Human Research Protection Program (HRPP)

Procedures for the Protection of Human Subjects in Research

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Table of Contents

I. Human Research Protection Program (HRPP) ................................................................. 5
   A. Purpose and Mission ........................................................................................................ 5
   B. Definitions .......................................................................................................................... 6
   C. Institutional Assurance ..................................................................................................... 20
   D. Scope of the HRPP .......................................................................................................... 21
   E. Ethical Foundations and Regulatory Mandates for the Protection of Human Subjects and Applicability to HSR at NF/SGVHS ....................................................... 21
   F. Requirements of Funding Sources .................................................................................. 22
   G. Applicability of FDA Regulations .................................................................................. 22
   H. Engagement in Human Subjects Research .................................................................... 22
   I. Special Considerations in NF/SGVHS Research ............................................................. 25
   J. Identifying and Disseminating New Information ............................................................. 26
   K. Allocation of Resources for the HRPP Program .............................................................. 27

II. Roles and Responsibilities in the NF/SGVHS HRPP ......................................................... 28
   A. The NF/SGVHS Director (“Director”) .............................................................................. 28
   B. Associate Chief of Staff/Research and Development (ACOS/R&D) ............................ 29
   C. Institutional Review Board (IRB) ..................................................................................... 30
   D. Administrative Officer/Research and Development (AO/R&D) .................................. 31
   E. HRPP Administrator ......................................................................................................... 32
   F. Research Compliance Officer (RCO) .............................................................................. 32
   G. Research Pharmacist ....................................................................................................... 33
   H. Information Security Officer (ISO) and Privacy Officer (PO) ....................................... 33
   I. Research and Development Committee ......................................................................... 33
   J. Subcommittee on Research Safety .................................................................................. 34
   K. Investigator ..................................................................................................................... 35

III. Requirements and Procedures related to Human Subjects Research at NF/SGVHS ................................................................................................................................. 40
   A. Research under the Auspices of NF/SGVHS ................................................................. 40
   B. Investigator Eligibility for VA Research Support .............................................................. 40
C. Protocol Submission, Reviews, and Approvals ........................................ 40
D. Human Subjects Protection and Other Training Requirements ...................... 42
E. Credentialing and Privileging ........................................................................ 42
F. Non Human Determinations ........................................................................... 43
G. Research Exempt from IRB Review .................................................................. 43
H. Expedited Review of Human Studies Research .............................................. 44
I. Informed Consent Process and Documentation ............................................... 44
J. HIPAA Authorization .......................................................................................... 46
K. Continuing review and Management of Protocols with Lapsed IRB Approval ...... 47
L. Protocol Conclusion or Termination ................................................................. 47
M. Departing Investigators ................................................................................... 48
N. Research Involving Vulnerable Populations ..................................................... 49
O. Contacting Veterans for Research Purposes .................................................... 49
P. Requirements for a VHA Health Record ............................................................ 49
Q. Flagging the VHA Health Record .................................................................... 51
R. Non-Veterans as Research Subjects ................................................................. 52
S. Payment of Research Subjects ........................................................................ 52
T. Conflict of Interest ............................................................................................ 53
U. Investigational Drugs in Research with Human Subjects ............................... 53
V. Investigational Devices in Research with Human Subjects .............................. 55
W. Research Involving Human Biological Specimens ......................................... 57
X. Research Involving Human Data ..................................................................... 57
Y. Use of Social Security Numbers in VA Human Research ............................... 57
Z. Use Preparatory to Research ......................................................................... 58
AA. Privacy, Confidentiality and HIPAA ............................................................... 58
BB. Information Security ....................................................................................... 60
CC. Treatment of Research Related-Injuries ....................................................... 60

IV. Unanticipated Problems, Serious Adverse Events and Non-Compliance Reporting .................................................................................................................. 62

A. Reporting Unanticipated problem involving risk to subjects or others and serious adverse events .......................................................................................... 62
B. Reporting Non-compliance

C. Reporting Requirement for Suspension or Termination of IRB approval, Serious or Continuing Non-Compliance and/or Unanticipated Problems

V. Outreach Program for Human Research Participants

A. Informational Brochures and Posters

B. NF/SGVHS Website

C. Community News

D. Research Week

E. Periodic Review of Research Week

F. Community Outreach

G. Inclusion of Community Members in Research Process

VI. Sponsored Research

A. Protection of Research Participants

B. Monitor of Study

C. Research Related Injuries

VII. References
Chapter I: North Florida South Georgia Human Research Protection Program (HRPP)

A. Purpose and Mission

The NF/SGVHS is responsible for protecting the rights and welfare of human research subjects. The NF/SGVHS HRPP is the comprehensive system to ensure the highest level of protection for human subjects participating in research within the NF/SGVHS. The HRPP coordinates and oversees the protection of human research subjects through this system consisting of a variety of individuals and committees including, but not limited to: the NF/SGVHS Director, Associate Chief of Staff (ACOS) for R&D, Administrative Officer (AO) for R&D, HRPP Administrator, Research Compliance Officer (RCO), R&D Committee, IRB, other committees or subcommittees addressing human subjects protection (e.g., Subcommittee on Research Safety (SRS), Radiation Safety Committee), Investigators and research staff, IRB staff and Research Service staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer), research pharmacy staff and others. The HRPP assists the institution in assuring that all activities related to human subjects research are guided by ethical principles and meet regulatory requirements for the protection of human subjects in research. Human research subjects participating in research at NF/SGVHS must receive the highest level of protection possible and any questions or any ethical or legal ambiguities will be resolved in favor of the human research subject.
The purpose of this manual is to establish, implement, and communicate responsibilities, procedures and requirements for the NF/SGVHS HRPP and to provide guidance to all individuals or entities involved in reviewing, approving, supporting, conducting, managing, or overseeing research involving human subjects.

B. Definitions and Acronyms related to VA Human Research Protections (from VHA Handbook 1200.05 unless otherwise noted)

1. **Accreditation.** Accreditation of a Human Research Protection Program (HRPP) is the process of obtaining independent recognition that a HRPP affords protection to human subjects by meeting and exceeding the prevailing ethical, professional, and regulatory requirements, and that the HRPP engages in continuous quality improvement.

2. **Accrediting Organization.** The accrediting organization is an independent body that has developed standards of performance to assess compliance with the prevailing ethical, professional, and regulatory guidelines for the conduct of human subjects research.

3. **Adverse Event (AE).** 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.

4. **Affiliated Institution.** An affiliated institution is an academic institution that has a relationship for the purpose of education, research, or enhanced patient care with a VA medical center documented by a formal Affiliation Agreement in conformance with VA requirements (also referred to as “academic affiliate”). In addition, special purpose agreements documented by a memorandum of understanding (MOU) approved by the Chief Research and Development Officer (CRADO) may be developed in research and development (R&D) areas, such as health services or rehabilitation R&D.

5. **Affiliation Agreement.** An Affiliation Agreement is a written agreement documenting the relationship for the purpose of education, research, or enhanced patient care between a VA medical center and an affiliated institution.

6. **Anonymous.** For the purposes of VA research, anonymous means de-identified in accordance with both:

   (a) The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule
(45 CFR 164.514(b) and

(b) The Common Rule provision that the identity of the subject cannot be readily ascertained by the investigator or associated with the information (38 CFR 16.102(f)).

7. **Assurance (Assurance of Compliance) or Federalwide Assurance (FWA).** For human research, an Assurance is a written commitment to protect human subjects participating in research and to comply with the requirements of 38 CFR Part 16. Assurances are reviewed and approved by the HHS Office for Human Research Protections (OHRP) and various other departments and agencies under the Federal Policy (Common Rule) for the Protection of Human Subjects (56 FR 28001, June 18, 1991). Under federal regulations, any institution conducting or engaged in federally supported research involving human subjects must obtain an Assurance in accordance with 38 CFR 16.103. NOTE: All research conducted under VA auspices is considered to be Federally-supported. This requirement also applies to any collaborating “performance site” institutions. Under 38 CFR 16.102(f), an institution is engaged in human subject research whenever its employees or agents: intervene or interact with living individuals for research purposes; or obtain, release, or access individually-identifiable private information for research purposes. **NOTE: The terms Assurance, Assurance of Compliance, and Federalwide Assurance (FWA) are synonymous.**

8. **Blinded.** A blinded study design is one comparing two or more interventions in which the research personnel, the subjects, or some combination thereof, do not know the treatment group assignments of individual subjects.

9. **Children.** Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted (45 CFR 46.402(a)).

10. **Clinical Investigation.** The FDA considers the term clinical investigation to mean any experiment that involves a test article and one or more human subjects, and that either:

    (a) Meets the requirements for prior submission to the FDA under § 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act; or

    (b) Does not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).
11. **Coded Data.** The term “coded data” means “coded private information” as defined in guidance published by HHS entitled Guidance on Research Involving Coded Private Information or Biological Specimens, currently available at: http://www.dhhs.gov/ohrp/humansubjects/guidance/cdebiol.htm.


13. **Credentialing.** Credentialing is the systematic process of screening and evaluating qualifications and other credentials, including licensure, education, training, and experience, and current competence and health status.

14. **Data.** Data means information derived directly from patients or human research subjects or indirectly through accessing databases. It includes information from Deoxyribonucleic Acid (DNA) sequencing. It does not include information derived from research involving animals or other types of research that do not involve human subjects.

15. **Database.** A database is a collection of data or information elements organized in a manner to permit systematic retrieval.

16. **Data Monitoring Committee (DMC), Data and Safety Monitoring Board (DSMB), or Data and Safety Monitoring Committee (DSMC).** A DMC, DSMB, or DSMC is group of individuals with relevant expertise that reviews accumulating data from one or more ongoing research studies. The DMC, DSMB, or DSMC independently advises the sponsor or the principal investigator (PI) regarding the continuing safety of the research study’s subjects, as well as the continuing validity and scientific merit of the study. DMC, DSMB, and DSMC are considered synonymous for the purposes of this Handbook.

17. **Data Repository.** A data repository (data warehouse) is a database or a collection of databases that have been created or organized to facilitate the conduct of multiple research protocols, including future protocols not yet envisioned. It also may have been created for other purposes such as administrative and clinical purposes.

18. **De-Identified Data**

   (a) For the purposes of VA research, de-identified data are data that have been de-identified in accordance with both:

   (i) The Health Insurance Portability and Accountability Act (HIPAA) Privacy
Rule (45 CFR 164.514(b), and

(ii) The Common Rule provision that the identity of the subject cannot be readily ascertained by the investigator or be associated with the information (38 CFR 16.102(f)).

(b) Such data may also be known as “anonymous.” NOTE: Coded data is data identifiable by the individual(s) who has access to the code. Therefore, for the purposes of this Manual, coded data are not considered to be de-identified or anonymous.

19. **Delivery.** In the context of pregnancy, delivery means complete separation of the fetus from the woman by expulsion, extraction, or any other means.

20. **Embryo.** An embryo is an organism in the early stages of development, which in humans is the first 6 weeks.

21. **Exempt Research.** Exempt research includes research activities in which the only involvement of human subjects is in one or more of the categories listed in 38 CFR 16.101(b). The exempt status must be determined by the Institutional Review Board (IRB) Chair or an IRB voting member designated by the Chair. NOTE: Such an exemption applies only to requirements found in 38 CFR Part 16. All other relevant VA and Federal requirements apply.

22. **Expedited Review Procedures for Research.** In contrast to a convened IRB review process, the expedited review process consists of a review carried out by the IRB Chair or by one or more experienced voting members of the IRB designated by the IRB Chair in accordance with 38 CFR 16.110(b).

23. **External AE.** In the context of a multi-site study, an external AE is an AE experienced by subjects, research staff, or others at another institution engaged in the trial.

24. **Facility.** For purposes of this Handbook, the term “facility” and “institution” are interchangeable.

25. **Fetus.** A fetus is the product of conception from the time of implantation until delivery.

26. **Generalizable Knowledge.** Information that is designed to expand the knowledge base of a scientific discipline (or other scholarly field of study) (draft VHA Handbook 1058.05)

27. **Health Care Agent.** A health care agent is an individual named by the patient in a Durable Power of Attorney for Health Care (38 CFR 17.32(a)(iii)).

28. **HIPAA Authorization.** The term HIPAA authorization means prior written
permission for use and disclosure of protected health information (PHI) from the information’s source person, research subject, or legally authorized personal representative, as required under law, including HIPAA. The written authorization must include all elements of a compliant authorization prior to any disclosure of information.

29. **Human Biological Specimens.** Human biological specimens are defined as 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.

30. **Human Research.** Human research is research involving human subjects or one or more identifiable human biological specimens. For FDA-regulated studies, human subject research also includes any activity that is a clinical investigation involving a human subject as defined above.

31. **Human Research Protection Program (HRPP).** A HRPP is a comprehensive system to ensure the protection of human subjects participating in research. At a local VA facility, the HRPP consists of a variety of individuals and committees including, but not limited to: the VA facility Director, Associate Chief of Staff (ACOS) for R&D, Administrative Officer (AO) for R&D, Research Compliance Officer (RCO), R&D Committee, IRB, other committees or subcommittees addressing human subjects protection (e.g., Subcommittee on Research Safety (SRS), Institutional Biosafety Committee, Radiation Safety Committee, Radioactive Drug Research Committee, Conflict of Interest Committee), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. 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.

32. **Human Subject.** This definition of human subject includes investigators, technicians, and others assisting investigators, when they serve in a “subject” role by being observed, manipulated, or sampled.

(a) Title 38 CFR Part 16 defines a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains either:

   (i) Data through intervention or interaction with the individual; interaction includes communication or interpersonal contract between the researchers
and the subject; or

(ii) Identifiable private information (38 CFR 16.102 (f)).

(b) For research covered by Food and Drug Administration (FDA) regulations, human subjects means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. (21 CFR 50.3(g), 21 CFR 66.102(c)).

(c) For research covered by FDA device regulations, subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease (21 CFR 812.3(p)).

33. **In Vitro Fertilization.** In vitro fertilization is any fertilization of human ova, which occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

34. **Institution.** An institution is any public or private entity or agency (38 CFR 16.102(b)). VHA Handbooks 1200.05 and 1058.03 distinguish VA from non-VA institutions.

   (a) **VA Institution.** A VA institution is any entity that is operated by VA, including but not limited to: VA hospitals, medical centers, clinics, and health care systems; space owned, leased, or rented by VA; and space that is "shared" with a non-VA entity (unless the VA space is leased to a non-VA entity and specifically designated in writing not to be used by VA or VA employees for research). A VA facility may include multiple campuses and satellite components. **NOTE:** For purposes of this Manual, the terms "facility," "VA facility," and "VA institution" are considered synonymous.

   (b) **Non-VA Institution.** A non-VA institution is an entity not operated by VA. Non-VA institutions include, but are not limited to:

      (i) Any entity that is not a legal component of VA or of a VA facility, including a contract research organization (CRO), industry or private sponsor, or public or private research company, foundation, or group.

      (ii) Entities operated under a contract with VA including, but not limited to, contract Community-based Outpatient Clinics (CBOCs), contract nursing homes, contract outpatient clinics. **NOTE:** Some entities (e.g., CBOCs) are VA institutions when they are part of the VA facility, but non-VA institutions when they are operated under a contract with VA (e.g., a contract CBOC).
(iii) Academic institutions, including VA–affiliated medical schools, dental schools, and other academic affiliates (see Affiliated Institution).

(iv) VA-affiliated Non-Profit Research and Education Corporations (NPCs).

(v) Other Federal, state, or local departments or agencies.

35. **Institutional Official (IO).** The IO is the individual legally authorized as Signatory Official to commit an institution to an Assurance. The IO serves as the official representative of the institution to external agencies and oversight bodies, and provides all written communication with external departments, agencies, and oversight bodies. The VA facility Directors are the IOs for local VA facilities. The IO is responsible for the HRPP as described in NF/SGVHS policies and procedures and as described in VHA Handbook 1200.05.

36. **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.

37. **Interaction.** Interaction includes communication or interpersonal contact between investigator and subject (38 CFR 16.102(f)(2)).

38. **Internal or Local AE.** In the context of a multi-center study, internal AEs are those AEs experienced by subjects, research staff, or others at the reporting individual’s own VA facility or VA-approved research site.

39. **International Research.** VA international research is any VA-approved research conducted at international sites (not within the United States (U.S.), its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research sending such specimens or data out of the U.S. **NOTE:** For the purposes of VA HRPPs, research conducted at U.S. military bases, ships, or embassies is not considered international research.

40. **Intervention.** Intervention includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes (38 CFR 16.102(f)(2)). Interventional studies are those in which the research subjects are assigned by the investigator to a treatment or other intervention, and their outcomes are measured.
41. **Investigational Device.** As defined by the FDA, an investigational device is a device that is the object of an investigation (21 CFR 812.3(g)).

42. **Investigational Device Exemption (IDE).** An IDE is an application to FDA that allows an investigational significant risk device to be used in a clinical investigation to collect safety and effectiveness data. If the device is a non-significant risk device, it is considered to have an approved application for IDE after IRB approval is obtained (see 21 CFR 812).

43. **Investigational Drug.** 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:

   (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 Investigational New Drug (IND) application, in a controlled, randomized, or blinded study.

44. **Investigational New Drug (IND) Application.** An IND is an application to the FDA allows an investigational drug or biological product to be studied in humans. An IND must be in effect prior to shipment and administration of investigational drug or biological products (see 21 CFR 312).

45. **Investigator.** An investigator is any individual who conducts research involving human subjects including, but not limited to, the 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.

   (a) **VA Investigator.** A VA investigator is any individual who conducts research approved by the VA 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.

   (b) **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.

(c) **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.

(d) **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.

46. **Legal Guardian.** A legal guardian is a person appointed by a court of competent jurisdiction to maintain and care for the property of an individual, or an individual who the court has declared incompetent due to physical or mental incapacity or age.

47. **Legally Authorized Representative (LAR).** A LAR 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)). For purposes of this manual, the following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority: Health care agent (i.e., an individual named by the individual in a Durable Power of Attorney for Health Care (38 CFR.17.32(a)(iii)); Legal guardian or special guardian; Next of kin in this order: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or close friend. The responsibilities of the LAR are described in VHA Handbook 1200.05.

**NOTE:** An individual who is qualified as a LAR to provide informed consent on behalf of a prospective research subject may not always qualify as a personal representative for purposes of consent to use or disclose a subject’s Protected Health Information (PHI) (i.e., signing a HIPAA authorization). Therefore, in circumstances involving authorization for use or disclosure of a human subject’s PHI, the investigator must ensure the LAR meets the requirements of a personal representative in HIPAA and the Privacy Act of 1974 (legal guardian or power of attorney) prior to the LAR’s signing a HIPAA authorization (VHA Handbook 1605.1).

48. **Minimal Risk.** Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (38 CFR 16.102(i)).

49. **Memorandum of Understanding.** An MOU is a written agreement between two VA facilities or between a VA facility and a non-VA institution documenting their relationship and defining their respective roles and responsibilities within that
relationship (VHA Handbook 1058.03).

50. **Neonate**. For the purposes of VA research, a neonate is an infant in the first 28 days of life.

51. **Observational Studies**. Observational studies are non-interventional studies in which individuals are observed and those observations are recorded. Outcomes, including health outcomes, may also be measured by the investigators.

52. **Office for Human Research Protections (OHRP)**. OHRP is an office within the Department of Health and Human Services (DHHS) that reviews and approves Assurances, monitors human research subjects protections through educational efforts, clarification and guidance, site visits, and reporting requirements. OHRP has the authority to suspend research for failure to adhere to the regulations.

53. **Office of Research and Development (ORD)**. Within VHA Central Office, ORD is the office responsible for the overall policy, planning, coordination, and direction of VA research activities.

54. **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.

55. **Personal Representative**. A personal representative is a person who, under applicable law, has authority to act on behalf of another individual. This may include power of attorney, legal guardianship of an individual, the executor of an estate of a deceased individual, or someone under Federal, state, local, or tribal law with such authority (e.g., the parent of a minor) (VHA Handbook 1605.1).

56. **Pilot Studies**. Pilot studies are full-fledged research studies that must be approved by the IRB(s), when human subjects are involved. They are not considered to be activities preparatory to research.

57. **Pregnancy**. Pregnancy encompasses the period of time from implantation until delivery.

58. **Preparatory to Research**. Within VHA, activities “preparatory to research” refer to activities that are necessary for the development of a specific protocol. PHI from data repositories or medical records may be reviewed during this process without IRB approval, subject authorization, or a waiver of authorization, but only aggregate data may be recorded and used in the protocol application (e.g., potential number of subjects meeting study criteria at each site). Within VHA, an activity preparatory to research does not include the identification of potential
subjects and recording of data for the purpose of recruiting these subjects or to link with other data. The preparatory to research activity ends once the protocol has been submitted to the IRB for review.

59. **Prisoner.** A prisoner is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

60. **Privacy Board.** Under HIPAA, a Privacy Board is a board that is established to review and approve requests for waivers or alterations of HIPAA authorizations in connection with use or disclosure of PHI. The UF IRB-01 acts as the privacy board NF/SGVHS except for research that falls under the VA CIRB.

61. **Private Information**

   (a) Private information must be individually identifiable in order for the information to constitute research involving human subjects (38 CFR 16.102(f)).

   (b) Private information includes:

   (i) Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and

   (ii) Information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record).

62. **Privileging**

   (a) For the purposes of this Manual, the terms “privileging” and "clinical privileging" are the same and are defined as the process by which a practitioner, licensed for independent practice (i.e., without supervision, direction, required sponsor, preceptor, mandatory collaboration, etc.), is permitted by law and the facility:

   (i) To practice independently; and

   (ii) To provide specified medical or other patient care services within the scope of the individual's license, based on the individual's clinical competence as determined by peer references, professional experience, health status, education, training, and licensure.
(b) Clinical privileges must be facility-specific and provider-specific per VHA Handbook 1100.19.

63. **Program for Research Integrity Development and Education (PRIDE).**
PRIDE is the program within ORD that is responsible for training, education, and policy development related to VA human subjects protection.

64. **Quorum.** A quorum is defined as a majority of the voting members. At meetings of the R&D Committee and its subcommittees, a quorum must be established and maintained throughout the entire meeting in order for business to be conducted. Some committees, such as the IRB have additional requirements for the establishment of a quorum, such as presence of a member whose primary concerns are in nonscientific areas. A member with a conflict of interest cannot:

(a) Contribute to a quorum,

(b) Be present for the discussion of the issue for which they are conflicted, except to answer questions from the committee, or

(c) Be present for the vote on the issue.

65. **Research.** Research means a systematic investigation including research development, testing, and evaluation designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities (38 CFR 16.102(d)).

66. **Research Compliance Officer (RCO).** The RCO is an individual whose primary responsibility is to audit and review research projects relative to requirements for the protection of human subjects, laboratory animal welfare, research safety, research laboratory security, research information protection, and other areas under the jurisdiction of and as specified by ORO. In addition to conducting required audits, the RCO may serve as a nonvoting consultant, as needed, to the facility’s R&D Committee, IRB, IACUC, Subcommittee on Research Safety (SRS), and other research review committees. The RCO may not serve as a voting or nonvoting member of these committees. The RCO may attend meetings of these committees when requested by the committee or as specified by local SOP’s.

67. **Research Records.** Research records include, but are not limited to, IRB and R&D Committee records, records of all observations, other data relevant to the investigation, progress notes, research study forms, surveys, questionnaires, and other documentation regarding the study per VHA Handbook 1907.01.
(a) **IRB Records.** IRB records include, but are not limited to: copies of all research proposals and amendments reviewed; scientific evaluations, if any, that accompany the proposals; approved informed consent documents; progress reports submitted by investigators; reports of injuries to subjects; reports of complaints from subjects; minutes of IRB meetings; reports of expedited review activities; records of continuing review activities; copies of all correspondence between IRB and the investigators; reports of deviations from IRB-approved protocol; a list of IRB members; written procedures for IRB in the same detail as described in 38 CFR 16.103(b)(4) and (5); and statements of significant new findings provided to subjects as required by 38 CFR 16.116(b)(5). A NF/SGVHS IRB of record must maintain prepare and maintain adequate documentation of IRB activities to the extent required by 38 CFR 16.115 and VHA Handbook 1200.05.

(b) **Investigators’ Research Records.** Research records include the following when relevant to the study: copies of all IRB-approved versions of the protocol and amendments; case report forms and supporting data (including but not limited to signed and dated informed consent forms and HIPAA authorization forms); documentation on each subject including informed consent, interactions with subjects by telephone or in person, observations, interventions, and other data relevant to the research study; reports of adverse events; data analyses; codes and keys used to de-identify and re-identify subjects’ PHI; reports (including, but not limited to abstracts and other publications); all correspondence (including, but not limited to, that with the funding source or sponsor) and with applicable oversight entities (including, but not limited to, IRB, R&D Committee, ORO, and FDA); and a master list of all subjects for whom informed consent has been obtained in the study.

68. **Researcher.** A researcher is an investigator.

69. **Sensitive Information**

   (a) VA sensitive information is all department data, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration, or destruction of the information.

   (b) The term includes information whose improper use or disclosure could adversely affect the ability of an agency to accomplish its mission; proprietary information; records about specific individuals requiring protection under various confidentiality provisions, such as the Privacy Act and the HIPAA Privacy Rule; and information that can be withheld under the Freedom of Information Act
70. **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.

71. **Sponsor.** For FDA studies, the FDA considers a sponsor to be the person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual, pharmaceutical company, governmental agency, academic institution, private organization, or other. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of their own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators (21 CFR 312.3 and 21 CFR 812.3).

72. **Surrogate.** A surrogate is an individual authorized under VHA policy to make decisions on behalf of a subject who lacks decision-making capacity.

73. **Suspension of IRB Approval.** A suspension of IRB approval is a determination by the IRB Chair, a qualified IRB voting member designated by the IRB Chair, or the convened IRB to temporarily interrupt some or all previously-approved research activities. The suspended activities could include, but not be limited to, recruiting of new subjects for the research. Suspended studies remain open and require continuing review.

74. **Systematic Investigation.** A systematic investigation is an activity that is planned in advance and that uses data collection and analysis to answer a question. (draft VHA Handbook 1058.05)

75. **Termination of IRB Approval.** A termination of IRB approval is a determination by the convened IRB to permanently halt some or all previously approved research activities including, but not limited to, enrollment of new subjects in research.

    **NOTE:** The terms “suspension” and “termination” apply to interruptions related to concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others. They do not include interruptions in human research resulting solely from the expiration of the IRB approval period (VHA Handbook 1058.01).

76. **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)).

77. **Unanticipated (or unexpected) Adverse Event (UAE).** An UAE is an AE that is new or greater than previously known, in terms of nature, severity, or frequency of occurrence, as documented in the protocol or other materials approved by IRB.

78. **Usual Care.** Usual care is medical or other treatment or services a research subject would receive if not participating in the research study (e.g., the chemotherapy an oncology patient would receive whether or not the patient was participating in a research study).

79. **VA Research.** VA research is research that is approved by the R&D Committee and conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments), utilizing VA resources (e.g., equipment), or on VA property including space leased to, and used by VA. The research may be funded by VA, by other sponsors, or be unfunded.

   **NOTE:** Research conducted by non-VA investigators that does not utilize VA resources and that occurs on space, or with equipment, leased from VA or covered under a use agreement between VA and a non-VA entity is not considered VA research.

80. **Without Compensation (WOC).** A WOC appointment is a VA appointment for a person who performs duties without any direct monetary compensation from VA.

**C. Institutional Assurance**

All human subject research conducted or supported by VA must comply with the Federal Policy (Common Rule) for the Protection of Human Subjects, 56 Federal Register (FR) 28001, June 18, 1991, as codified at 38 CFR Part 16. Each VA facility engaged in human subjects research must provide a written Assurance, acceptable to the Secretary of Veterans Affairs, committing the facility to comply with 38 CFR Part 16. The NF/SGVHS has a Federalwide Assurance (FWA) approved by the Office for Human Research Protections (OHRP) and a VA addendum approved by the VA Office of Research Oversight. The NF/SGVHS FWA covers all human subjects research conducted within the NF/SGVHS and by NF/SGVHS investigators acting in their official VA capacity. The NF/SGVHS Director is the signatory official to the FWA and the Institutional Official responsible for the oversight of the HRPP. Information on the components of the NF/SGVHS Assurance is listed on the OHRP website or is available upon request from the Research Service Office.

As part of its Assurance, NF/SGVHS has designated the University of Florida (UF) IRB-01 and the VA Central IRB (VA CIRB) as IRBs of record through Memoranda of
Understanding. NF/SGVHS investigators conducting human subjects research must comply with the requirements and determinations of the applicable IRB. IRB policies and procedures are available on the respective IRB websites.

D. Scope of the HRPP

The NF/SGVHS HRPP applies to activities meeting the definition of human subjects research or clinical investigation in which NF/SGVHS is engaged regardless of funding source, type of research or place of conduct. All activities that are determined to meet these definitions fall under the auspices of the NF/SGVHS HRPP and are subject to the all applicable regulations and requirements as described in NF/SGVHS HRPP policies and procedures. Definitions of “research,” “human subjects” and “clinical investigation” are provided in Chapter I.B. Procedures for obtaining a determination of whether an activity meets the definition of human subjects research are described in Chapter III.

Human Research Studies conducted at NF/SGVHS include but are not limited to: clinical investigations; health services research; rehabilitation research and may include patients, healthy volunteers, staff, and/or students.

E. Ethical Foundations and Regulatory Mandates for the Protection of Human Subjects and Applicability to HSR at NF/SGVHS

Ethical Foundations

NF/SGVHS assures that all of its human subjects research activities are guided by the ethical principles as set forth in the report of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research Ethical Principles and Guidelines for the Protection of Human Subjects of Research (The Belmont Report). The three guiding ethical principles of The Belmont Report include:

(1) Respect for Persons (applied in such ways as obtaining informed consent, giving consideration to privacy and confidentiality, and including special protections for those with diminished autonomy);

(2) Beneficence (applied by weighing risks and benefits); and

(3) Justice (applied by the equitable selection of subjects).

Regulations for the Protection of Human Subjects

All research involving human subjects must comply with applicable Federal regulations and VA requirements that address the protection of human subjects.
VA is one of the seventeen Federal departments and agencies that have agreed to follow the Federal Policy for the Protection of Human Subjects (Common Rule), effective June 18, 1991. For VA, this policy is incorporated in 38 CFR Part 16. All human subject research conducted or supported by VA must comply with 38 CFR Part 16.

VHA Handbook 1200.05 defines the procedures for implementing 38 CFR Part 16 and other applicable Federal requirements for the protection of human subjects. VHA Handbook 1200.05 and provisions of the manual apply to all research involving human subjects (domestic or international) in which NF/SGHVS is engaged. The research may be funded by VA, by other sponsors, or be unfunded.

As a component of the VA research program, NF/SGVHS supports and rigorously abides by the Federal Policy for Protection of Human Subjects of Research (the Common Rule) and the ethical principles outlined in the Belmont Report (http://ohsr.od.nih.gov/guidelines/belmont.html). All research involving human subjects must comply with all Federal regulations and VA requirements that address the protection of human subjects. State laws may apply in special circumstances. These regulations and requirements must be met before any research involving human subjects is initiated, and adherence must be sustained throughout the conduct of the research.

**F. Requirements of Funding Sources**

Investigators receiving support from other Federal departments or agencies (e.g., the Department of Health and Human Services (DHHS), the National Institutes of Health (NIH)), or from non-Federal sources (e.g., the American Heart Association) must meet the requirements of the funding source, in addition to those of VA and other applicable Federal entities, for the protection of human subjects. When NF/SGVHS is engaged in human subjects research conducted or supported by the Department of Health and Human Services (HHS), the Institution will comply with all subparts of the HHS regulations at Title 45 Code of Federal Regulations part 46 (45 CFR part 46, subparts A, B, C, and D).

**G. Applicability of FDA Regulations**

When FDA-regulated products are used, FDA regulations apply regardless of funding source.

**H. Engagement in Human Subjects Research**

In general a VA facility is considered engaged in human subjects research activity when an individual with a VA appointment (including full and part-time employees,
WOC employees, and employees under the IPA of 1970) obtain for purposes of a research study:

- Data about subjects through intervention or interaction;
- Identifiable private information about the subject; or
- Informed consent from the subjects of the research.


If there are questions about engagement in human subjects research, the Research Service Office or IRB should be consulted.

All research in which the NF/SGVHS is engaged must have a VA investigator. A VA investigator must be compensated by VA, be appointed to work without compensation (WOC), or may be an employee assigned to VA through the Intergovernmental Personnel Act (IPA) of 1970.

**NOTE:** All members of the research team for a VA research study must be VA employees (paid, WOC, or IPA). The only individuals outside VA who do not need a VA appointment or VA-specific training are those who perform a service for the research study in the course of their usual clinical duties.

When conducting human research studies involving more than one engaged institution, each institution is responsible for safeguarding the rights and welfare of human subjects entered at its site, and for complying with all applicable local, VA and other Federal requirements including those described in VHA Handbook 1200.05.

(1) NF/SGVHS engaged in human subjects research

When NF/SGVHS is engaged in human subjects research:

- There must be a VA Principal investigator (PI), Co-PI or Site investigator for the study (definitions for what constitutes a VA PI is in Chapter 1B).
- A NF/SGVHS IRB (UF IRB-01 or VA CIRB as applicable) and the NF/SGVHS R&D Committee must approve the study.

(2) NF/SGVHS and another VA institution engaged in Human Subject Research
When NF/SGVHS and another VA are engaged in multi-site research, each facility must hold an effective FWA.

- The FWA for each VA facility covers all research conducted at the facility or by the facility’s investigators acting in their official VA capacity for the engaged facility.
- The IRB for each VA facility must review the research unless an IRB Authorization Agreement (or similar agreement) is in place.
- Each VA facility must have a Principal Investigator (PI), Co-PI or Site Investigator (SI).
- The R&D Committee from each facility must approve the research in which it is engaged.
- Each participating site is responsible for research in which it is engaged and investigators must follow requirements as described in local policies and procedures.

(3) NF/SGVHS and non-VA institution engaged

When NF/SGVHS and a non-VA institution are engaged in multi-site research, each VA and non-VA facility engaged in research involving human subjects must hold an effective FWA.

- The FWA for each facility covers all research conducted at the facility or by the facility’s investigators acting in their official institutional capacities.
- The IRB for each facility must review the research unless there is an IRB authorization or similar agreement in place.
- Each facility must have a Principal Investigator (PI), Co-PI or Site Investigator (SI).
- The NF/SGVHS R&D Committee will approve and have jurisdiction over research in which the VA is engaged.
- VA research is research that is approved by the R&D Committee and conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments), utilizing VA resources (e.g., equipment), or on VA property including space leased to, and used by VA. The research may be funded by VA, by other sponsors, or be unfunded. The provisions of 1200.05 apply to all VA research involving human subjects.
- Each participating site is responsible for research in which it is engaged and investigators must follow requirements as described in local policies and
procedures including but not limited to training requirements, other approvals by non-research entities, etc. Each institution retains responsibility for ensuring compliance with IRB determinations and terms of institutional assurances.

(4) Engagement of Non-VA Investigators in VA supported research

Non-VA investigators who conduct VA-supported research must be covered under an Assurance. FWAs for VA facilities may not include or apply to any non-VA institutions or non-VA personnel without written approvals as described in VHA Handbook 1058.03.

I. Special Considerations in NF/SGVHS Research

(1) Classified research involving human subjects cannot be approved by a VA IRB or R&D Committee or performed at a VA facility, including space leased to, and used by VA.

(2) Planned emergency research may not be approved by a VA IRB or R&D Committee and cannot be conducted by VA.

(3) Research in which the subject is a fetus, in-utero or ex-utero (including human fetal tissue) must not be conducted by VA investigators while on official duty, or at VA facilities, or at approved off-site facilities.

(4) Research related to neonates including, but not limited to, observational or interventional research, must not be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities.

(5) Research related to in vitro fertilization must not be conducted by VA investigators while on official duty, or at VA facilities, or at approved off-site facilities.

(6) Research involving pregnant women must follow the requirements of VHA Handbook 1200.05 and as delineated in IRB policy.

(7) Research involving children cannot be conducted by VA investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. The criteria and process for obtaining a CRADO waiver is described in VHA Handbook 1200. Research involving children cannot be approved until all requirements are met.

(8) Research involving prisoners cannot be conducted by VA investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a
VA-approved off-site facility unless a waiver has been granted by the CRADO. If such a waiver is granted by the CRADO, the research must be in accordance with applicable Federal regulations pertaining to prisoners as research subjects (see 45 CFR 46, Subpart C 46.301–46.306, Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects) and in accordance with IRB policies and procedures. Procedures for subjects who become incarcerated during the course of a study are described in VHA Handbook 1200.05.

(9) International research requires the approval of the facility Director and CRADO prior to its initiation. All requirements of VHA Handbook 1200.05 must be met prior to engaging in international research.

J. Identifying and Disseminating New Information

New information that may affect the NF/SGVHS HRPP, including laws, regulations, policies, procedures, emerging ethical and scientific issues are disseminated in a variety of ways. New information may come from new or revised VHA Handbooks, Directives, Memoranda, Guidance, OHRP, FDA, ORD, ORO, IRB, or other sources. The ACOS/R&D has the primary responsibility for identifying and disseminating new information. The Administrative Officer/R&D, HRPP Administrator, Research Compliance Officer (through the Director’s Office) and others assist in identifying any new information and provide guidance to assist in implementation and education.

The ACOS/R&D and AO/R&D decide whether this new information requires a new policy and procedure or whether it replaces existing policy and procedures. After the decision is made the new information and any needed actions will be disseminated in the most efficient forum. The NF/SGVHS uses several different media to disseminate relevant information and changes important to the conduct of Human Subjects Research:

(1) E-Mail is used to forward new policies and memos either from the local research office or from Central Office. All IRB monthly newsletters and educational events are forwarded from the IRB to the Research Office who then forwards to all VA researchers.

(2) The ACOS/R&D schedules bi-annual Investigator meetings to present and discuss any new or emerging Human Research Protection Policies, procedures or areas of interest.

(3) The University IRB in addition to the monthly newsletter offers educational opportunities to all Investigators. The Research Office forwards the notice of events to all VA investigators. In addition The University of Florida IRB will repeat these events at the VA to assure dissemination of information to VA investigators.
(4) Applicable information to the University IRB and VA IRB members from the Institution is done through the Research Compliance Officer and/or Research Service's Designee.

K. Allocation of Resources for the HRPP Program

NF/SGVHS ensures that adequate and appropriate financial and personnel resources are provided to carry out the policies and procedures of the HRPP. The R&D Committee and its subcommittees assess the HRPP resources through an ongoing QA/QI program and, as needed, provide recommendations to the Medical Center Director (Reference: Research and Development Committee SOP; Quality Assurance/Quality Improvement Program SOP)
Chapter II: Roles and Responsibilities in the NF/SGVHS HRPP

A. The NF/SGVHS Director (“Director”)

The Director is responsible for the NF/SGVHS research program (VHA Handbook 1200.01) and implementation of the HRPP (VHA Handbook 1200.05).

(1) In accordance with VHA Policy, the Director is responsible for the R&D program of the institution, advised and assisted by an R&D Committee (VHA Directive 1200). The Director is responsible for implementing the R&D program, policies and procedures, including establishing and appointing members to the R&D Committee and subcommittees. The Director, through the R&D Committee, ensures appropriate resources (funds, staffing, and facilities) are available supporting the HRPP. One source of HRPP support is hospital funds and facilities.

(2) The Director is responsible for the integrity, operations and implementation of the HRPP Program and is advised and assisted by the Chief of Staff (COS), the Associate Chief of Staff for Research (ACOS/R), and the R&D Committee in meeting these responsibilities.

(3) Maintains and signs the FWA (as the IO) and as such, completes Assurance training prior to signing the FWA and every three years thereafter in accordance with VHA requirements.

(4) Fosters an institutional culture that supports the ethical conduct of human subjects research and ensures effective coordination of the activities of the HRPP.

(5) Oversees the IRB, R&D Committee, research office, and all investigators and research team members.

(6) Appoints at least one full-time research compliance officer to conduct annual research consent audits and triennial regulatory audits, and implements a research compliance program in accordance with requirements of VHA Handbook 1058.01.

(7) Ensures adequate resources to support the operations of the HRPP including adequate administrative personnel, equipment and space for the Research Service office (through activities such as annual review of the HRPP budget) and appropriate human research protection educational opportunities.

(8) Ensures that IRB members, relevant administrative staff, Researchers and Research Staff are appropriately knowledgeable to fulfill their respective duties in accordance with ethical standards and all applicable local, VA and other Federal requirements.
(9) Develops and implements an educational plan for IRB members, staff, Researchers, and Research Staff including initial and continuing education as described in local SOPs.

(10) Serves as the point of contact for correspondence addressing human subjects research with OHRP, FDA, VHA Central Office and other applicable entities.

(11) Ensures HRPP accreditation by the applicable organization approved by ORD to perform this function and reports changes in accreditation status in accordance with VHA Handbook 1058.01 and annual reports as required by the Accrediting Organization.

(12) Designates IRBs to review research and ensures designated IRBs of record comply with all applicable VA and other Federal requirements including the provisions of VHA Handbook 1200.05.

(13) Appoints members of the R & D Committee and all appropriate subcommittees including the appointment of VA representatives to IRB-01 in accordance with the requirements of VHA Handbooks 1058.03 and 1200.05 and UF IRB policies and procedures.

(14) Ensures an annual evaluation of the HRPP as described in the R&D Committee SOP.

B. Associate Chief of Staff for Research and Development (ACOS/R&D).

The ACOS/R is delegated the authority for the overall responsibility for the R & D Program including the HRPP at NF/SGVHS. Specifically, the ACOS/R

(1) Reports to the Director through the Chief of Staff.

(2) Is the designated Human Protections Administrator on the NF/SGVHS FWA.

(3) Manages the R&D Program including implementation of policies and procedures, oversight of resources, and oversight of research conducted at NF/SGVHS.

(4) Administers and coordinates the day-to-day implementation and oversight of the HRPP.

(5) Disseminates information regarding the NF/SGVHS HRPP as described in HRPP written procedures.

(6) Maintains all appropriate records related to the management of the research program including the HRPP.
(7) Monitors changes in VA and other Federal regulations and policies that relate to human research protections and notifies the MCD, the R&D Committee and others as appropriate.

(8) Ensures that the FWA and IRB Registration are current and updated as required.

(9) Monitors mandatory Human Research Protection Training of HRPP staff, research personnel, PIs and other personnel to ensure that human subjects protection training requirements are met as required by VHA Handbook 1200.05 and NF/SGVHS policies and procedures.

(10) Ensures all personnel involved in human subjects research are appropriately credentialed and privileged to perform research related duties.

(11) Ensures a local Research Subject Outreach Program.

C. **Institutional Review Board (IRB)**

NF/SGVHS has designated the University of Florida (UF) IRB-01 and the VA Central IRB (VA CIRB) as IRBs of record through Memoranda of Understanding. The University of Florida IRB-01 reviews and oversees all research involving human subjects conducted at NF/SGVHS except those falling under the purview of VA CIRB.

NF/SGVHS IRBs of record have the authority (per the Common Rule) to approve, require modification in, or disapprove research; observe or have a third party observe the consent process and the research; and suspend or terminate approval of research not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to subjects. The IRB is responsible for ascertaining the acceptability of proposed research in terms of commitments and policies, applicable law, the effect of study design as it relates to risk and benefits, sensitivity to community standards and attitudes, as well as standards of professional conduct and practice. The IRB complies with the provisions of 38 CFR 16 and VHA Handbook 1200.05.

The designated IRBs function independently and members have direct access to the IO for appeal if they experience undue influence or have concerns about the IRB. Research approved by a NF/SGVHS IRB of record is subject to further appropriate review and approval or disapproval by officials (e.g. Director) and other committees (e.g. R&D Committee); however, officials or committees cannot approve research if it has been disapproved by a NF/SGVHS IRB of record.

(1) UF IRB-01
The NF/SGVHS has designated the UF IRB-01 as an IRB of record on its FWA and the Director has signed an MOU with UF for the use of IRB-01. The MOU defines the roles and responsibilities of both NF/SGVHS and UF in accordance with VHA requirements including those outlined in VHA Handbook 1058.03 and ORO guidance. For additional information on the IRB-01, including review processes and operational issues, IRB-01 Policies and Procedures Manual is available online. Investigators conducting research under the oversight of the IRB-01 must follow all applicable IRB policies, procedures and guidance.

The NF/SGVHS Director must ensure the UF IRB-01 complies with all applicable VA and other Federal requirements including, but not limited to, 38 CFR 16 and the provisions of VHA Handbook 1200.05 when reviewing VA research. If the terms of the MOU are not met, the NF/SGVHS must make alternative IRB arrangements.

The NF/SGVHS Director appoints VA representatives to IRB-01 in accordance with the requirements of VHA Handbooks 1058.03 and 1200.05 and UF IRB policies and procedures. These VA requirements apply only to UF IRB-01 which is the only UF IRB designated to review NF/SGVHS research.

(2) VA Central IRB (CIRB)

The NF/SGVHS has designated the VA CIRB as an IRB of record on its FWA and the Director has signed an MOU with VHA Central Office for the use of the VA CIRB for studies meeting criteria for review by VA CIRB (i.e. VA funded, multisite). The roles and responsibilities of both NF/SGVHS and VA CIRB are outlined in the MOU between the entities. As required by the MOU, the Director has appointed a NF/SGVHS representative to: (1) Comment and Respond to VA Central IRB Review and (2) Serve as Liaison.

More information on procedures for use of VA CIRB are available in the SOP entitled “Use of VA Central IRB” located on the Research Service website. Investigators conducting research under the oversight of the VA CIRB must follow all applicable VA CIRB policies, procedures and guidance. Information on VA CIRB is available on the ORD website through a link on NF/SGVHS Research Service website.

D. Administrative Officer for Research (AO/R)

(1) Assists the ACOS/R in the implementation of the NF/SGVHS research program.

(2) Supervises daily operations of the Research Office and provides staff support to the R&D Committee.

(3) Maintains the NF/SGVHS FWA as described in VHA Handbook 1058.03 and local policies and procedures.
(4) Remains up-to-date and knowledgeable about human research protection requirements and advises the ACOS, the facility, investigators and others as applicable concerning relevant issues.

(5) Ensures that R&D Committee meetings are scheduled, review materials are complete and distributed prior to the meetings, minutes are recorded timely and accurately, decisions are communicated to investigators, reports are obtained and generated on time, and records are maintained.

E. Human Research Protection Program (HRPP) Administrator

(1) Primary responsibility is human research protection program oversight for Research Service. Responsible through the ACOS/R.

(2) Keeps abreast of HRPP changes and interpretations of laws and regulations.

(3) Reviews and revises local policies and procedures to ensure compliance with applicable requirements.

(4) Reviews human research protocols and applications for compliance with VA specific requirements.

(5) Develops and designs compliance processes for human subject projects.

(6) Assists with the program of quality assurance and performance improvement for the HRPP and the training program for R&D members, administrative staff, investigators, and investigators’ staff.

(7) Attends committee meetings and serves as a technical advisor in areas of Human Research Oversight regulation.

F. Research Compliance Officer

(1) Appointed by and reports directly to the Director.

(2) Primary responsibility is oversight of research projects. The RCO conducts study and informed consent audits in accordance with VHA Handbook 1058.01.

(3) Keep abreast of changes and interpretations to laws and regulations and review local policies and procedures to ensure compliance.

(4) Assists with the program of quality assurance and performance improvement for the HRPP and the training program for R&D members, administrative staff, investigators, and investigators’ staff.
(5) Attends committee and subcommittee meetings and serves as a technical advisor in areas of Human Research Oversight regulation.

G. Research Pharmacist

(1) Assumes responsibility for implementing FDA regulations concerning investigational drugs.
(2) Receives and dispenses all drugs used in research.
(3) Maintains records accounting for the use of the drugs.
(4) Monitors investigators’ compliance with local and FDA requirements.
(5) Disposes of drugs at the end of the study.

H. Privacy Officer (PO) and Information Security Officer (ISO)

(1) Provide specialized knowledge of applicable legal, policy, and technical requirements related to the protection of information and additional expertise to the review of human research.
(2) Review all proposed human research protocols and document such reviews prior to R&DC initial approval and as applicable during the conduct of the research if changes are made.
(3) Ensure proposed research complies with all applicable local, VA and other Federal requirements for privacy and confidentiality, and for information security, respectively, by identifying, addressing, and mitigating potential concerns about proposed research studies.
(4) Serve in an advisory capacity to the R&D Committee as nonvoting members.
(5) Provide documentation of reviews to NF/SGVHS Research Service for distribution as applicable and maintenance with project files.

I. R&D Committee

The NF/SGVHS R&D Committee has oversight of all R&D activities within the NF/SGVHS. The R&D Committee must review and approve all proposed research in which NF/SGVHS is engaged prior to initiation. Research that has been approved by a NF/SGVHS IRB is subject to further review and approval or disapproval by the R&D Committee; however, the R&D Committee cannot approve research if it has been disapproved by a NF/SGVHS IRB (38 CFR 16.112).

The R&D Committee’s primary purposes, in conjunction with the other oversight committees, are to:
(1) Maintain high scientific standards throughout the VA R&D program.

(2) Assure that the research conducted at the NF/SGVHS is consistent with the broad objectives of the VHA and its research program and supports the facility’s patient care mission.

(3) Evaluate the quality, appropriateness, and feasibility of research proposals.

(4) Review the research facilities available at the Medical Center to assure that they are of high quality to support the R&D program.

(5) Recommend the distribution of R&D funds, space, personnel, supplies, equipment facilities and other common resources when these issues are brought to the attention of the committee.

(6) Advise the ACOS/R&D and the Director on professional and administrative aspects of the R&D program.

(7) Oversee the operations of subcommittees charged with evaluating human research. With regard to human research protections, subcommittees include the Subcommittee for Research Safety (SRS), UF IRB-01 and the Oversight Committee on Clinical Research (OCCR). For more information on subcommittees, their functions and their purview, please refer to the R&D Committee Standard Operating Procedure at [http://www.northflorida.va.gov/research/policies.asp](http://www.northflorida.va.gov/research/policies.asp).

(8) Receive and investigate reports of complaints, allegations of research non-compliance or improprieties, and research QA/QI activities.

(9) Set institutional policy for research personnel training.

(10) The R&D committee assesses its performance, and that of its subcommittees, and the IRB, with regard to compliance with established policies and procedures. By audits or reports, there is a determination of NF/SGVHS compliance with research subject protection requirements and assurance that subcommittees fulfill their roles meeting HRPP objectives.

Additional information on the R&D Committee, including review processes and other operational issues, is available in the R&D Committee Standard Operating Procedure on the Research Service Website.

**J. Subcommittee on Research Safety**

(1) Ensures the safety of VA personnel conducting VA research.

(2) Conducts initial review of all VA human research submissions prior to final R&D Committee approval and distinguishes those with hazards that require subsequent review by the full SRS from those which do not have hazards and do not require SRS review. Safety approval must be updated annually as described in SRS policies. If an amendment to a VA human research study relates to bio-safety, radiation safety or
other safety issues, the Subcommittee for Research Safety must approve the amendment prior to implementation of the change.

Additional information on the SRS including review processes and other operational issues is available through links on the Research Service Website.

**K. Investigator Responsibilities**

VHA Handbook 1200.05 defines investigator and VA Investigator (see Chapter 1B).

Research utilizing VA resources (i.e. equipment) or on VA property or involving VA patients (including their medical information or PII, III or PHI) is considered a VA study and must have a VA PI, Co-PI or Site Investigator.

Investigators (including but not limited to PIs and LSIs) must uphold professional and ethical standards and practices and adhere to all applicable VA and other Federal requirements, including but not limited to the NF/SGVHS SOPs, regarding the conduct of research and the protection of human subjects. Responsibilities of VA investigators are described in VHA Handbook 1200.05, protocol documents submitted to the IRB (including Addendum A and V for IRB-01) and in other NF/SGVHS and IRB policies and procedures.

Specifically, investigators must:

1. Submit requested materials for review to IRB and R&D Committees and other appropriate subcommittees in accordance with IRB and NF/SGVHS policies and procedures.

2. Obtain written approvals of the IRB, SRS as applicable, and R&D Committee before initiating human subjects research at the NF/SGVHS. Research cannot be initiated until the investigator has obtained written notification that the research can be initiated from the NF/SGVHS ACOS/R&D. Investigators must also obtain approval for all changes to the research protocol (e.g., amendments or modifications), including changes to the IRB informed consent form prior to implementing the changes. The only exception is when it is necessary to change the protocol to eliminate apparent immediate hazards to the subject. The investigator must promptly report these changes to the IRB in accordance with IRB policy on adverse events and/or unanticipated problems. Investigators must ensure that any revisions submitted to and approved by the IRB-01 are also submitted to the NF/SGVHS HRPP Office along with the appropriate cover form. Additional VA reviews (i.e. Safety Committee, ISO, PO) may be required depending on the nature of the revision.

3. Responds to participants’ complaints and/or concerns.
(4) The PI, as the individual responsible for the implementation of research, is directly responsible for all aspects of a research project, ensuring the protection of every human subject in the research project. This responsibility starts with protocol design that is scientifically valid, minimizes risks to subjects and contains a description of the data and safety monitoring plan (DSMP) when appropriate; ensuring adequate resources to carry out the research safely; ensuring all members of the research team are qualified to perform procedures; and complying with the findings, determinations and requirements of the IRB and R&D Committees. Investigators must maintain appropriate oversight of project(s) and staff in order to conduct research effectively and to ensure that the rights and welfare of human participants are protected. At all times, the PI must ensure the research is being implemented in accordance with the approved protocol and in compliance with all applicable regulatory requirements and the determinations of the IRB and R&D Committees.

(5) Disclose to the IRB and the NF/SGVHS any potential, actual, or perceived conflict of interest (COI) of a financial, professional, or personal nature that may affect any aspect of the research, and complying with all applicable VA, Federal and local requirements regarding conflict of interest. Procedures for disclosing, evaluating, mitigating and managing conflicts of interest are described in IRB-01 and NF/SGVHS policies and procedures. IRB and NF/SGVHS forms solicit information on COI.

(6) Ensure research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials and, when relevant, privileges) to perform procedures assigned to them during the study.

(7) Develop a research plan that is scientifically valid, minimizes risk to subjects, and contains a description of the data and safety monitoring plan (DSMP) when applicable. IRB-01 forms have been designed to solicit information for NF/SGVHS investigators to comply with this requirement. It is incumbent on investigators to provide complete, accurate and consistent information to the IRB. VHA Handbook 1200.05, paragraph 10 describes requirements for VA research protocols.

(8) Maintain written documentation on file that the protocol is being implemented as approved by IRB and in accordance with other required approvals as required by VHA Handbook 1200.05. The case history must show that informed consent was obtained prior to study participation when informed consent is a requirement of the approved protocol. Investigator research records must be maintained in accordance with VHA VHA’s Records Control Schedule (RCS 10-1) (see definition of investigator research records). All original signed and dated consent forms must be maintained in the investigator’s research files, readily retrievable, and secured in accordance with VA requirements.

(9) Ensure the requirements for research involving investigational drugs or devices are met (see Chapter IV).
(10) Obtain and Document Informed Consent as required by the IRB using the most current version of the IRB-approved VA consent form (VA Form 10-1086). Investigators must ensure that no human being is involved as a subject in research unless legally effective informed consent of the subject or the subject’s LAR has been obtained (38 CFR 16.116) unless the requirement has been waived by the IRB. The informed consent must be obtained and documented prior to any research-related screening, interaction or intervention involving a human subject. Information on the general requirements for informed consent including required and additional elements, documentation of informed consent and waivers of consent/documentation of consent is available in IRB-01 policies and procedures and Informed Consent Instructions.

(11) Ensure consistency of the language in the Informed Consent Form with that in the Protocol and HIPAA Authorization and ensure that no human subject is involved in research unless the investigator (or designee) has obtained legally effective HIPAA authorization for the use and disclosure of the subject’s PHI, unless this requirement is waived by the IRB (or Privacy Board).

(12) Make every reasonable effort to make available the informational brochure, “Volunteering in Research – Here Are Some Things You Need To Know,” to prospective subjects, and their surrogates where applicable, when the individuals are approached to take part in a study and document efforts in the subjects consent process note. Investigators are provided with copies of the brochure with initial notification of VA approval and upon request from the Research Service Office.

(13) Ensure that subjects are contacted in accordance with VHA policy. During recruitment, when making initial contact, investigators and the research team must makes initial contact with the potential subject in person or by letter prior to any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research. (Note: Cold Calling is NOT Allowed) During the initial contact the researcher must provide a telephone number or other means that veterans can use to verify the validity of the study, e.g. http://www.clinicaltrials.gov or the veteran can contact the VA Research Office at 352-376-1611 ext. 6069. This information should also be included in the consent form.

During subsequent contacts, Investigators and/or the research team should begin any telephone calls to the subject by referring to previous contacts and, when applicable, the information provided in the informed consent form, and should ensure that the scope of telephone contacts with the subject is limited to topics outlined in IRB-approved protocols and informed consent forms.

Investigators and research team members are prohibited from requesting Social Security numbers by telephone.
(14) Submit continuing review materials in a timely manner to provide IRB sufficient time to review and approve the study before IRB approval expires. IRB approval automatically expires if the continuing review and approval does not occur by the expiration date of the current approval. Requirements for continuing review, VA annual renewal and procedures for management of protocols with lapsed approval are described in NF/SGVHS SOP on continuing review and in applicable IRB policies and procedures. At completion of the research study, investigators must complete all required documentation and storing research records according to all applicable VA and Federal records retention requirements.

(15) Report deviations from the protocol and subject complaints to the IRB in accordance with IRB policy.

(16) Report unanticipated problems involving risks to subjects or others, and all SAEs, whether related or unrelated to the research, in accordance with IRB and NF/SGVHS policies and procedures and VHA Handbook 1058.01.

(16) Transfer records to NF/SGVHS in the event the investigator leaves the facility (described in Chapter III section on departing investigators).

(17) Ensure that all individuals involved in the conduct of VA human subjects complete training as outlined in the Research Service Policy on training to conduct research and in accordance with IRB policy.

(18) Ensure all VA research staff (clinical and non-clinical including volunteers) conducting human research (exempt or non-exempt) only perform those activities in a research study for which they have the relevant credentials, privileges, research scope of practice or functional statement and licenses, registrations and certifications.

(19) Maintain and retain all research records in accordance with the VA Records Control Schedule. Required records, including investigator's research records must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA’s Record Control Schedule. Until a schedule for local research records is published, all records including identifiers must be retained. Consent forms and HIPAA authorizations should not include a timeframe for destruction.

(20) Participate in audits as described in NF/SGVHS and UF IRB-01 policies and procedures.

(21) Maintain a “master list” of subjects for whom informed consent has been obtained (either a signed consent or consent obtained with a waiver of the requirement to sign a consent) that includes at a minimum, subject name. The
master list does not require submission to the IRB but the PI must certify to the IRB at CR that all subjects entered onto the master list of subjects for the study signed an informed consent form prior to undergoing any study interactions or interventions, unless the IRB has granted a waiver of informed consent or waiver of documentation. The list should be maintained with the investigator records.

(22) Create or update VHA health records in accordance with VHA requirements (described in Chapter III).

(23) Flag VHA health records in accordance with VHA requirements (described in Chapter III).

(24) Fulfill responsibilities for use of investigational drugs or devices in accordance with VHA requirements (described in Chapter III).
Chapter III: Requirements and Procedures related to Human Subjects Research at NF/SGVHS

A. RESEARCH UNDER THE AUSPICES OF NF/SGVHS

All research involving human subjects under the auspices of NF/SGVHS regardless of funding source is subject to the oversight and approval of the NF/SGVHS R&D Committee and applicable subcommittees (i.e. IRB and SRS) and non-research entities. This includes research involving human subjects and recruitment of NF/SGVHS veterans conducted completely or partially in NF/SGVHS facilities including approved leased space on or off site. It also includes research conducted by individuals with VA appointments as well as WOC status while on official VA duty and research deriving data from intervention or interaction with human subjects (e.g. tissue banks, medical records, databases, etc.). NF/SGVHS may not engage the services of another IRB for the purposes of avoiding the rulings of UF-IRB 01 or VA CIRB (when applicable). The use of commercial IRBs is prohibited.

B. INVESTIGATOR ELIGIBILITY FOR VA RESEARCH SUPPORT

An investigator may apply to for VA research funding if s/he meets eligibility standards established by the ORD. Specific requirements of the research service to which the investigator wishes to apply must be met. For more information on investigator eligibility, refer to VHA Handbook 1200.15 as well as any additional guidance issued by the respective research service. Guidance for investigator is normally posted on the VA ORD web site (www.research.va.gov).

An investigator may apply to the NF/SGVHS Research Service for other support (laboratory space, access to clinical materials, etc.) if s/he has a VA appointment of any kind (1/8 or more of salary, WOC status, etc.), and if s/he makes a significant contribution to the VA mission as defined by the Director, Chief of Staff, ACOS/R, and/or R&D Committee.

C. PROTOCOL SUBMISSION, REVIEWS AND APPROVALS

Research proposals involving human subjects, medical records or databases, or human tissue must be submitted to IRB and R&D Committee for review and approval prior to any study initiation. All human research studies must also be reviewed by SRS and the Information Security Officer and Privacy Officer. Other reviews may be necessary depending on the nature of the research. An investigator cannot initiate a new study until he or she receives notifications from the ACOS/R that all required committee and subcommittee initial approvals have been obtained, including initial approval from the R&D Committee in accordance with VHA Handbook 1200.01.

1. Protocol submission guidelines are available on the UF IRB-01 and NF/SGVHS Research Service websites.Investigators involved in studies reviewed by the VA
CIRB should consult with the VA CIRB website and with the applicable Coordinating Center or Protocol PI staff. Regardless of reviewing IRB, NF/SGVHS submission requirements and approvals are applicable. Investigators must follow all applicable policies and procedures of the reviewing IRB throughout the conduct of the research.

2. All human research submissions (including exempt or those with an IRB non-human determination) must be submitted to the NF/SGVHS Grants Administration Core-HRPP Office for processing and distribution.

3. New protocol submissions are placed on the R&D Committees agenda when all applicable subcommittees (i.e. IRB and SRS when applicable) have approved the research and non-research entities (e.g. ISO, PO) have verified that VHA requirements have been met. After a research project has been approved by all applicable R&D Committee subcommittees and non-research entities and the R&D Committee, the ACOS/R&D notifies investigators, in writing, that a research project can be initiated. Once R&D Committee approval has been given the research becomes VA-approved research. The R&D approval date is the date at which final R&D approval is given. The R&D approval date is not the same as the IRB approval date, which determines when IRB continuing review occurs.

The NF/SGVHS R&D Committee must review and approve all proposed human subjects research in which NF/SGVHS is engaged prior to initiation. Research that has been approved by a NF/SGVHS IRB is subject to further review and approval or disapproval by the R&D Committee (i.e. the R&D Committee can disapprove research even if the research has been approved by the IRB); however, the R&D Committee cannot approve human subjects research if it has not been approved or if it has been disapproved by a NF/SGVHS IRB. Reasons for R&D disapproval may relate to such issues as scientific design, ethical issues regarding subject protection, feasibility due to lack of VA resources, impact on patients, safety concerns, etc.

All formal communications of the R&D Committee/designated subcommittees are in writing.

An investigator may appeal any R&D Committee decision. If a study is disapproved, the proposal may be resubmitted with a cover letter detailing how the concerns and/or objections to the previous submission have been addressed or providing additional clarifications for areas that may have been not correctly reviewed due to lack of details. For other actions such as suspension or termination of a study, an appeal letter may be sent to the R&D Committee. Since the R&D Committee cannot override the disapproval action for a research activity made by any of its subcommittees, the objections and concerns of the subcommittee(s) must be addressed before the R&D Committee take final action.
R&D Committee operations and procedures for the oversight of VA research are described in the R&D SOP.

4. All changes in an approved protocol (any changes in a research activity) (e.g. protocol amendments, revisions to consent forms, changes to recruitment materials, investigator changes) must be reviewed and approved by the IRB (in accordance with applicable IRB written procedures) and any other appropriate subcommittees prior to implementation of the change unless necessary to eliminate an immediate apparent hazard to subjects. Other non-research entities (e.g. ISO, PO) may review revisions to approved research as applicable.

5. All research involving human subjects (including those determined exempt by the IRB) must be renewed annually at the VA. Further information on VA annual renewal procedures is available in the NF/SGVHS SOP, Continuing Review Process for Human Research.

D. HUMAN SUBJECTS PROTECTION AND OTHER TRAINING REQUIREMENTS

All individuals involved with human subjects research at NF/SGVHS are required to complete training as required by Research Service SOP, Education for Conducting Research and facility policy. The Research Service Office will monitor completion and renewal of research-specific educational requirements and will maintain documentation of training. Investigators are responsible for ensuring that individuals involved in human subjects research complete applicable training in the time frames specified and maintain documentation of such training.

All applicable training must be completed by all VA research team members (as indicated in the IRB submission and VA Coversheet) prior to inclusion of a new protocol on the R&D Committee agenda. Research team training is reviewed at new protocol submission and at continuing review (VA annual renewal) to confirm compliance. Individuals who are noncompliant with VA required human subjects training cannot participate until applicable training has been completed. If noncompliant training is identified, an e-mail will be sent to the Principal Investigator notifying them of the noncompliant training and that the individual cannot participate in the conduct of the study until confirmation of training has been received. If training is not completed within 2 weeks of the email request, a letter from the ACOS-R will be sent to the investigator, the Chief of Service and the Chief of Staff notifying them of the failure to resolve the delinquency.

E. CREDENTIALING AND PRIVILEGING

All VA research staff (clinical and non-clinical) conducting human research (exempt or non-exempt) must be credentialled and privileged (if applicable) as required by local, VA, VHA, and ORD requirements. Research staff (including volunteers) may
only perform those activities in a research study for which they have the relevant credentials, privileges (when relevant), scopes of practice or functional statements and licenses, registrations and/or certifications. Credentialing and privileging information will be maintained by the applicable Service of the individual. Individuals involved in VA research will be asked to provide information related to C & P in HRPP submission documents. Research scopes of practice for all non-privileged research personnel must be provided with initial submission, annual renewal and with the addition of any new research personnel. Copies of research scopes of practice will be retained by the Research Office. See the NFSG/VHS SOP: Credentialing, Verification of Education, Scope of Practice and Training for Research Staff for more detailed information.

**F. NON-HUMAN DETERMINATIONS**

Any activity that meets the following definitions requires review and approval by the IRB prior to initiation:

- Common Rule definitions of “research” and involves “human subjects”
- FDA definition of “clinical investigation/research” and involves “human subjects” as defined by the FDA.

Not all activities meet the federal regulatory definitions of human subjects’ research or clinical investigation. Investigators who are unsure whether a proposed activity meets the definition of human subjects’ research should contact the IRB for guidance. Only the IRB can make the determination that an activity does not meet the definitions and therefore does not require prospective IRB review. If there is any question that an activity could constitute human subjects’ research (based upon the definitions in this manual) the Investigator must obtain a determination from the IRB in accordance with IRB procedures. Refer to UF IRB-01 Policies and Procedures and website for more information on non-human determinations.

Research determined to be non-human must be reviewed and approved by the NF/SGVHS R&D Committee and any applicable subcommittees and non-research entities initially and then annually thereafter.

**G. RESEARCH EXEMPT FROM IRB REVIEW**

NF/SGVHS research investigators who intend to involve human subjects in research activities do not have the authority to make an independent determination that research involving human subjects is exempt from applicable requirements; only the IRB makes determinations of exemption. The IRB may deny protocol exemption and require IRB review.

IRB-01 Policies and Procedures describe procedures related to exempt determinations.
Research determined exempt by the IRB must be reviewed and approved by the NF/SGVHS R&D Committee and any applicable subcommittees and non-research entities initially and then annually thereafter. Requirements of VHA Handbook 1200.05 apply to exempt research.

H. EXPEDITED REVIEW OF HUMAN RESEARCH STUDIES

An expedited review process consists of a review carried out by the IRB Chair or by one or more experienced voting members of the IRB designated by the IRB Chair in accordance with 38 CFR 16.110(b). The IRB may use expedited review procedures to review and approve specific categories of research activities as defined in the Federal Register: Volume 63, Number 216, Pages 60364-60367, November 9, 1998.

Information on the types of research that may qualify for expedited review and expedited review procedures is available in IRB-01 Policies and Procedures, the IRB Introductory Questionnaire and applicable appendices on the IRB-01 website.

I. INFORMED CONSENT PROCESS AND DOCUMENTATION

Legally effective informed consent of a subject, or the subject's legally authorized representative (LAR), must be obtained prior to an investigator involving a human being as a subject in research unless the requirement has been waived by the IRB. If someone other than the investigator conducts the interview and obtains consent, the investigator should formally delegate this responsibility. Any person obtaining consent should receive appropriate training and be knowledgeable about the research to be conducted and the consenting process and be able to answer questions about the study.

An investigator must seek subject consent to participate in a research study under circumstances that:

1. Provide the prospective subject or the subject's representative sufficient opportunity to consider whether or not to participate, and

2. Minimize the possibility of coercion or undue influence.

The informed consent must be obtained and documented prior to any research-related screening, interaction or intervention involving a human subject.

Under some conditions (as described in VHA Handbook 1200.05 and IRB policies and procedures), investigators may obtain consent from the LAR of a subject (i.e., surrogate consent). To obtain consent from an LAR, VA investigators must provide the IRB with information to ensure the requirements of 1200.05 are met. For IRB-01, Addendum V solicits this information. Requirements for research involving
persons lacking decision making capacity and surrogate consent are detailed in VHA Handbook 1200.05.

Informed consent must be documented prospectively using the most recent IRB approved written consent form unless documentation of informed consent has been explicitly waived by the IRB in accordance with applicable regulations (see IRB-01 ICF Instructions for criteria to waive documentation of consent). The written IRB approved informed consent document must be signed and dated by the subject or the subject's legally authorized representative and the person obtaining consent. A witness signature is needed only if required by the IRB. If a witness signature is required, the witness is required to witness only the subject's or subject's LAR's signature, not the informed consent process (e.g., if the subject does not want the witness to know the nature of the research study), unless the sponsor or IRB requires the witness to witness the informed consent process.

VA Form 10-1086, which includes the required elements and any additional elements, is used as the consent form for VA research. The requirement to utilize VA Form 10-1086 to document informed consent applies to all VA-approved research. Approval is documented by a stamp or preprinted box on each page of the consent form indicating the recent IRB approval date. The consent form may be read to the subject or the subject's legally-authorized representative. The investigator must ensure that the subject (or representative) is given adequate opportunity to read the form and ask questions before signing it. The original signed consent form is filed in the subject's case history. A copy of the signed and dated informed consent must be provided to the subject or the subject's legal representative. A copy is provided to the VA Investigational Drug Service (IDS) when IDS services are utilized by the study. For more details on informed consent documentation see IRB online policies and procedures.

The original signed and dated informed consent form must be filed in the investigator's research file for that subject so that it is readily accessible for auditing. If the subject submits the signed and dated informed consent form to the investigator or designee by facsimile, the person who obtains informed consent must sign and date the facsimile, and then the facsimile can serve as the original informed consent document. If facsimile is used for the informed consent document, measures must be employed to ensure the confidentiality of the information, and the privacy of the subject. Where applicable, a copy of the signed and dated informed consent form must be placed in the medical record in accordance with VHA Handbook 1907.01.

Use of a short form ICF is described in IRB-01 P&P. If a short form ICF is utilized: 1) A copy of the summary and a copy of the short form must be given to the subject or the LAR; 2) the original signed short form and summary must be filed in the investigator's research file for that subject; 3) where applicable, a copy of the signed short form informed consent form must be placed in the medical record in accordance with VHA Handbook 1907.01); and 4) the investigator must file all
original, signed and dated, short form informed consent forms in the investigator’s research file for that subject, so that they are readily accessible for auditing.

Information on the general requirements for informed consent including required and additional elements, documentation of informed consent and waivers of consent/documentation of consent can be found at the IRB-01 website.

J. HIPAA AUTHORIZATION

NF/SGVHS investigators may not involve human subjects in research that involves the use, review, creation or disclosure of Protected Health Information, unless the investigator (or a designee formally and prospectively designated in writing) has obtained legally effective HIPAA authorization for the use and disclosure of the subject’s PHI, or has obtained an IRB-approved waiver of HIPAA authorization.

VHA requires a written HIPAA authorization signed by the individual to whom the information or record pertains if the information is for research purposes. The HIPAA authorization for the use or disclosure of individually-identifiable health information for a VA research study must be a standalone document for all new research protocols approved by the IRB after March 31, 2011 as required by VHA Handbook 1200.05 and confirmed with ORD and ORO. All research protocols approved by the IRB before March 31, 2011, can continue to use the traditional VA informed consent that contains the authorization (ie: combined document). This combined document can be used for the duration of these approved protocols (ie: continuing review and revisions). VA investigators must use the most current version of the combined ICF/HIPAA Authorization or NF/SGVHS HIPAA Authorization template and ensure information in the HIPAA authorization is consistent with the protocol and informed consent form in either case. If an investigator chooses to split the ICF and HIPAA Authorization either at revision or continuing review, the initial separation of documents requires review by the VA Privacy Office. Signed HIPAA Authorizations must be scanned into CPRS along with the VA 10-1086 and be retained with the investigators research records.

For new studies, the IRB cannot approve the HIPAA authorization unless it is incorporated into the informed consent document; therefore, the IRB cannot approve a HIPAA authorization for a new VA research study because it must now be a standalone document. However, the IRB, as the VA Privacy Board, may waive the requirement for a HIPAA authorization in accordance with applicable requirements (see IRB-01 policies and procedures for Waivers of HIPAA Authorization).

NF/SGVHS investigators must be aware that an individual who is qualified to be a LAR for research purposes may not always qualify as a personal representative for purposes of signing a HIPAA authorization. Therefore, in circumstances involving authorization for use or disclosure of a subject’s PHI, the investigator must ensure the LAR meets the requirements of a personal representative in HIPAA and the
Privacy Act of 1974 (court appointed legal guardian or power of attorney) prior to the LAR’s signing a HIPAA authorization (VHA Handbook 1605.1).

The NF/SGVHS Privacy Officer (PO) is responsible for the content of the standalone NF/SGVHS HIPAA Authorization template and for reviewing a proposed study-specific standalone authorization to ensure all applicable requirements have been met or identify deficiencies and require changes to correct those deficiencies. Privacy Office reviews will be documented and maintained in Research Service Files.

Any changes to approved research that may impact privacy may require re-review by the PO to ensure that applicable requirements are met.

**K. CONTINUING REVIEW, VA ANNUAL RENEWAL AND MANAGEMENT OF PROTOCOLS WITH LAPSED IRB APPROVAL**

The IRB is responsible for conducting continuing review of ongoing non-exempt research to ensure that the rights and welfare of human subjects are protected and to review the progress of the entire study. Protocols must continue to have ongoing IRB approval as long as the research continues to involve human subjects, even when research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions and only long term follow-up is being conducted or the only remaining activity is limited to data analysis of personally identifiable information.

At the time of initial approval and then with subsequent continuing review, the IRB determines the frequency and extent of continuing review for each study appropriate to the degree of risk, but not less than once per year. If continuing review does not occur within the timeframe set by the IRB, IRB approval automatically expires. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. The IRB notifies the PI [and VA Research Office] of the expiration of approval. Protocols with lapsed approval do not automatically require reporting to oversight agencies as a suspended protocol (OHRP Guidance and VHA Handbook 1058.01).

Requirements for continuing review, VA annual renewal and procedures for management of protocols with lapsed approval are described in NF/SGVHS SOP on continuing review and in applicable IRB policies and procedures.

**L. PROTOCOL CONCLUSION OR TERMINATION**

At the conclusion or termination of a human research study (including those determined exempt by the IRB), VA investigators must submit a closure report to the IRB and the R&D Committee. For more detailed information on criteria for closing a research protocol and study closure processes, refer to IRB policies and procedures.
Once the IRB has officially closed a protocol, the submission including the closure letter should be submitted to the VA HRPP Office for closure.

Once a study is closed, investigators are responsible for:

1. ensuring that reasonable ongoing procedures, as described in the IRB-approved protocol, are in place to protect subject privacy and confidentiality of research data;
2. storing research records according to all applicable VA and Federal records retention requirements; and
3. as appropriate, communicating study results to subjects or the community from which subjects were recruited.

M. DEPARTING INVESTIGATORS

Investigators terminating their relationship with the NF/SGVHS must contact the Research Service Office to obtain instructions for completing necessary documentation. Research investigators leaving NF/SGVHS must submit final reports to the IRB and R&D Committee for all of their VA projects and must complete the necessary clearance forms to ensure proper and appropriate disposition of all research matters, including laboratory chemicals, equipment, experimental drugs dispensed through Pharmacy Service and research employees appointed specifically for the investigators’ program. A Checklist for Departing Investigators will be provided by the Research Service Office and must be completed prior to departure.

When a protocol changes from one principal investigator (PI) to another (as a result of resignation or retirement, for example), the change must be approved locally by the R&D Committee and the IRB and, if VA funded, by the appropriate research service within ORD at VACO. In such changes, care will be exercised to assure that any identifiable subject information remains confidential and becomes the responsibility of the new PI.

If an investigator leaves NF/SGVHS, all original research records must be retained by the facility. If a grant is ongoing and the investigator leaves NF/SGVHS to go to another VA facility, the investigator must obtain approval for a copy of relevant materials to be provided to the new VA facility’s research office. The approval must be obtained from the NF/SGVHS Research Office (ACOS/R), other relevant individuals or offices as applicable including but not limited to the PI’s supervisor, Information Security Officer, Privacy Officer, and CIO and the sponsor.

If an investigator leaves the NF/SGVHS without formally closing a study or transferring responsibility to another VA investigator, the Principal Investigator’s supervisor will be contacted to complete close-out procedures. The ACOS/R may
administratively close the study after assuring that all the research has ended and the study can be safely closed.

N. RESEARCH INVOLVING VULNERABLE POPULATIONS

VHA Handbook 1200.05 describes VA requirements for the protection of vulnerable individuals or vulnerable populations as research subjects in VA research; when VA requirements are more stringent than HHS requirements, all VA requirements must be met.

VA considers fetuses, neonates, pregnant women, prisoners, children and subjects who lack decision-making capacity as categorically vulnerable. VA requirements for the inclusion of any of these categories of subjects in research must always be met. Additional information on VA requirements involving these populations is included in Chapter I.I of this manual and in VHA Handbook 1200.05.

Additional requirements of 1200.05 that pertain to pregnant women, children, prisoners, and persons with impaired decision making capacity have been incorporated into the applicable Introductory Questionnaire Addenda.

O. CONTACTING VETERANS FOR RESEARCH PURPOSES

Requirements for contacting veterans for research purposes are described in Chapter 3, Investigator Responsibilities.

P. REQUIREMENTS FOR A VHA HEALTH RECORD

Investigators must create or update the VHA health record in CPRS and write a progress note for all veteran or non-veteran research subjects admitted to VA facilities as in-patients, treated as outpatients at VA facilities, or when research procedures or interventions are used in the medical care of the VA research subject at a VA facility or at facilities contracted by VA to provide services to Veterans (e.g., contract CBOCs or contract nursing homes).

A record must also be created:

(1) When the research requires use of any clinical resources, such as: radiology, cardiology (e.g., electrocardiogram, stress test, etc.), clinical laboratory, and pharmacy; or

(2) If the research intervention may lead to physical or psychological AEs (VHA Handbook 1907.01).
When created or updated for research purposes, at a minimum, the health record must include the following information for an approved research study:

(1) The name of the study;

(2) The person obtaining the subject’s informed consent;

(3) A statement that the subject or the subject’s LAR was capable of understanding the informed consent process;

(4) A statement that the study was explained to the subject or the subject’s LAR;

(5) A statement that the subject or the subject’s LAR consented before participation in the study began;

(6) A statement that the subject or the subject’s LAR was given the opportunity to ask questions;

(7) A copy of the signed and dated research informed consent form (i.e., VA Form 10-1086);

(8) A copy of the HIPAA authorization for data use or disclosure;

(9) A copy of the initial enrollment progress note and other applicable progress notes;

(10) Information on possible drug interactions and/or toxicity of the pharmaceutical agents that are being administered to the subject because of the research (i.e., investigational drugs);

(11) VA Form 10-9012, Investigational Drug Information Record, or superseding forms for investigational drugs;

(12) A copy of any research results that are used for medical care;

(13) Information on all research and experimental interventions including potential risks, indications, and applicable progress notes; and

(14) VHA Form 10-3203, Consent for Use of Picture and/or Voice, if applicable.

The entry must also be placed in the progress note when the human subject is actually entered into the study and when the human subject’s participation has finished. **NOTE: Consent and entry notes can be combined when both occur at the same visit.**
For details on documentation of informed consent and research in the medical record refer to the Documentation of Research in CPRS policy on http://www.northflorida.va.gov/Research/indexResearchers.asp.

Requirements related to VHA health records and research is described in VHA Handbooks 1907.01 and VHA Handbook 1200.05.

Investigators/Coordinators must have VA computer access to enter research information in the electronic medical record (CPRS) for all VA subjects. Contact the Human Resource Service (x.6009) for VA computer access and Research Service (x.4204) for CPRS access.

Q. FLAGGING THE VHA HEALTH RECORD

VHA Handbook 1200.05 (October 15, 2010), Paragraph 44, describes the requirements for flagging the VHA health record. ORD has implemented mandatory flagging in CPRS for subjects participating in research involving certain activities as outlined below. Investigators must flag the VHA health record (CPRS) for any research involving:

(a) Any invasive research procedure (e.g., muscle biopsy or bronchoscopy);

(b) Interventions that will be used in the medical care of the subject, or that could interfere with other care the subject is receiving or may receive (e.g., administration of a medication, treatment, or use of an investigational device);

(c) Clinical services that will be used in the medical care of the subject (e.g., orders for laboratory tests or x-rays ordered as a part of the study), or that could interfere with other care the subject is receiving or may receive; or

(d) The use of a survey or questionnaire that may provoke undue stress or anxiety unless the IRB determines that mandatory flagging is not in the best interests of the subject (e.g., an interview study of victims of sexual assault).

The IRB must make a flagging determination for any research involving the above; under the provisions of 1200.05 (October 15, 2010), the IRB is not required to make a flagging determination for any research not involving the above. The IRB may determine other situations that would warrant flagging in CPRS. Investigators are required to flag the health record if any of the above criteria are met or if the IRB determines that flagging outside of these criteria trigger this requirement. If there are any questions about the procedures for flagging VHA health records, investigators and/or staff should contact the NF/SGVHS Research Service Office or consult with instructions on the NF/SGVHS website.
R. NON-VETERANS AS RESEARCH SUBJECTS

Most regulations pertaining to the participation of veterans as research subjects applies also to non-veteran subjects enrolled in VA approved research.

Non-veterans can be included in VA research under certain circumstances. VHA Handbook 1200.05 specifies the circumstances when non-Veterans can be included in VA research. VA investigators wanting to enroll non-veterans in VA approved research must provide justification for including non-Veterans in the IRB submission documents (for IRB-01, Addendum V solicits this information). The IRB must review the justification for inclusion of non-Veterans and approve entering non-Veterans into the study before any non-Veterans can be recruited.

S. PAYMENT OF RESEARCH SUBJECTS

VHA Handbook 1200.05 describes the requirements for payment of subjects in VA research. VA policy prohibits paying human subjects to participate in research when the research is an integral part of a patient's medical care and when it makes no special demands on the patient beyond those of usual medical care. Payment may be permitted, with approval of the IRB, in the following circumstances:

1. **No direct subject benefit.** When the study to be performed is not directly intended to enhance the diagnosis or treatment of the medical condition for which the volunteer subject is being treated, and when the standard of practice at the affiliate (University of Florida) is to pay subjects in this situation.

2. **Others being paid.** In multi-institutional studies, when human subjects at a collaborating VA or non-VA institution, such as the University of Florida, are to be paid for the same participation in the same study, subjects may be paid at a rate comparable to that proposed at the other sites, if deemed reasonable by the local IRB.

3. **Comparative situations.** In other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate.

4. **Transportation expenses.** When transportation expenses are incurred by the subject, that would not be incurred in the normal course of receiving treatment, and that are not reimbursed by any other mechanism.

Prospective investigators who wish to pay research subjects must include in their IRB submission: (1) Substantiation that proposed payments are reasonable and commensurate with the expected contributions of the subject; (2) The terms of the subject participation agreement, the amount of payment and the time frame for payment in the informed consent form; (3) Substantiation that subject payments are
fair and appropriate and that they do not constitute (or appear to constitute) undue pressure, influence, or coercion on the prospective research subjects to volunteer for or continue to participate in the research study.

The IRB will review all proposals for payment of subjects to assure conformity with VA policies. This review includes consideration of the payment schedule to avoid any coercion that might result from withholding all or most payment until the end of a long trial.

The NF/SGVHS Research Service is responsible for ensuring that the approved payment to subjects is made from a VA-approved funding source for research activities.

For VA-funded research, the informed consent should indicate that payments to subjects made through Austin Financial Services Center generate Internal Revenue Service (IRS) Form 1099 regardless of amount. The informed consent form must include this information and the fact that the SSN will be used for payment purposes. Gift cards are not subject to these reporting requirements.

T. CONFLICT OF INTEREST

For detailed information on Conflict of Interest, see IRB Policies and Procedures and R&D SOP “Conflict of Interest”.

U. INVESTIGATIONAL DRUGS IN RESEARCH WITH HUMAN SUBJECTS

VA human research involving investigational drugs must be conducted in accordance with all applicable VA and other Federal requirements including, but not limited to VHA Handbooks 1200.05 and 1108.04 and FDA regulations. If the research involves FDA-regulated drugs, both VA requirements and FDA regulations apply. FDA regulations supersede VA requirements for human subjects research under FDA jurisdiction unless VA requirements are more restrictive than applicable FDA regulations.

Details of these requirements may be found in the Pharmacy Service Investigational Drug Service (IDS) policies and SOPs. Further information on IND requirements and exemptions may be found in the IND SOP, and Emergency use of a test article in the corresponding SOP.

VHA Handbook 1108.04, paragraph 2f defines an investigational drug as a chemical or biological drug that is used in a clinical investigation. An investigational drug can be: a chemical compound that has not been released by the FDA for general use or it can be 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 clinical trial.
VA investigators must complete applicable IRB documents when proposing to use drugs or biologics in proposed research. Investigators will be required to submit an IND application to FDA for a clinical investigation on products that are subject to section 505 of the Food, Drug, and Cosmetic Act or to the licensing provisions of the Public Health Service Act (58 Stat. 632, as amended (42 U.S.C. 201 et seq.) unless the clinical investigation meets the exemption criteria set forth in 21 CFR 312.2(b) as determined by the IRB. Further information on IRB review of research involving investigational drugs is available in IRB-01 policies and procedures.

**Investigator Responsibilities.** To receive an investigational drug as defined above, in addition to FDA regulations for the conduct of research under an IND and other investigator responsibilities defined in this manual, the investigator must:

1. Provide the Investigational Drug Service information on each subject receiving an investigational drug through the electronic medical record or other locally approved means. Documentation is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements, i.e., herbals, nutriceuticals.

2. Provide the Investigational Drug Service with the following:
   
   (a) Documentation of IRB and any other relevant approvals;
   
   (b) A copy of VA Form 10-9012, Investigational Drug Information Record, when applicable;
   
   (c) A copy of the current approved protocol;
   
   (d) A copy of the informed consent form for each participating subject with all appropriate signatures;
   
   (e) Documentation of the IRB continuing review approval;
   
   (f) Copies of sponsor-related correspondence specific to the drug(s) as appropriate;
   
   (g) Copies of all correspondence addressed to the investigator from the FDA (and other involved authorities) specific to the investigational drug(s) as appropriate;

3. Inform the Clinical Research Pharmacist (Investigational Drug Service) and the IRB, in writing, when a study involving investigational drugs has been suspended, terminated, or closed;

4. Comply with all dispensing requirements;
(5) Comply with all documentation requirements and make relevant records accessible to the Investigational Drug Service when requested (VHA Handbook 1108.04 6.a.(4));

(6) Comply with all VHA pharmacy requirements regarding receiving, dispensing, storing, and record-keeping for investigational drugs.

V. INVESTIGATIONAL DEVICES IN RESEARCH WITH HUMAN SUBJECTS

IRB review and approval and investigator conduct of all investigational device studies must be in accordance with all applicable VA and other requirements including, but not limited VHA Handbook 1200.05 and FDA regulations (e.g., 21 CFR Parts 50 and 56, and Investigational Device Exemptions (IDE) (21 CFR 812)). If the research involves FDA-regulated devices, both VA requirements and FDA regulations apply. FDA regulations supersede VA requirements for human subjects research under FDA jurisdiction unless VA requirements are more restrictive than applicable FDA regulations.

(1) **Delivery.** Devices should be delivered only to the principal investigator after full approval for the research has been secured. If this is not feasible (e.g., due to required installation, testing, training, etc.) the investigator should work with the Clinical Research Office to secure permission to bring the device on station. Please note, in many cases it may be necessary to secure a number of approvals, such as Biomedical Engineering, prior to bringing the device on station. All receipts and invoices of delivery must be kept with the Investigator.

(2) **Management.** The protocol and/or application should describe how the device will be managed on station. This includes a discussion of who will have access to the device and assurance that investigational stock will not be used in place of approved devices for non-research patients.

(3) **Storage.** Devices should be stored in a separate, locked area, away from approved devices and clearly marked ‘CAUTION: Investigational Device – For Research Use Only.’

(4) **Use.** Investigational Devices may only be used by an approved investigator in conjunction with a fully approved protocol (IRB and R&D) and for patients who have given their consent to participate.

(5) **Disposal.** The investigator or manufacturer should provide guidance for disposition of unused, damaged or faulty devices and for the disposition of all stock and/or equipment at the termination of the research. Under no circumstances may devices be maintained after conclusion of the research unless they have received
full FDA approval and the investigator has secured appropriate local approvals to maintain the device for clinical use.

(6) **Principal Investigator Responsibilities.**

The investigator must ensure the procedures, in the conduct of research involving an investigational device, are in accordance with all applicable local, VA and other Federal requirements, including FDA regulations. Specifically:

a. Submitting the protocol and all required documentation, including the informed consent form and the Investigational Device Information Sheet (Appendix A) to the IRB and R&D Committee review prior to beginning the study. An IDE must be obtained from the sponsor for significant risk devices prior to project review.

b. Submitting continuing review documentation and all adverse events to the IRB and R&D as required by applicable policy.

c. Using the investigational device only after notification of IRB and R&D approval and after informed consent is obtained as required by the IRB.

d. Adhering to the Investigational Device Exemption regulations at 21CFR812. Research projects involving non-significant risk devices must adhere to the abbreviated requirements at 21CFR812.2 (d).

e. Providing secure storage for all investigational devices according to their storage requirements and as outlined in the research protocol.

f. Ensuring proper dispensing and utilization of the investigational devices as defined in the research protocol.

g. Dispensing and using the investigational device by appropriate personnel as outlined in the research protocol and as permitted by appropriate training in the proper use of the device.

h. Obtaining and documenting informed consent for each individual prior to using the investigational device.

i. Maintaining the appropriate research records and tracking of the investigational device per 21 CFR 812.140 (Appendix B).

j. Reporting any protocol modifications to the IRB immediately.

Guidelines for Investigators using Investigational Devices for further information and guidance in preparing for study that includes investigational device(s) is available at http://www.northflorida.va.gov/NORTHFLORIDA/research/files/InvestigationalDevice.doc
W. RESEARCH INVOLVING HUMAN BIOLOGICAL SPECIMENS

All activities involving the collection of human biological specimens for research purposes, as well as the research use of specimens collected for clinical care, must be conducted under the terms of a research protocol approved by the IRB and R&D Committee. The collection and use of human biological specimens (either identifiable or de-identified) must comply with all applicable VA and other Federal requirements including, but not limited to: 21 CFR 50, 21 CFR 312, 38 CFR 16, 45 CFR 160 and 164 (HIPAA), VHA Handbook 1200.8, and current VA requirements for research involving human biological specimens or superseding requirements.

Research that proposes the use of de-identified human samples requires a determination from the IRB that the research is non-human or exempt.

When informed consent is being obtained in studies involving tissue banking, consent forms must include the following elements:

(1) If applicable, that the investigator believes that the human biologic specimens obtained could be part of, or lead to the development of, a commercially valuable product.

(2) If the specimens are to be retained after the end of the study for future research, where the specimens will be retained, who will have access to them, and how long they will be retained. Current applicable institutional, VA and other Federal requirements must be met for handling, use and storage of biologic specimens.

X. RESEARCH INVOLVING HUMAN DATA

Use of VA or non-VA human data and data repositories (whether developed for health care, administration of VA programs, or research) for research purposes must be consistent with the mission of VA including:

a. Having relevance to the health of Veterans,

b. Protecting the privacy of the individuals from whom the data were collected, and

c. Being consistent with all applicable ethical and regulatory standards, and all applicable VA and other Federal requirements. All applicable requirements of VHA Handbook 1200.12 must be met for the use of data and data repositories for VHA research purposes.

Y. USE OF SOCIAL SECURITY NUMBERS IN HUMAN RESEARCH

Investigators can obtain and use real Social Security numbers only when real Social Security numbers are required to meet the specific aims of the research protocol (i.e. access CPRS for subject’s protected health information, to search databases, to
match data from different databases, etc) or to enter information into the subjects’ health records (i.e. the SSN is the medical record number in VHA).

Investigators must provide the justification for the use of the SSN and the security measures to protect them in the IRB submission. The collection and use of real Social Security numbers must be approved by IRB, and the investigators must follow all applicable VA and other Federal requirements for obtaining and using real Social Security numbers.

If obtaining and using the SSN for research-related purposes is approved, the key that holds the SSN, the subject’s name and study number must be secured at all times, be stored separate from the other research files and be accessible only to a limited number of research staff who have need and awareness to only use the SSN for the approved, designated purpose(s).

The SSN as the medical record number must be included on any document that is entered into the medical record, including scanning into the Computerized Patient Record System (CPRS). Research consents and HIPAA Authorization forms should include the SSN if they will be entered into the medical record; if a medical record is not required, then the SSN does not need to be obtained from the subject unless the use of the SSN is for specific research purposes, described in the approved protocol and in the informed consent documents.

Z. USE PREPARATORY TO RESEARCH

Data repositories (including VA medical records) may be used (i.e., accessed) by VA investigators for activities that are preparatory to VA research without the requirement to obtain either a HIPAA authorization from the subject or waiver of HIPAA authorization by an IRB or Privacy Board. This includes use of PHI for the preparation of a research protocol prior to submission to the IRB(s). Requirements for uses preparatory to research are described in VHA Handbook 1200.05, the NF/SGVHS SOP Access to Individually Identifiable Information for Use in Research Studies and IRB-01 policies and procedures that describe IRB review of HIPAA documentation in human subject research.

AA. PRIVACY, CONFIDENTIALITY AND HIPAA

Investigator must include provisions to protect the privacy of subjects and maintain the confidentiality of research data in their submission to the IRB. At the time of initial review, the IRB ensures that there are adequate provisions to the privacy and confidentiality of research subjects is protected. The IRB assesses whether there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data by evaluating the methods used to obtain information:

1. About subjects
2. About individuals who may be recruited to participate in studies
3. The use of personally identifiable records
4. The methods to protect the confidentiality of records

The PI provides the information regarding the privacy and confidentiality of research subjects at the time of initial review through submission of applicable IRB forms and documents, any necessary HIPAA forms, and/or other submitted, applicable materials.

The NF/SGVHS Privacy Officer must review human research submissions (protocol and any other relevant materials submitted to the IRB such as the HIPAA authorization and/or HIPAA Waiver) to ensure compliance with all applicable local, VA and other federal requirements for privacy by identifying, addressing, and mitigating potential concerns about proposed research studies. The PO completes the privacy review on the applicable privacy checklist. The PO will indicate either that all applicable local, VA and other Federal requirements for information security have been met or identify deficiencies and require changes to correct those deficiencies.

The UF IRB-01 serves as the Privacy Board for research at the VA NF/SGVHS and abides by the Health Insurance Portability and Accountability Act (HIPAA) of 1996 and applicable VHA requirements. The UF IRB-01 and the VA R&D recognize the importance of protecting subject privacy, and carefully evaluates each protocol for the privacy measures taken. Only those authorized by the UF IRB, as described in the approved protocol, can collect, use and share individually-identifiable patient information. Individuals must have prior approval by the IRB, ISO, PO and R&D Committee before receiving individually identifiable patient data for research purposes. VHA Handbook 1200.12 describes the requirements that must be met for use of data in VA research.

In accordance with VHA requirements, investigators must obtain a HIPAA authorization (see section on HIPAA Authorization above) to use and disclose protected health information unless a waiver of HIPAA Authorization has been granted by the UF IRB-01. In addition, all investigators and research staff must complete the VA Privacy Policy Training.

Notice of Privacy Practices (NOPP): Notices of privacy practices must be given to non-veterans. The NF/SGVHS Privacy Office is responsible for this requirements. VHA Handbook 1605.04 requires that VHA Notice of Privacy Practices be provided to all non-Veteran patients receiving care or treatment at a VHA healthcare facility and non-Veteran research subjects enrolled in a VA-approved research study with clinical trials.

Principal Investigators of a VA-approved research study must provide a copy of IB 10-163, VHA Notice of Privacy Practices, to any non-Veteran research subject at their first research visit and have the subject sign and date an Acknowledgment of the Notice of Privacy Practices, VA Form 10-0483 at this first episode of care. The
subject must be given the Notice of Privacy Practices to take with them. In situations where the non-Veteran has a personal representative, the VHA Notice of Privacy Practices may be given to and written acknowledgement obtained from the subject’s personal representative. If an acknowledgement is not received from the subject, the research team member obtaining informed consent must enter an administrative note into CPRS (or the subject’s research record if there is no VHA health record) indicating a good faith effort was made to obtain the written acknowledgement and the reason it was not received.

BB. INFORMATION SECURITY

NF/SBVHS Investigators must provide an information security plan in the IRB submission for new studies (approved after March 31, 2011) and upon request for older studies (for IRB-01 Addendum V solicits this information). The NF/SBVHS Information Security Officer must review human research submissions (protocol and any other relevant materials submitted to the IRB) to ensure compliance with all applicable local, VA and other federal requirements for information security by identifying, addressing, and mitigating potential concerns about proposed research studies. The ISO completes the information security review on the applicable information security checklist. The ISO will indicate either that all applicable local, VA and other Federal requirements for information security have been met or identify deficiencies and require changes to correct those deficiencies.

Any changes to the research that may impact information security must be re-reviewed by the ISO.

CC. TREATMENT OF RESEARCH-RELATED INJURIES TO HUMAN SUBJECTS

VA medical facilities must provide necessary medical treatment to a research subject injured as a result of participation in a research study approved by a VA R&D Committee and conducted under the supervision of one or more VA employees (38 CFR 17.85). This does not apply to:

1. Treatment for injuries due to non-compliance by a subject with study procedures (38 CFR 17.85(a)(1)); or
2. Research conducted for VA under a contract with an individual or a non-VA institution (38 CFR 17.85(a)(2)).

Care for VA research subjects under 38 CFR 17.85 must be provided in VA medical facilities, except in the following situations:

1. If VA facilities are not capable of furnishing economical care or are not capable of furnishing the care or services required. Under these circumstances, VA facility Directors may contract for such care (38 CFR 17.85(b)(1)).
(2) If inpatient care must be provided to a non-Veteran under 38 CFR 17.85, VA facility Directors may contract for such care (38 CFR 17.85(b)(2)).

(3) If a research subject needs treatment in a medical emergency in a non-VA facility for a condition covered by 38 CFR 17.85, VA facility directors must provide reasonable reimbursement for the emergency treatment in a non-VA facility (38 CFR 17.85(b)(3)).

VA regulations pertaining to the treatment of research-related injuries to human subjects (38 CFR 17.85) apply to minimal and greater than minimal risk research.

Language explaining VA’s authority to provide medical treatment to research subjects injured by participation in a VA research project must be included in the informed consent.

If a subject is injured as a result of participation in VA-approved research, this must be reported to the IRB within the timeframe specified in IRB and NF/SGVHS policy.
Chapter IV: Unanticipated Problems, Serious Adverse Events and Non-Compliance Reporting

A. Reporting UNANTICIPATED PROBLEM INVOLVING RISK TO SUBJECTS OR OTHERS AND SERIOUS ADVERSE EVENTS

Investigators and other members of the NF/SGVHS research community must report unanticipated problems involving risk to subjects or others and serious adverse events (whether related or unrelated to the research) to the IRB regardless of funding source, study sponsor or type of study in accordance with VHA Handbook 1058.01, NF/SGVHS SOPs and applicable IRB policies and procedures. If an investigator has a question on what must be reported and such timeframes for reporting, the IRB or NF/SGVHS Research Service office should be consulted.

The principal investigator is ultimately responsible for ensuring the prompt reporting of unanticipated problems involving risks to subjects or others to the IRB. All adverse events and unanticipated problems that require reporting under UF IRB Policy must be included on the Cumulative Table submitted at continuing review.

For purposes of reporting, the UF IRB has approved an algorithm for reporting unanticipated problems and/or adverse events available at http://irb.ufl.edu/docs/AEGuide.pdf. Each category has an established time frame for reporting to the IRB that include:

Events that may represent unanticipated problems involving risks to subjects or others (including a subset of adverse events that are serious and unexpected) occurring either:

1. At study sites with UF IRB approval or
2. At another center participating in the same protocol

Must be reported by the Principal Investigator, in writing to the IRB within five working days of discovery (five working days from notification for off-site events).

B. Reporting Non-compliance

Within 5 business days of discovery, members of the NF/SGVHS research community must report (in writing) any apparent serious or continuing noncompliance with applicable human research protection requirements, to the UF IRB-01 (or VA Central IRB as applicable) in accordance with VHA Handbook 1058.01, NF/SGVHS SOPs and applicable IRB policies and procedures. Examples of apparent serious or continuing noncompliance that require reporting are outlined NF/SGVHS policies and procedures. Investigators should consult with applicable IRB policies and procedures for additional reporting requirements.
C. Reporting Requirement for Suspension or Termination of IRB approval, Serious or Continuing Non-Compliance and/or Unanticipated Problems

NF/SGVHS is required to report certain research events to the Office of Research Oversight in accordance with VHA Handbook 1058.01 and NF/SGVHS SOP “Research Compliance Reporting Requirements.”

Federal regulations (38 CFR 16 and 21 CFR 56) and VHA Handbooks require that suspensions or terminations of IRB approval, serious or continuing non-compliance, and/or unanticipated problems involving risk to subjects or others be promptly reported to the IRB, institutional officials, and regulatory agencies. For VA Research, if the IRB suspends or terminates IRB approved research and/or makes a determination of serious and/or continuing noncompliance with the determinations or requirements of the IRB or that the protocol has been associated with an unanticipated problem involving risk to subjects or others, the IRB will notify the PI, NF/SGVHS IO and others as described in IRB and NF/SGVHS policy.

Following notification of a reportable event, the ACOS-R or designee and/or other individuals as applicable, will draft a report to be sent to applicable individuals and agencies. The contents of the report should be in accordance with oversight agency requirements. The requirements for ORO reports are described in the Research Compliance Reporting Requirements SOP. Procedures for reporting to OHRP are available on the OHRP website.

The draft report is sent to the IO for review and modification as needed. The final report is approved and signed by the IO and distributed by the ACOS/R or designee to the following, as appropriate:

1. Office of Research Oversight (ORO) as described in Reporting SOP
2. The Office of Research and Development, as described in Reporting SOP
3. The VISN Director, as described in Reporting SOP
4. FDA, if the study is subject to FDA Regulations, within 30 days of final IRB determination
5. OHRP within 30 days of the final IRB determination
6. Any “Common Rule” Federal Agency that is supporting the research, within 30 days of the final IRB determination
7. Principal Investigator
8. Principal Investigator’s Supervisor
9. Sponsor, if the study is sponsored
10. IRB of record for the protocol (IRB-01 or VA CIRB)
11. The VA Privacy Officer if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information
12. The VA Information Security Officer if the event involved violations of information security requirements

For research that involves the VA only (not UF), the VA IO or designee is responsible for reporting to applicable individuals and entities.

For research that involves both UF and the VA, a decision may be made by the respective IO’s that a joint report is authored and distributed to applicable agencies. This will be determined on a case by case basis; otherwise individual reports will be made by each institution.

As stated above, interruptions in research resulting solely from the expiration of IRB approval is not considered a suspension under VHA regulations and thus does not require reporting to ORO (VHA Handbook 1058.01). Expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under DHHS regulations (OHRP Guidance).
Chapter V: Participant OUTREACH

Several activities and efforts are available to ensure that participants, prospective participants and the community have an understanding of human research at NF/SG VHS.

A. Informational Brochures and Posters

The following informational pieces are available for display and distribution throughout NF/SGVHS:

1. Booklet. “I’m a veteran. Should I participate in research? Here are some things you NEED to know.” Department of Veteran Affairs, Center on Advice and Compliance Help (COACH) www.research.va.gov/programs/PRIDE/veterans/default.cfm.

   There is an accompanying video also available for distribution.

2. Brochure. “Volunteering in RESEARCH. Here are some things you need to know” Department of Veterans Affairs, Center on Advice and Compliance Help (COACH) www.research.va.gov/programs/PRIDE/veterans/default.cfm.

   There are accompanying handout and poster available for distribution as well as a video that can be view on-line.

3. Posters. The poster “Volunteering in Research. What questions should I ask before I volunteer?” published by Department of Veterans Affairs, Center on Advice and Compliance Help (COACH) is displayed throughout the NF/SGVHS as appropriate.

Spanish versions of all the above materials are also available from COACH.

The Volunteering in RESEARCH brochures are distributed:

1. Throughout the VA Medical Center to include the clinics, credit union, cafeteria, canteen and entry areas for the convenience of the patients. For quality assurance purposes, the number of brochures placed in each area is recorded in a log maintained by Research Service staff. On a bi-weekly basis, Research Service staff account for such brochures and replenish as necessary. A monthly review is conducted to determine how many brochures have been distributed.

2. To investigators with their notification of initial approval and as requested. NF/SGVHS investigators should make every reasonable effort to provide the brochure to prospective subject and their surrogates when applicable, when
the individuals are approached to take part in research and to document in the consent progress note that the brochure was provided.

Each brochure includes information on obtaining more information (e.g. Research Service Phone number and website URL)

**B. NF/SGVHS Website**

Information about participating in research is available online through the Research Service website at [http://www.northflorida.va.gov/Research/indexResearchers.asp](http://www.northflorida.va.gov/Research/indexResearchers.asp). The following links to other informational resources about research are included on this website:

1. Clinical Trials.gov
2. US Department of Health and Human Services
3. Food and Drug Administration (FDA)
4. National Institutes of Health (NIH)
5. Office of Research Oversight (ORO)
6. The President’s Council on Bioethics
7. MyHealtheVet
8. AAHRPP

**C. Community News**

News releases can be prepared by the NF/SGVHS Public Affairs Office as events surface. These releases of information to the community should cover the research activities currently being conducted, and the dates and topics for Research Day.

**D. Research Week**

Each year the Department of Veteran Affairs celebrates research week typically during late April, early May. NF/SGVHS takes this opportunity to present the research activities taking place in the service. Most recently NF/SG VHS has provided a two-day program during the week, including a research day with scientific presentations, and a community day, including brief presentations on research topics of interest to the veteran and community. The community, veterans, investigators and staff are encouraged to attend both days, although the community day is developed and directed toward the veteran and community.

In addition to the brief presentations on research and service topics of interest to the veteran and community, booths and posters are provided that include information on local service and veteran organizations. Other activities may also be provided during the day including health and wellness checks, literature distribution and brief respite care for the veteran so their caregiver can take part in the activities.
Investigators and staff are encouraged to attend this day and interact with the veterans and community.

Research Day is directed toward the research community, although the community and veterans are encouraged to attend. A theme is selected annually and speakers are chosen in accordance with the theme.

Posters announcing Research Week, along with locally generated information highlighting the current research theme are displayed in lobby areas in the hospital, throughout the research laboratories, and distributed to employees. Announcements are made by the local media, and local veteran and service groups are directly notified of the event.

Public officials are invited to this event, which also entails added media coverage and protocol.

In general, Research Week gives the NF/SGVHS a chance to highlight the research activities and achievements of the service and help the veterans and community better understand the research advancements made for veterans by our investigators and research staff.

E. Periodic Review of Research Week

The organization evaluates the Research Week event after the event to determine how it can be made better for the upcoming year. Informally, the research office discusses what worked well, what did not work well, and what can be done to improve for future events. Investigators, attendees and community organization that provided booths and information are surveyed for their comments and ideas. Research week typically includes all areas of research. Investigators and staff work together with the administrative office to bring the event together. Ideas for future events are welcomed and if practical implemented as necessary.

All other outreach activities are periodically reviewed (at least annually, and when new materials become available) and coordinated with the Public Affairs Office to ensure a constant flow of information to the public about the potential of research, at the same time as ensuring efforts are maintained to safeguard individuals' participation in research. The goal of Research Service is to keep individuals informed as much as possible through the use of various available media.

As new materials and ideas arise, the outreach program makes appropriate changes under the direction of the organization.

F. Community Outreach

Investigators are encouraged to present information related to their research at local community and veteran support groups. The directory of Veterans Service
Organizations and their contact information is available online at: http://www1.va.gov/vso. The information presented may be general information that relates to the investigator’s field of research.

G. Inclusion of Community Members in the Research Process

NF/SFVHS encourages investigators to involve community members in the research process, when appropriate. Research can be enhanced when individuals from the local area are involved in the design, conduct, and analysis of the data from the study. Considerations for reviewing research that involves community members in the research process at NF/SGVHS may include the use of veterans groups and organizations participating in all or a portion of the research process or to act as an advisory board. Additionally, when appropriate, investigators are encouraged to inform the community members about the results of the research study and utilize them to help disseminate the results.

The research centers located in NF/SGVHS are encouraged to include community and/or veteran members on their advisory boards/committees. The advisory boards/committees are responsible for advising the centers on strategic planning of their research portfolios and future directions. In addition, the UF IRB-01 includes a community member on its Review Committee.
Chapter VI: Sponsored Research

Clinical Trial Cooperative Research and Development Agreements (CT CRADAs) are used when a VAMC is interested in participating in a study for which a commercial company 1) owns the investigational new drug (IND) or device; 2) designs the protocol; and 3) funds the project. Additional information on VA CRADAs and other model agreements is available on the VHA R&D website at http://vaww.research.va.gov/programs/tech_transfer/model_agreements/default.cfm or can be obtained from the North Florida Foundation for Research and Education (NFFRE).

A. Protection of Research Participants

VA CT CRADAs include provisions for the protection of human subjects. Research conducted under a CRADA must conform to laws, regulations and VA policies and procedures pertaining to protections for human subjects.

B. Monitor of Study

In studies where sponsors bear responsibility for monitoring of the research, NF/SGVHS and the sponsor shall immediately notify each other and NFSFVHS will promptly notify the IRB upon identifying any aspects of the protocol, including unanticipated problems involving risk and information discovered during site monitoring visits or in the study results that may:

1. adversely affect the safety, well-being, or medical care of participants;
2. affect the willingness of participants to continue participation in the research;
3. influence the conduct of the study; or
4. alter the IRB’s approval to continue the study.

When participant safety or medical care could be directly affected by study results, VA will send study participants a written communication about the results. Any communication with participants must be approved by the IRB.

C. Research Related Injuries

Provisions for coverage of cost for research related injuries should be included in research awards and contracts.

The sponsor is responsible for reasonable and customary costs incurred for treatment of injury reasonably related to the subject’s participation in the study described in the scope of work except to the extent that:
(a) The injury is attributable to the negligence or willful misconduct of an indemnitee; or

(b) The injury is attributable to failure to administer the test article as required in the protocol or to otherwise substantially follow the protocol.

Information on the responsibility for research-related injury must be included in the consent form.
Chapter VII: References

Title 38 CFR Chapter I, Department of Veterans Affairs, Part 16, Protection of Human Subjects.

Title 38 CFR Chapter I, Department of Veterans Affairs, Part 17, Medical

Title 45 CFR Subparts A, B, C, and D, Department of Health and Human Services, Part 46, Protection of Human Subjects

Title 21 CFR Food and Drug Administration, Parts 50, 56, 312, 812
VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research and its references

VHA Handbook 1058.01, Reporting Adverse Events in Research to the Office of Research Oversight, Office of Research Oversight.

VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research, Office of Research Oversight.

VHA Handbook 1108.04, Investigational Drugs and Supplies, Pharmacy Service


VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research

VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research

VHA Handbook 1605.01, Privacy and Release of Information, Information Assurance Service

VHA Handbook 1907.01, Health Information Management and Health Records, Information Assurance Service