vets is justified and appropriate. A summary of the justification for enrollment of non-vets as subjects must be submitted by the PI to the R&D Committee for review and approval. All regulations pertaining to the use of veterans as research subjects pertain to non-veteran subjects enrolled in VA-approved research.

**h. Organizational Structure and Responsibilities of the HRPP:** The essential functions of the STVHCS HRPP include comprehensive review of protocols, ethically sound participant-

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investigator interactions, ongoing (risk appropriate) safety monitoring, quality improvement/compliance activities, and education and training of investigators and research staff. It is the responsibility of all individuals involved in the HRPP to understand and apply their obligation to protect human subjects.

### **(1) Medical Center Director:**

(a) The Director is the institutional official ultimately responsible for the implementation and performance of the STVHCS HRPP. The Director delegates authority for all respective roles and responsibilities within the HRPP.

(b) The Director is the Assurance signatory official and is responsible for overseeing the protection of human subjects within the facility.

(c) The Director is ultimately responsible for overseeing the R&D Committee and research office. The Director ensures that policies and procedures for the HRPP are developed and maintained. The Director is responsible to see that sufficient resources, including funding, space and staff to support the activities of the HRPP are provided.

(d) The Director ensures that an environment that fosters safe human subjects research is promoted and training and education for all participants in the HRPP is provided.

(e) The Director is ultimately responsible for overseeing the IRB in its review and monitoring of VA human subject research, and assuring that IRB members are appropriately knowledgeable in the protection of human subjects and understand their ethical obligation to do so.

(f) The Director is ultimately responsible for the oversight of VA investigators and research team members to assure they are appropriately knowledgeable and understand their obligation to conduct research in accordance with ethical standards and all applicable regulations.

(g) Fulfills all educational requirements mandated by the VA Office of Research and Development (ORD) and OHRP.

(h) Appoints one or more research compliance officers to conduct annual research consent document audits and triennial regulatory audits, and to assist in the VA facility's assessments of regulatory compliance.

1. Unless a waiver for a part-time research compliance officer is approved by the under secretary for health, each VA facility conducting research must designate at least one full-time research compliance officer.

2. The medical center director must report any appointment, resignation, or change in status of the research compliance officer to ORO VHA Central Office, with a copy to the relevant ORO research officer, within 10 business days after the appointment, resignation, or change takes effect.

(i) Reports to ORO in writing within five business days after being notified of a research problem or event (including serious and continuing non-compliance, unanticipated problems involving risks to subjects or others, and suspensions and terminations) for which such reporting is required.

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1. The medical center director's written report is required regardless of whether disposition of the event has been resolved at the time of the report.

2. Follow-up reports detailing any additional findings and appropriate remedial actions must be provided to the relevant ORO office at intervals and in a manner specified by that office.

(j) Provides a copy of any ORO compliance reports regarding the research program to the ACOS for Research, Research and Development Committee, any relevant research review committee(s), and the research compliance officer in a timely fashion.

(k) Reports the following research events to ORO Central Office, with a simultaneous copy to the appropriate ORO research officer, as indicated in the following:

1. IRB changes in number of IRBs and changes in membership rosters.

2. Substantive memorandum of understanding changes must be reported to ORO Central Office within five business days.

(l) Reports accreditation problems to ORO Central Office within five working days.

(m) Ensuring provision of adequate resources to support the operations of the HRPP so that those operations are in compliance with all VA and other federal requirements that govern human subjects research protection.

(n) Ensuring an annual evaluation of the facility's HRPP by delegating this authority to the Research and Development Committee.

(o) Delegating authority to one or more individuals to:

1. Provide comments or suggestions to VA Central IRB, in response to VA Central IRB's initial review considerations to the ACOS for R&D.

2. Responds to VA Central IRB's approval of the study on behalf of the VA facility as to whether the VA facility chooses to participate or declines to participate in the study to the ACOS for Research.

3. Serve as liaison between the VA facility and both the local site investigator and VA Central IRB to the ACOS for R&D or their designee.

(p) Ensuring a local research subject outreach program is implemented that includes a reliable mechanism for research subjects to communicate with investigators and with an informed VA representative who is independent of the research study in question (e.g., providing contact information in the consent document).

(q) Ensuring a local research subject outreach program is implemented that includes:

1. Researchers making every reasonable effort to provide the informational brochure, "Volunteering in Research – Here Are Some Things You Need To Know," at: <http://www.research.va.gov/programs/pride/veterans/tri-fold.pdf>, to prospective research subjects in settings where subjects might be recruited (e.g., clinic waiting areas) and to each prospective subject when that individual is approached to take part in a study.

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2. Providing venues for research subjects and their designated representatives to obtain information, discuss their questions and concerns, and offer their input.

3. When appropriate, making educational activities available for research subjects and their communities.

(r) Ensuring appropriate auditing of local human subjects research studies to assess compliance with all applicable local, VA, and other federal requirements including, but not limited to, Office of Research Oversight requirements.

(2) **R&D Committee:** The R&D Committee has a central role in the oversight of research at the STVHCS. The responsibilities and function of the R&D Committee are detailed in STVHCS Research and Development (R&D) Committee Charter. In broad terms, the R&D Committee is responsible through the Chief of Staff to the facility Director for the following:

(a) Maintaining high standards throughout the R&D program, including the protection of human research subjects.

(b) Ensuring that the resources available for the proposed research are adequate to successfully and safely perform the research.

(c) Overseeing the implementation and performance of the HRPP and providing oversight to assure regulatory compliance. It has the responsibility to assure that there is adequate resource allocation to maintain the HRPP.

(d) Reviewing all subcommittee activities and ensuring that the procedures followed for the review of research by the subcommittee are appropriate and free from undue influence.

(e) Evaluating quality improvement activities, supporting implementation of needed changes, and making recommendations to the Medical Center Director.

(f) Developing plans and processes for improvement of research oversight, and evaluating research audit reports, reports of UPIRSOs, research non-compliance, and research-related concerns or complaints. Audit reports may include audits conducted by the STVHCS Compliance Office, Office of R&D, other STVHCS sections, or non-STVHCS audits such as by the UTHSCSA Compliance Office or external study monitors.

(g) Approving all research to be conducted within the STVHCS. No STVHCS research can be initiated without the approval of the R&D Committee.

### (3) **Subcommittee for Human Studies (Institutional Review Board; IRB):**

(a) The STVHCS Director, as authorized by VHA Handbook 1200.05, has designated the VA Central IRB and UTHSCSA Institutional Review Board (IRB) as the IRB's of record that will review all human subject research at the STVHCS. The STVHCS has established an MOU with the UTHSCSA and the VA Central IRB outlining the responsibilities and conditions of this arrangement. The STVHCS does not allow the use of another IRB for the purposes of avoiding the rulings of an IRB of record. The STVHCS or UTHSCSA IRB may not use a commercial IRB for review of VA research.

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(b) The UTHSCSA IRBs are registered with OHRP: IRB 1 (Registration #IRB00000553); IRB 2 (Registration #IRB00002691); and IRB 3 (Registration #IRB00002692); and IRB 4 (Registration # IRB00009608). The VA Central IRB is registered with OHRP as IRB00006332 Veterans Health Administration Central Office IRB #1

(c) The IRB is responsible to review and monitor research involving human subjects in accordance with Veterans Health Administration (VHA) guidelines, and will function as a subcommittee of the R&D Committee. The IRB has the authority to approve, require modifications necessary for approval, and disapprove all research activities involving human subjects at the STVHCS. No VA research involving human subjects may be initiated without approval of the IRB. The IRB will confirm that FDA regulated research has a valid IND or Investigational Device Exemption (IDE), as appropriate.

(d) The IRB has the authority to suspend or terminate the approval of research that is not being conducted in accordance with the IRB's requirements, or that has been associated with unexpected serious harm to subjects.

(e) The IRB has the authority to observe, or have a third party observe, the consent process and the conduct of human subject research.

(f) The IRBs of record provide the relevant documents (e.g. protocols, copies of the minutes and IRB actions) to the R&D Committee to enable it to oversee the IRB review process. The R&D Committee may not approve research projects disapproved by an IRB.

(g) The IRB or designated reviewer, not the investigator, makes the determination of when a protocol is exempt from federal regulations based on criteria detailed in 45 CFR 46.101(b)(1)-(6) and in accordance with VHA Handbook 1200.05.

(h) The IRB is responsible for the dissemination of its policies, SOPs, and other materials necessary for the protection of human subjects.

### (4) **ACOS for R&D and R&D Office:**

#### (a) ACOS for R&D and Deputy ACOS for R&D:

1. The responsibility to administer the R&D program and ensuring day-to-day operation (implementation, maintenance, and improvement) of the HRPP is delegated to the ACOS for R&D from the Medical Center Director through the Chief of Staff. This includes the financial management of the facility's HRPP program, funds allocated to each project, and any non-VA monies available in the Facility's General Post Fund designated for R&D activities by the Medical Center Director.

2. The ACOS for R&D serves as a non-voting member of the R&D Committee, reporting on the status of all aspects of research.

3. The ACOS for R&D is the primary point of contact for communication between the IRB and the UTHSCSA Office of Clinical Research and the STVHCS HRPP components.

4. The Deputy ACOS for R&D assists the ACOS for R&D in all aspects of the operational management of the STVHCS clinical research program and HRPP.

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5. Any recommendations approved by the R&D Committee are implemented by the Associate Chief of Staff (ACOS) for R&D or designee.

6. The ACOS for R&D ensures that all research personnel have designated roles and responsibilities delegated by the Principal Investigator that are appropriate to their education, training, licensure and experience, by reviewing and approving (along with the Chief of Staff) a written Research Scope of Practice.

(b) The Administrative Officer (AO) for R&D and the R&D Office administers the operational function of the HRPP. The AO for R&D is responsible for developing and implementing control procedures for fiscal matters, supplies, equipment, and services such as common resources and administrative support. The R&D Office responsibilities include:

1. Administration of the R&D Committee and its subcommittees.
2. Administration of the protocol review, management, and monitoring processes.
3. Processing research complaints or reports of noncompliance.
4. Verification, documentation, and tracking of required human research training and credentialing of research study personnel.

5. Preparation, submission, and maintenance of communications, reports, and correspondence required for the program administration.

6. Development, dissemination and implementation of VA Central Office policies and directives, and local policies and procedures. This requires the continual monitoring of VA and external guidance that affects HRPP activities and developing/implementing new or revised policies/procedures as required. Dissemination of information, and the provision of individualized consultation, related to new regulations, policies, and guidelines to research investigators, research staff, the R&D Committee, and the UTHSCSA Office of IRB are of critical importance to the function of the HRPP.

7. Providing an annual HRPP report to the R&D Committee to include a review of HRPP activities, changes in the HRPP, policies, budget and resources, training/credentialing, and Strategic Improvement and Quality Assurance/Quality Improvement activities.

### **(5) Research Pharmacist:**

(a) The Research Pharmacist, under the direction of Research Service with oversight by the STVHCS Pharmacy Service, is responsible for implementation and monitoring of HRPP requirements associated with the use of investigational drugs and devices. The policies and procedures related to the handling of Investigational Drugs and Investigational Devices and the research pharmacist's role are detailed in STVHCS Research Pharmacy Standard Operating Procedures for Handling Investigational Drugs and Investigational Devices in Human Research, respectively.

(b) The research pharmacy is involved in all phases of investigational drug studies, from planning through completion.

(c) The Research pharmacist is an ex officio, non-voting member of the R&D Committee. For all submitted research protocols that include administration of test agents or devices, the

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Research Pharmacist provides for the R&D Committee a review of the safety, feasibility, and appropriateness of the study for the STVHCS, and ensures that pharmacy resources are adequate to support the research study.

**(6) Research Compliance Officer (RCO).** The RCO is appointed by the Medical Center Director and is responsible for the development and implementation of a Research Compliance Program to provide oversight on the day-to-day activities of human research through systematic audits.

(a) The RCO reports directly to the medical center director. The activities of the research compliance officer are not determined or managed by the Research Service, research investigators, or any other research personnel.

(b) The RCO will maintain oversight to ensure adequacy of the STVHCS Research Program processes, such as, the effectiveness of communication with all applicable committees, persons, and officials. The RCO will also ensure documentation and reporting requirements of the auditing program are met to include: Content of the reports; persons, officials or committees that must receive and review reports (e.g., the Principal Investigator, Medical Center Director, IRB Director, R&D Committee, ACOS for Research), and other administrative persons or entities (e.g., ORO, OHRP, FDA) as appropriate. Ensure adherence to time frames for reporting and timelines for corrective actions required by the IRB, R&DC, Subcommittee for Research Safety, or other appropriate entities to be taken based on the findings. The RCO will also be cognizant of who should implement and review the corrective actions; and how to evaluate the results of any corrective actions.

(c) The RCO serves as a nonvoting consultant to the following facility committees: R&D, IRB, Institutional Animal Care and Use Committee (IACUC), Subcommittee for Research Safety (SRS), and other research review committees. The RCO will attend committee meetings to provide information and serve as a subject matter expert on research compliance issues. The RCO does not contribute to quorum or deliberate or vote with the committee. The Committee Chair may elect to exclude the RCO from any or all proceedings of the committee meeting if it is felt, by the Committee Chair that a conflict of interest exists. The RCO will also evaluate their presence at a committee meeting for potential conflict of interest and act accordingly.

(d) The RCO will communicate audit findings determined to be serious or continuing non-compliance to oversight agencies as appropriate.

**(7) Principal Investigators and their research staff:** All individuals involved in research at the STVHCS must have either a salaried or WOC appointment. Principal Investigators have the primary responsibility to safeguard the rights and welfare of each research subject, and to ensure that the subject's rights and welfare take precedence over the goals and requirements of society and the research. Any questions related to this responsibility, or the policies and procedures for protection of human subjects, should be directed to the IRB Director or ACOS for R&D. The Principal Investigator and research staff must abide by all determinations of the IRB and R&D Committee. The responsibilities of the Principal Investigator include but are not limited to those listed on the Statement of Commitment and Understanding signed by the PI located at <http://www.southtexas.va.gov/Research/Protocol.asp>, and those listed in VHA Handbook 1200.05. To obtain additional information regarding the HRPP, investigators and research staff are encouraged to contact the IRB or the R&D office by phone and/or refer to the IRB and R&D websites.

(a) R&D Contact Information: <http://www.southtexas.va.gov/Research/Contacts.asp>

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(b) IRB Contact Information: <http://research.uthscsa.edu/irb/irboffice.shtml>

**(8) Information Security Officer (ISO):** The ISO works closely with the R&D Office to ensure that all research data is collected, handled, and stored in a secure manner. The ISO reviews each research protocol that is submitted to the R&D Committee, and no protocol will be approved that does not meet the VA research data security standards. The ISO is an ex officio, non-voting member of the R&D Committee and is responsible to communicate to the R&D Committee on any matter of concern related to information security in research.

**(9) Privacy Officer:** The Privacy Officer works closely with the R&D to ensure that approved research meets all VHA, HIPAA, and other regulatory requirements. The Privacy Officer reviews each research protocol that is submitted to the R&D Committee to ensure that legal authority exists prior to the use of Protected Health Information (PHI) for research, and that legal authority exists prior to the disclosure of PHI to outside entities for research purposes. The Privacy Officer participates as an ex officio, non-voting member of the R&D Committee in order to provide expertise related to research documentation and privacy related issues. The Privacy Officer is also responsible to monitor the accounting of disclosures of PHI related to research.

**(10) Medical Staff Office:** The Medical Staff Office has the responsibility of verifying the appropriate credentials of Licensed Independent Practitioners and unlicensed personnel who have a degree that makes them potentially eligible for a license involved in research, and for providing current information to the R&D Office for verification and tracking of credentials and privileges for research investigators and study staff.

**(11) Human Resources Management Service (HRMS):** The HRMS has the responsibility of processing and maintaining appointments of all personnel involved in STVHCS research. The VetPro section of HRMS has the responsibility for credentialing all licensed dependent practitioners and for providing current information to the R&D Office for verification and tracking of credentials for research investigators and study staff.

**(12) Financial Conflict of Interest (FCOI) Administrator:** The FCOI Administrator is appointed by the Medical Center Director to review research investigator's FCOI disclosure forms to determine if a real or perceived FCOI may exist. The Administrator will consider the FCOI evaluation by the IRB FCOI Committee in determining the actions required to manage, reduce, or eliminate FCOI, and will make referrals to Regional Counsel when necessary. The findings and recommendations of the FCOI Administrator will be communicated to the IRB and R&D Committee. No protocol will be approved by the R&D Committee unless all of the concerns of the FCOI Administrator and the IRB FCOI Committee evaluation are satisfied.

**(13) Radiation Safety Committee (Medical Radioisotope and Radiation Control Committee; MRRCC):** The IRB and R&D Committee cannot approve research involving the use of radioactive substances or radiation at the STVHCS unless it has been approved by the MRRCC. The MRRCC is responsible to:

(a) Review and approve or deny, on the basis of scientific validity, safety, feasibility, and appropriateness for the STVHCS, any research protocol that involves the use of radioactive materials and radiation producing devices.

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(b) Review and approve or deny a proposed authorized user, based on the training and experience of the individual, to ensure that the qualifications of all investigators involved in protocols that use radioactive materials are adequate.

(c) Review investigation reports of all alleged occupational overexposures, recorded events, misadministration and unusual occurrences as they pertain to the use of radioactive materials and radiation devices.

(d) Recommend actions indicated to reduce or minimize radiation exposure, and direct termination of those activities, involving radiation or radioisotopes, that seriously threaten the health of any individual.

(e) Ensure the safety review of the use of potentially hazardous sources of non-ionizing radiation for the STVHCS.

**(14) Subcommittee for Research Safety (SRS):** The SRS is a subcommittee of the R&D Committee that is responsible for overseeing compliance with the VHA Handbook 1200.8 Safety of Personnel Engaged in Research. The details of the STVHCS Research safety program and function of the SRS can be found in the SRS Policy at:

<http://www.southtexas.va.gov/Research/Documents/16-02ResearchSOPSafetyProgram.pdf>.

The responsibilities of the SRS include the following:

(a) Reviewing research proposals for compliance with all applicable regulations pertaining to biological, chemical, physical, and radiation hazards. This includes all research proposals to be conducted at the VA, or by VA personnel off-site while on-duty. The SRS will approve or disapprove all proposals that involve safety hazards unique to the research environment, and will provide written communication of the committee's findings to the PI and the R&D Committee. The R&D Committee will consider the findings of the SRS prior to its approval of the research protocol.

(b) Making general recommendations to the R&D Committee, ACOS/R&D, Chief of Staff, facility safety official, and when appropriate, facility Safety Committee regarding research safety.

(c) Identifying the need for health surveillance of personnel involved in individual research projects; and if appropriate, advising R&D Committee and Employee Health Practitioner on the need for such surveillance.

(d) Communicating with, and serving as an information resource to, investigators and research staff concerning all aspects of research safety.

(e) Reporting annually to the R&D Committee an evaluation of the STVHCS research safety program, to include a review of all active research protocols involving biological, chemical, physical, and radiation hazards, regardless of funding status or source, an assessment of the effectiveness of the research safety program, and recommendations for quality improvement.

**(15) Health Information Management Section (HIMS).** HIMS is responsible to assist in the documentation of research activities in the medical record. HIMS is responsible to scan the signed Research Informed Consent Document (VA 10-1086 form) and the Investigational Drug record document (VA 10-9012 form) into the electronic medical record (attached to the Consent Enrollment Note).

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**(16) Research Integrity Officer (RIO):** The ACOS for R&D is designated by the STVHCS Director as the institution's RIO. The RIO is responsible to receive, and ensure the appropriate investigation of any allegations of misconduct according to STVHCS Policy Memorandum entitled "Research Misconduct" and VHA Handbook 1058.2.

**(17) Clinical Staff:** The STVHCS clinical staff (nurses, physicians, respiratory therapists, etc.) has the responsibility of contributing to the protection of human subjects when they interact with research subjects and investigators as part of their routine clinical duties. This includes communication with research staff, the research compliance office, or R&D Office staff when they have a question or concern about a research activity. The clinical staff is responsible to read the documentation of research activities in the medical record and use the information as appropriate in the routine clinical care of the patient.

**(18) UTHSCSA Office of Clinical Research:** The STVHCS research program is closely aligned with the research program at the UTHSCSA because many investigators and research staff are dually salaried by the two institutions and may be principally located at either institution, research protocols are often active at both sites, and parts of VA-approved research may be performed at the UTHSCSA. The UTHSCSA Office of Clinical Research is the counterpart of the R&D Office at the STVHCS. These offices recognize that the optimal protection of human subjects requires full cooperation between the two institutions; therefore, the offices work together in efforts such as jointly providing training for research personnel, using a shared evaluation tool for defining research Scope of Practice, sharing of research resources, and jointly implementing compliance activities.

**(19) External sponsors:** External sponsors of human subject research have a role in the protection of research subjects during all phases of the research.

(a) Prior to initiation of a sponsored research protocol, the written agreement between the organization and sponsor must specify that the sponsor will use procedures that protect research participants; address medical care for research participants with a research-related injury; promptly report to the STVHCS findings that could affect the safety of participants or their willingness to continue participation, influence the conduct of the study, or alter the IRB's approval to continue the study; address plans for disseminating findings from the research and the roles that investigators and sponsors will play in publication or disclosure of results; and address in the written agreement with the Sponsor how results will be communicated to study participants.

(b) During the active phase of the research the sponsor must promptly report to the Principal Investigator any finding that could affect the safety of participants or their willingness to continue participation, influence the conduct of the study, or alter the IRB's or R&D Committee's approval to continue the study. The PI must ensure that the IRB and STVHCS R&D Office are notified, as appropriate.

### **i. Protection of Confidential Information about Research Subjects:**

(1) **VA investigators must obtain written authorization or a waiver of authorization** from the IRB to use VHA individually-identifiable health information involving non-employee research subjects for research purposes. The requested data may only be used in a manner consistent with the approved research protocol.

(2) **All protocols involving the collection, use and/or storage of research information** including subject identifiers and PHI that are submitted to an IRB and R&D Committee for

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approval must contain specific information on all sites where the data will be used or stored, how the data will be transmitted or transported, who will have access to the data, and how the data will be secured.

(3) **The details of the STVHCS policy and procedures that have been established to ensure the security of VA-sensitive research data and protected health information can be found in the STVHCS Research Service Standing Operating Procedure (SOP) entitled "Protection of VA-Sensitive Research Information."**

### **j. Interaction and Communication Between the Components of the HRPP:**

(1) **Independence of review and oversight:** The STVHCS HRPP functions as a coordinated system of checks and balances provided by the multiple different review components (IRB, R&D, Privacy, and Compliance). Each of the components functions independently in its review and oversight of research, and one component cannot exert undue influence on the independent review and conclusions of another. The R&D Committee and IRB do not answer to individuals, departments, or units that rely on them for the review of their research. The PI is responsible to assure that no undue influence will be asserted by any member of the research team toward any review or oversight committee, committee member, or individual involved in the HRPP. The IRB is the final authority of all decisions regarding the welfare and protection of human subjects participating in research at the STVHCS. Attempts to unduly influence the IRB will be reported to the Medical Center Director and the R&D Committee for appropriate action. The R&D Committee cannot approve any human subjects research activity that has not been approved by the IRB. Likewise, Institutional Officials do not have the authority to approve research that has not been approved by the IRB and R&D Committee. The R&D Committee is responsible to ensure that the review process for each component is appropriate, without exerting undue influence on the outcome of a review of a specific protocol or activity. Attempts to exert undue influence on the review or approval process should be reported. Committee and subcommittee chairs and members have direct access to the IRB Director, ACOS for R&D, and Medical Center Director for appeal if they experience undue influence or if they have concerns.

(2) **Coordinated effort and effective communication:** The effective function of the multi-component and multi-tiered HRPP requires coordination at all levels and frequent and effective communication at all levels. The lines of communication and coordination are described in multiple Standard Operating Procedures and Policies.

(3) **Dissemination of Information:** All policies and Standard Operating Procedures related to the HRPP are made available to investigators and research staff through electronic dissemination, posting on the STVHCS Research Service website, and through paper copy in the R&D Office.

### **k. Resources Committed to the HRPP:**

(1) **The STVHCS will provide the resources appropriate to the volume of research at the STVHCS to ensure the effective function of the HRPP.** It will engage in a systematic budgeting process for the HRPP resources including personnel, materials, space, equipment, training and education. Funding for the various components of the HRPP may come from the medical care allocation or R&D Service administrative funds.

(2) **The R&D Office will report annually to the R&D Committee a review of resources provided by organization to support the HRPP.** The R&D Committee will evaluate the effective

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function, quality, and compliance of the program, and will communicate its findings and any recommendations to the Medical Center Director.

**I. Strategic Improvement and Quality Assurance-Quality Improvement** related to the HRPP: The STVHCS program for the protection of human subjects is accomplished through a system of continuous education, evaluation, implementation, and oversight activities.

(1) **Education of research personnel:** The STVHCS recognizes that a proactive program of education for all individuals involved in human subjects research is critical to the success of the HRPP. To this end several educational programs and activities have been implemented.

(a) On-line standardized training: All individuals involved in human subjects research at the STVHCS, whether they are salaried or have a WOC appointment, are required to complete the online Collaborative Institutional Training Initiative (CITI) Course in The Protection of Human Research Subjects. The CITI certification is good for three years. A link to this training course is available on the STVHCS Research Service website.

(b) IRB and Office of Clinical Research-sponsored training: The STVHCS participates with the UTHSCSA in providing an 8-hour training course on "Conducting Clinical Research". All personnel involved in human subjects research at the STVHCS are strongly encouraged to participate in this course, which is offered 3 times per year. The UTHSCSA IRB also provides periodic Forums for education of STVHCS investigators and their research staff related to human subjects research issues.

(c) Training seminars, conferences and webinars sponsored by outside organizations (e.g. Public Responsibility in Medicine and Research [PRIM&R] annual conference and PRIM&R at your doorstep): The STVHCS participates with the UTHSCSA in providing onsite seminars and webinars for IRB and R&D committee members and IRB and R&D office staff. Additional training that has been provided by the VA nonprofit organization, FAVHR, through UTHSCSA it is The Association of Clinical Research Professional (ACRP).

(d) Investigator Handbook: The STVHCS Investigator Handbook is available in text form and on the STVHCS research website to serve as a practical guide to assist research teams in following policies, regulations, and laws to protect the rights and welfare of human participants. In addition, the Investigator Handbook provides information regarding where investigators can go to find more information or to have questions addressed.

(e) Individualized training: The R&D Office staff, the ACOS/Research, and the Deputy ACOS for Research are readily available to provide individualized training and facilitation of the responsible conduct of human subjects research.

(f) Policies and Standard Operating Procedures (SOPs): The policies and SOPs of the STVHCS R&D Office and UTHSCSA IRB are posted on their respective websites to facilitate their use by investigators and their research staff.

### (2) **Educational outreach to research participants:**

(a) The STVHCS recognizes that people who understand research will be better protected as research subjects. Therefore, a program of educational outreach is in place to improve the understanding of research in the community. This includes the display of posters and pamphlets in public areas of the STVHCS, providing community speakers to discuss VA research when the opportunity arises, and maintaining a STVHCS research website that is

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accessible to the public. Past, current, or prospective participants in research have the opportunity to pose questions, concerns, complaints, or suggestions to investigators, the R&D Office, and the IRB through the required contact information provided in the Informed Consent document, and listed on posted pamphlets and posters. Investigators are reminded at the time of study approval to use the “Volunteering in Research – Here Are Some Things You Need To Know,” (<http://www.research.va.gov/programs/pride/veterans/tri-fold.pdf>) when individuals are approached to take part in a study.

(b) National VA Research Week celebrates the achievements of VA researchers in providing high quality care for veterans and advancing medical science. It also serves to educate Veterans, the public, and the media about the research being conducted at medical centers, and its impact on treating and preventing disease and disability. The STVHCS coordinates activities of National VA Research Week with local events to educate and provide information to the community.

(c) There may be special circumstances in which an ad-hoc committee will need to be formed to address issues involved in the review of a VA R&D protocol. The purpose of the ad-hoc committee would be to provide Veteran input on issues requiring Veteran input for a specific protocol and/or a specific issue. The convened R&D committee can request the formation of an ad-hoc committee composed of Veterans. The Office of General Counsel will be consulted to ensure that appropriate federal regulations and requirements regarding formation of committees involving non-federal employees are followed.

(d) VA Central Office has a number of initiatives to solicit ideas for future research from the community of veterans the VHA medical centers serve. As these ideas are transformed into requests for applications our local investigators apply for potential funding of local research projects that are directly applicable to the veterans we serve.

(3) **Compliance plan:** The RCO is responsible for creating an auditing plan that will ensure that all active human subjects research at STVHCS is reviewed, at a minimum, as outlined in the ORO guidance. Refer to STVHCS Policy Memorandum entitled “Research Compliance Program” for additional details.

(4) **Procedures for addressing research-related complaints and concerns,** and allegations and findings of research non-compliance:

(a) Complaints, concerns, or allegations related to research: The STVHCS HRPP maintains an open door policy. Any individual is welcome to contact the research office or any other component of the HRPP with a question, concern, complaint, comment, or suggestion. All Informed Consent documents contain the contact information for the IRB so that a research subject may bring any questions, concerns, complaints, comments, or suggestions to the attention of the IRB, who will in turn communicate those to the ACOS for Research as appropriate. The ACOS for Research is responsible for insuring that complaints, concerns, or allegations related to research are reviewed and appropriate actions are taken. The process for reviewing and addressing complaints, concerns, or allegations related to research is detailed in STVHCS Policy Memorandum entitled “Human Subject Concerns, Complaints, and Allegations of Research Improprieties.

(b) Findings of research non-compliance: Research non-compliance may be identified through self-reporting by a principal investigator, receipt and subsequent review of an allegation by the ACOS for R&D, or through a routine or for-cause audit of a research protocol by the Research Compliance office. Potential research non-compliance involving human subjects

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research will be immediately reported to the IRB, who will take appropriate actions as outlined in UTHSCSA IRB Policy. The IRB determination of the findings will be reported to the investigator, the ACOS for R&D, the R&D Committee, and the Medical Center Director. The final course of action regarding the complaint or allegation is entirely dependent upon the nature, severity, and degree of seriousness of the findings. All actions taken shall be at the institutional level most appropriate for the circumstances.

(c) Reporting of research non-compliance: The IRB Director, or ACOS for R&D through the Medical Center Director as the Institutional Official for the HRPP, will report all actions requiring reporting to regulatory bodies outside the medical center, such as the Regional ORO, VHA ISO if information security is at issue, OHRP, the FDA if investigational devices or drugs are involved, and/or any other federal agencies overseeing research who require separate reports from OHRP. If the noncompliance is related to VA-funded research, it will also be reported to the VA Office of Research and Development. Reports shall be made as soon as possible after recognition of a reportable event and within the maximum allowable time required by the applicable regulatory body. Instances that may require such notification include findings of serious or continuing noncompliance with the regulations for the protection of human subjects or with the requirements of the IRB.

### (5) **Monitoring and reporting of unanticipated problems and adverse events**

(a) Reporting to and evaluation by the IRB: The purpose of reporting unanticipated problems involving risk to subjects or others is to protect the rights and welfare of participants in human subject research. Investigators involved in human subject research at the STVHCS are required to promptly report all UPIRSO. Research conducted at the STVHCS must adhere to the UTHSCSA UPIRSO and Unanticipated Adverse Device Event (UADE) Policy [http://research.uthscsa.edu/irb/Policy/UPIRSO and UADE Policy.pdf](http://research.uthscsa.edu/irb/Policy/UPIRSO_and_UADE_Policy.pdf)

(b) Reporting to the STVHCS: Effective communication between the UTHSCSA IRB and STVHCS research program is essential to the function of the HRPP of the STVHCS. The ACOS/Research, or the Deputy ACOS/Research should the ACOS for Research and Development be unavailable, is the point of contact for all communications from the IRB. If the ACOS for R&D becomes aware of an UPIRSO or UADE, either directly through the PI or any other component of the STVHCS HRPP, that has not been reported to the IRB, the Principal Investigator will be informed of the requirement to promptly notify the IRB. The ACOS for R&D will also promptly report the possible UPIRSO or UADE to the IRB. The procedures for effective communication between the IRB and STVHCS are detailed in the Research Service Standard Operating Procedure entitled "Correspondence and Communication between the Research and Development (R&D) Office and Components of the Human Research Protection Program and Regulatory Agencies".

(c) Reporting to regulatory agencies: The IRB Director, or ACOS for R&D through the Medical Center Director as the Institutional Official for the HRPP, will report all UPIRSOs to external regulatory agencies, such as the Regional ORO, VHA ISO if information security is at issue, VHA Privacy Officer if the privacy/confidentiality of a research subject was compromised, OHRP, the FDA if investigational devices or drugs are involved, and/or any other federal agencies overseeing research who require separate reports from OHRP. If the UPIRSO is related to VA-funded research, it will also be reported to the VA Office of Research and Development. Reports shall be made as soon as possible after recognition of a reportable event and within the maximum allowable time required by the applicable regulatory body.

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(6) **Expiration of research protocol approval:** Approval for a research protocol may expire because of failure to meet reporting (e.g. Continuing Review) deadlines. In this case, the Principal Investigator will be notified that activities related to the research protocol must immediately cease, with the exception of those activities that are determined by the IRB or IRB Chair, in consultation with the Chief of Staff, to be required to ensure the safety of subjects already enrolled in the protocol. In this case, the IRB will notify investigators to immediately submit a list of participants for whom stopping research activities would cause harm. The expiration in approval of the protocol will be updated upon receipt and satisfactory review and approval of the required documentation by the IRB and R&D Committee.

(7) **Suspension or termination of research protocol approvals:** The IRB has the authority for suspension/termination of approvals at the STVHCS if research is not being conducted in accordance with IRB requirements, or is associated with unexpected harm to subjects. Suspensions or terminations must be reported to the appropriate oversight agencies. The STVHCS Director, R&D Committee, and/or the ACOS for R&D as the designated representative of the STVHCS Director, have the independent authority to disallow the conduct of any research protocol at the STVHCS that is not being conducted in accordance with R&D Committee requirements or institutional policies and regulations.

(8) **Oversight of External Research Study Monitors:** The evaluation of STVHCS human subjects research by external research study monitors, from the research sponsor or other outside regulatory agency, will be monitored by the R&D Office and reported to the R&D Committee. The Policies and procedures related to the conduct of external Research Study Monitors are detailed in Research Service Memorandum entitled "External Clinical Research Monitoring Visits".

(9) **Annual evaluation of the HRPP:** With input from investigators, IRB members, the R&D Office, and Research Compliance Office, the R&D Committee will annually evaluate the allocated resources, implementation, performance, and improvement activities of the HRPP, and will communicate its findings and any recommendations to the Director.

(10) **Institutional Conflict of Interest:** The STVHCS has instituted policy and procedures to ensure that the welfare of human participants and the integrity of research will not be compromised, or appear to be compromised, by competing institutional interests or obligations. The policy and procedures are detailed in STVHCS Policy Memorandum entitled "Managing Institutional Conflict of Interest". Regional Counsel for the STVHCS will be consulted on questions related to Institutional Conflict of Interest.

**m. Accreditation:** In accordance with VA Office of R&D requirements, the STVHCS will maintain Association for Accreditation of Human Research Protection Program (AAHRPP) accreditation, a program of independent external review of human research protection programs.

## 4. REFERENCES:

- a. Department of Health and Human Services (DHHS) Code of Federal Regulations Title 45, Public Welfare, Part 46, Protection of Human Subjects (45 CFR 46, 46.101)
- b. VA Code of Federal Regulations Title 38, Pensions, Bonuses, and Veteran's Relief, Chapter 1 Department of Veterans Affairs, Part 16, Protection of Human Subjects
- c. Code of Federal Regulations Title 21, Chapter 1, Food and Drug Administration (FDA) Department of Health and Human Services regulations pertaining to rights and welfare of

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human subjects participating in research involving investigational drugs and devices [21 CFR parts 50, 56, 312, 312.3, and 812, 812.3 (g), 812.3(r)]

d. VA Code of Federal Regulations Title 38, Pensions, Bonuses, and Veteran's Relief, Chapter 1 Department of Veterans Affairs, Part 17 Medical (38 CFR 17.33a, 17.45, 17.85, 17.92)

e. Department of Health and Human Services (DHHS) Code of Federal Regulations Title 45, Public Welfare, Parts 160 and 164, Standards for Privacy of Individually Identifiable Health Information and Security Standards for the Protection of Electronic Protected Health Information

f. VHA Handbook 1200.05 Requirements for the Protection of Human Subjects in Research, dated November 12, 2014

g. VHA Directive 1605.1, Privacy and Release of Information, dated August 31, 2016

h. VHA Handbook 1108.4, Investigational Drugs and Supplies, dated February 29, 2012

i. VHA Handbook 1200.08, Safety of Personnel Engaged in Research, dated March 6, 2009

j. VHA Handbook 1058.2, Research Misconduct, dated February 7, 2014

k. STVHCS Policy Memorandum 151-16-06, Research Misconduct, dated August 24, 2016

l. STVHCS Policy Memorandum 151-16-10, Managing Institutional Conflict of Interest, dated August 30, 2016

m. STVHCS Research and Development (R&D) Committee Charter

n. STVHCS Pharmacy Research Standard Operating Procedures (SOP)119PR-15-004, Handling of Investigational Drugs and Devices, dated December 12, 2014

o. STVHCS Research Service Standard Operating Procedure 11-35, Protection of VA-sensitive Research Information, dated March 2, 2011

p. STVHCS Research Service SOP 16-02, Safety Program, dated January 20, 2016

q. Master Agreement between the Department of Veterans Affairs and the American Federation of Government Employees, dated March 2011

**5. RESPONSIBILITY:** Associate Chief of Staff for Research and Development (151)

**6. RESCISSION:** STVHCS Policy Memorandum 151-11-03, dated July 25, 2011

**7. RECERTIFICATION:** March 2022

(Signed original on file)

ROBERT M. WALTON  
Director

DISTRIBUTION: A & B