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Institutional Authority

The President of the University of Florida (UF) is the authority responsible for compliance with federal and state laws and regulations and University policies concerning activities involving human subjects and for assuring the protection of human subjects. The President delegates this authority to the Vice President for Research. As UF’s Signatory Official, the Vice President (VP) for Research is legally authorized to act for the Institution and to assume, on behalf of the Institution, the obligations under UF’s Federal Wide Assurance (FWA) with the Department of Health and Human Services (DHHS) through the Office for Human Research Protections (OHRP). The UF FWA sets forth the principles and guidelines that govern the institution, and its faculty, staff, and students in the discharge of responsibilities for protecting the rights and welfare of human subjects taking part in research conducted at, conducted by, or sponsored by, the institution. Through its assurance, UF agrees to comply with the ethical principles of the Belmont Report and the provisions of the Common Rule (45 CFR 46, Subpart A) for all research regardless of funding source.

Under UF’s FWA, the VP for Research has designated three internal Institutional Review Boards (IRBs) (IRB-01 Health Science Center, IRB-02 Main Campus, and IRB-03 Jacksonville) and one external IRB (IRB-04, Western IRB or WIRB) to review and provide oversight for all research. Additional Boards may be established as necessary. The IRBs act under the authority of the VP for Research. The IRBs function in coordination with UF officials, other review committees and research investigators, but at all times maintain their independence to appropriately review, approve and monitor human research.

UF bears full responsibility for the performance of all research involving human subjects and for the protection of the rights and welfare of human subjects under its FWA, including complying with federal, state, or local laws and regulations as they may relate to such research and protections.

UF has delegated to Department Chairs and their equivalents the authority to review human subject research protocols submitted to the IRB by research investigators under their supervision. The Department Chairs or their equivalents must approve the submission of human subject research protocols prior to their submission to the IRB.

Limitation on Institutional Authority

Human research that has been approved by a University IRB may be subject to further review and approval or disapproval by officials of the institution (including the VP for Research) and other review bodies. In the case of IRB approved human subjects research, the VP for Research or designee may conclude that a project does not comply UF policies or obligations and may disapprove, suspend, or terminate the project on behalf of the institution. Additionally, university committees will have the authority to approve as submitted, require modifications in (to secure approval), disapprove or terminate all reviewed protocols. Any action that may affect subject safety should be forwarded to IRB-01.

For research to be conducted at the VA, the Institutional Official, designee, or R&D Committee may conclude that a project does not comply with VA policies or obligations and may disapprove, suspend, or terminate the project on behalf of the institution. Additionally, VA committees will have the authority to approve as submitted, require modifications in (to secure approval), disapprove or terminate all reviewed protocols. Per the VA R&D Committee SOP, any action that may affect subject safety will be forwarded to IRB-01.
In the case of a decision by a UF IRB to disapprove, suspend, or terminate a project, the decision may not be reversed by any other person or entity including any affiliated Institutional Official/designee, or any other officer/agency of the UF, state government, or federal government.

Applicability

With the exception of research in which the only involvement of humans is in one or more of the categories exempted or waived under 45 CFR 46.101(b)(1-6) or 101(i) UF's FWA extends the provisions of the Common Rule to:

(1) all human subjects research conducted by UF faculty, staff and students, regardless of sponsorship;
(2) all other activities (even in part) which involve such research, regardless of sponsorship;

45 CFR 46 Subparts B-D are only applicable to HHS funded or supported human subjects research.

UF considers its employees or agents to be engaged in research under the conditions described in OHRP's Guidance document titled "Engagement of Institutions in Research" located at: http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm.

The UF IRBs evaluate research protocols on a case by case basis to determine if our local research activities rely on engaging (as defined in the OHRP guidance) sites or investigators outside of our assured institutions (UF, Shands, or VA).

(1) If an outside site is engaged in the research and already possesses an FWA, that site must obtain approval from its listed IRB. This approval must be reviewed and approved by the UF IRB.

(2) If an outside site is engaged in the research and does not possess an FWA, that site must obtain an FWA which names either

(a) a UF IRB (if the University will agree to OHRP's "IRB Authorization Agreement") or
(b) other registered IRB - whose approval must be obtained and subsequently reviewed and approved by the UF IRB.

(3) If the research will engage individuals who are not employees or agents of our assured institutions, one of the following must occur:

(a) the individual must obtain approval from their local IRB if they are affiliated with another assured institution and are performing the research activities in affiliation with their institution, or

(b) the individual may be covered under the UF FWA as an "Unaffiliated Investigator" if they submit an Unaffiliated Investigator Agreement (aka Individual Investigator Agreement; available on the IRB-01 website at http://irb.ufl.edu/docs/frm-uia.doc).
This agreement commits them to comply with appropriate federal, state, and local laws, regulations, and policies regarding human subjects’ research. The Unaffiliated Investigator may not engage in the research until the agreement is signed by the IRB Chair and Institutional Official, and then approved by the UF IRB, via the appropriate Expedited or Full Board mechanism.

Investigators who wish to conduct research at an outside site and the site itself is not actually engaged (per OHRP’s guidance) in the research must (a) obtain written permission from the site to access their facility or population and (b) obtain UF IRB approval prior to accessing the site.

Faculty, staff, and students at other institutions relying on any UF IRB for oversight are required to review their institutional FWA with DHHS to insure they are conducting their research in accordance with the applicable assurance.

All human subjects research which is exempt under Section 101(b)(1-6) or 101(i) will be conducted in accordance with: (1) the Belmont Report, (2) this institution’s administrative procedures to ensure valid claims of exemption, and (3) orderly accounting for such activities.

**Authority of the IRB**

The VP for Research grants the IRB the authority to ensure that research is conducted in a manner that protects the rights, safety and welfare of human subjects. Specifically, the IRB has the authority to:

i. Approve, require modifications to secure approval, or disapprove all research activities, including proposed changes in previously approved human subject research.

ii. Suspend or terminate approval of research:
   1. in order to protect the rights and welfare of current, previous, or future research subjects;
   2. if information indicates that there may be serious and unexpected harm to subjects;
   3. if a particular study or other studies by a particular researcher are not being conducted in accordance with applicable requirements; or
   4. any other appropriate reason to insure subject safety (such as an increase in the risk to benefit ratio) or regulatory compliance (such as failure of sub-recipient sites to obtain appropriate IRB approval for the collection of data that UF researchers will rely on).

iii. To observe, or have a third party observe, the conduct of the research

iv. To observe, or have a third party observe, the consent process.

**Undue Influence**

Any IRB or IRB staff member who believes that he or she has have been subject to inappropriate attempts to influence the IRB process should report this immediately to the IRB Chair. The IRB Chair will then report the attempt at influence to the VP for Research (or the applicable IO), and if necessary, to the University President. Anyone who believes the IRB Chair is attempting to inappropriately influence the IRB should report their concerns to the VP for Research either directly or through the Assistant Director of IRBs or Director of Sponsored Research and Compliance. If the VP for Research is attempting to influence the IRB process, reports should be made directly to the University President. The UF President, VP for
Research, Director of Sponsored Research and Compliance or a designee will investigate the attempt to inappropriately influence the IRB and the VP for Research has the authority to respond and determine an appropriate response to such attempts.

Mission and Purpose

UF IRBs are established in accordance with federal regulations in order to accomplish their mission of protecting the rights and welfare of human subjects participating in biomedical and behavioral research at UF or affiliated institutions. The UF IRBs accomplish this mission by

(a) reviewing and approving all research that involves human subjects under appropriate FWAs (unless the IRB, through its members or designated staff, determines the research is exempt as described in this manual); and

(b) monitoring approved research to insure ongoing protection.

This document sets forth policies and procedures for UF’s Health Science Center IRB (IRB-01) under which the Institution, the IRB and Investigators will comply with all applicable laws and regulations, and University policies for the protection of human subjects.

Ethical Mandate to Protect Human Subjects

All of the Institution’s human subject research, regardless of funding source, and all activities of the IRBs are guided by the basic ethical principles that underlie the conduct of biomedical and behavioral research involving human subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled Ethical Principles and Guidelines for the Protection of Human Subjects of Research (“The Belmont Report”). The Belmont principles are central to the ethical conduct of research involving human subjects as follows:

**Respect for persons** requires that potential subjects be given the opportunity to choose what will or will not happen to them. This principle forms the basis for obtaining informed consent and the consent process (including information, comprehension and voluntariness). Respect for persons also provides additional protections for potentially vulnerable subjects. The principle is reflected in regulatory mandate that legally effective informed consent be sought and appropriately documented; and that additional safeguards for subjects with diminished capacity and others who are vulnerable to coercion or undue influence be considered and included in the research.

**Beneficence** is exemplified in the expressions of “do no harm” and “maximize possible benefits and minimize possible harms.” The principle of beneficence is reflected in the regulatory mandate that the IRB approve research

(a) that minimizes risk through sound research design, and

(b) where risks to subjects are reasonable in relation to both the anticipated benefits (if any) to subjects and the importance of knowledge reasonably expected to result.

**Justice** requires fairness in the distribution of benefits and burdens of research and that persons be treated fairly both individually (by offering potentially beneficial research to all who might benefit) and socially (based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons). The principle
of justice is reflected in the regulatory mandate that subject selection be equitable and representative of those likely to benefit from the research.

All institutional and non-institutional performance sites for this institution, domestic or foreign, will be obligated by UF to conform to ethical principles which are at least equivalent to those of this institution or as may be determined by the Department of Health and Human Services (DHHS) Secretary.

Regulatory Mandate to Protect Human Subjects

Department of Health and Human Services (DHHS) Regulations (45 CFR Part 46 Protection of Human Subjects Subpart A) constitute the Federal Policy (Common Rule) for the protection of human subjects. The Common Rule applies to any human subject research supported or conducted by federal agencies that have adopted the Common Rule, including, but not limited to DHHS. The Department of Veterans Affairs (VA) incorporated the Common Rule in 38 CFR 16. VHA Handbook 1200.05 (Requirements for the Protection of Human Subjects in Research) defines the procedures for the implementation of 38 CFR 16.

Food and Drug Administration Regulations (21 CFR 50 and 56) codify FDA requirements for the protection of human subjects (21 CFR Part 50 Subparts A, B, and D which includes general provisions, informed consent, and additional protections for children, respectively) and institutional review boards (21 CFR 56).

The FDA regulations at 21 CFR §50 (Protection of Human Subjects) applies to all clinical investigations regulated by the Food and Drug Administration under sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Additional specific obligations and commitments of, and standards of conduct for, persons who sponsor or monitor clinical investigations involving particular test articles may also be found in other parts (e.g., parts 312 and 812). Compliance with these parts is intended to protect the rights and safety of participants involved in investigations filed with the Food and Drug Administration pursuant to sections 403, 406, 409, 412, 413, 502, 503, 505, 510, 513-516, 518-520, 721, and 801 of the Federal Food, Drug, and Cosmetic Act and sections 351 and 354-360F of the Public Health Service Act. [21 CFR §50.1]

The FDA regulations at 21 CFR §56 (Institutional Review Boards) contains the general standards for the composition, operation, and responsibility of an IRB that reviews clinical investigations regulated by the Food and Drug Administration under sections 505(i) and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Compliance with this part is intended to protect the rights and welfare of human participants involved in such investigations. [21 CFR §56.101]

Except as provided in 38 CFR §18.101(b), VA Regulations38 CFR §18 applies to all research involving human participants conducted, supported or otherwise subject to regulation by any
Federal Department or Agency which takes appropriate administrative action to make the policy applicable to such research. [38 CFR §16.101(a)] [45 CFR §46.101(a)]

- This includes research conducted by Federal civilian employees or military personnel, except that each Department or Agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint.
- It also includes research conducted, supported, or otherwise subject to regulation by the Federal Government outside the United States.
- Research that is conducted or supported by a Federal Department or Agency, whether or not it is regulated as defined in 38 CFR §18.102(e), must comply with all sections of 38 CFR §18.
- Research that is neither conducted nor supported by a Federal Department or Agency but is subject to regulation as defined in 38 CFR §18.102(e) must be reviewed and approved, in compliance with 38 CFR §18.101, §18.102, and §18.107 through §18.117 of this policy, by an Institutional Review Board (IRB) that operates in accordance with the pertinent requirements of 38 CFR §18.

For all research involving the North Florida / South Georgia Veterans Health System (NF/SGVHS) NFG VHS UF IRB-01 will defer to current versions of the VHA Handbook 1200.05 (REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH) and the VHAVA Handbook 1058.01 (RESEARCH COMPLIANCE REPORTING REQUIREMENTS) to assure that study conduct and reporting guidelines are consistent with current Veteran Health Administration regulations.

Scope of Authority of the IRB

It is the policy of UF that all research involving human subjects under the oversight of the institution in accordance with its FWA will be conducted in accordance with applicable federal law and regulations that include but are not limited to 45 CFR 46, 21 CFR 50 and 56, and HIPAA regulations in 45 CFR 160 and 164, the Belmont Report, applicable Florida statutes and regulations, University policies, and requirements of the applicable IRB. Any activity meeting the regulatory definitions of research involving human subjects or clinical investigations involving human subjects (as outlined below) must be prospectively reviewed and approved by the appropriate UF IRB. The involvement of human subjects in research will not be permitted until the IRB reviews and approves the research protocol, generates the letter of approval (and informed consent form, if appropriate) for such research to be conducted, and until informed consent has been obtained from the subject or the subject's legal representative and documented in writing unless waived by the IRB in accordance with applicable federal regulations.

IRB-01 functions as the review board for human subjects research conducted by Health Science Center Faculty, staff and students, and those entities holding OHRP approved assurances designating IRB-01 including, but not limited to, the North Florida/South Georgia Veterans Health System (NF/SGVHS) and the institutions owned by Shand’s Teaching Hospital and Clinics, Inc. in accordance with the Memoranda of Understanding signed with those entities.

The UF IRB-01 operates as a Privacy Board as described in the Standards for Privacy of Individually Identifiable Health Information (the Privacy Rule; 45 CFR 160 and 164) of the Health Insurance Portability and Accountability Act (HIPAA)
when research involves Protected Health Information. IRB-01 acts as the Privacy Board for UF (Health Sciences Center), Shands, and the NF/SG VHS.

**DHHS and Definitions of Human Subjects, Research, and other terms**

The Federal regulations [45 CFR 46.102 (d)] [38 CFR 16.102 (d)] define *research* as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge and *human subject* as a living individual about whom an investigator (whether professional or student) conducting research obtains either

1. Data through intervention or interaction with the individual, or
2. Identifiable private information [45 CFR 46.102 (f)] [38 CFR 16.102 (f)].

*Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes [45 CFR 46.102 (f)(1)] [38 CFR 16.102 (f)(1)]. *Interaction* includes communication or interpersonal contact between investigator and subject [45 CFR 46.102 (f)(2)] [38 CFR 16.102 (f)(2)].

*Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects [45 CFR 46.102 (f)(2)] [38 CFR 16.102 (f)(2)].

*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 [§46.102(i); 21 CFR 50.3 (k)].

**NOTE:** 45 CFR 46 and 38 CFR 16 are considered the “Common Rule”. Future references to 45 CFR 46 may be referenced in the identical section in 38 CFR 16. Additional information regarding definitions relating to VA research is available in VHA Handbook 1200.05.

**FDA Definitions of Human Subjects, Clinical Investigation/Research, and other terms**

FDA regulations define "clinical investigation" (synonymous with “research”) as any experiment that involves a test article and one or more human subjects and that is one of the following: [21 CFR 50.3 (c) and 56.102 (c)]:

- Subject to requirements for prior submission to the Food and Drug Administration under §505(i) or §520(g) of the act.
  - Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act” means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]
  - Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act” means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]
"Act" means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

- Not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
  - Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]
- The term does not include experiments that are subject to the provisions of 21 CFR §58, regarding non-clinical laboratory studies.

FDA IDE Regulations [21 CFR §812.3(h)] define investigation as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device and FDA IND Regulations [21 CFR §312.3(b)] define clinical investigation as any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.

Under FDA regulations "human subject" means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A "subject" may be either a healthy individual or a patient [21 CFR 50.3 (g)]. The FDA’s Investigational Device Exemption (IDE) regulations [21 CFR 812.3 (p)] define subject as 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. Similarly, a subject may be in normal health or may have a medical condition or disease.

FDA IND Regulations [21 CFR §312.3(b)] define subject as a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.

Test article means any drug, biological product or medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act [21 CFR 50.3(j)] [21 CFR 56.102 (l)]

FDA Regulations for the Protection of Human Subjects apply to all clinical investigations regulated by the FDA under sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. [21 CFR 50]

Research includes, for instance, clinical trials, surveys and interviews, behavioral investigations, retrospective reviews of medical information, experiments with blood and tissue, and demonstration and service programs. The creation or use of a data or tissue repository for research purposes is considered research. In addition, the FDA includes under the definition of reviewable research, any use of a FDA regulated product (investigational or previously approved) except for use of a marketed product in the practice of medicine.
Research involving Human Subjects (“Human Research”)

Any activity that meets the following definitions for human subject research or clinical investigation (synonymous with “Research involving Human Subjects”, Human Research”, or similar terms, including all appropriate DHHS, VA, and FDA definitions) requires review and approval by the applicable UF IRB prior to initiation:

- Meets the DHHS and VA definitions of “research” and involves “human subjects” as defined by DHHS and the VA.

- Meets the 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. The federal regulations do not apply to such activities that do not meet applicable definitions. Investigators who are unsure whether a proposed activity meets the definition of human subjects’ research should contact the IRB office for guidance. As described in section “Determinations of Exemption” (page 14) and “Non-Human Subject Research//Indefinite Plans” (page 51), only the IRB can make the determination that an activity does not meet the definitions and therefore does not require prospective review. The IRB cannot retroactively approve non-exempt human subjects’ research. Contact information for the IRB-01 Office is available at http://irb.ufl.edu/irb01/officeinfo.htm. If there is any question that an activity could constitute human subjects’ research (based upon the definitions above), the Investigator is instructed by IRB Staff to submit applicable paperwork. Qualified IRB Staff or a Chair will determine, based upon information provided by the investigator, if the activity is human subject research requiring review and approval by the IRB. Decisions can be communicated to Investigators verbally or via written correspondence.

Human Subjects Research Exempt from IRB Review

Research activities involving human subjects that are exempt from IRB review are identified in 45 CFR 46.101(b)(1)-(6).

Exceptions to Exempt Criteria

The following are exceptions to the exempt categories

Criteria (Categories 1-5) allowing exemption from the federal regulations (45 CFR 46) only pertain to research that is not subject to FDA Regulation.

Category 6 is exempt under FDA regulation (21 CFR 56.104(d)). FDA also allows emergency use of a test article under certain conditions without prospective IRB approval (see section Emergency Use of Test Article).

Federally funded research involving prisoners as participants is not exempt from the federal regulations (45 CFR 46).

All Exempt criteria apply equally to children except for category 2. Exempt category 2 only applies to children for studies involving (a) educational testing or (b) observation of public behavior if the investigator does not take part in activities being observed.
Determinations of Exemption

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 the applicable regulations and thus, investigators should submit exempt studies to the IRB Administrative Office for review and determination. For further information on exempt submission and review procedures see Review of Exempt/Non-Human Research.

IRB-01 Relationships

UF Administration

Division of Sponsored Programs(DSP)

The DSP has the authority to review all human subjects research proposals (exempt or nonexempt) and decide whether the institution will permit the research to be conducted. If a project is approved by the IRB, but not permitted by the DSP, the DSP will promptly convey notice to the investigator and the IRB Chair. Neither the DSP nor any other office of the Institution may approve a research activity that has been disapproved by the appropriate IRB.

The DSP will forward certification of IRB approval of proposed research to the appropriate Federal department or agency only after all IRB-required modifications have been incorporated to the satisfaction of the IRB and will arrange for inspection of IRB records as required by Federal Regulations.

The DSP is responsible for ensuring constructive communication among the research administrators, department heads, research investigators, clinical care staff, human subjects, and Institutional Officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.

Additionally, DSP, with the assistance of the IRB, will ensure:

1. solicitation (or confirmation where applicable assurances to comply already exist), receipt, and management of all assurances of compliance (whatever the appropriate format)
2. certifications of IRB review (where appropriate) for all performance sites to this institution and subsequent submission of new documents to the proper Federal department or agency authorities (e.g., OHRP for DHHS) as a condition for involvement of each site in human subject research activities sponsored by DHHS or any other Federal department or agency for which its Assurance applies
3. that all affiliated performance sites that are not otherwise required to submit assurances of compliance with federal regulations for the protection of research subjects at least document mechanisms to implement the equivalent of ethical principles to which this UF is committed
4. that procedural and record-keeping audits will be conducted not less than once every year for the purpose of detecting, correcting, and reporting (as required) administrative and/or material breaches in uniformly protecting the rights and welfare of human subjects as required at least by the regulations and as may otherwise be additionally required by this institution.
Office of Vice President and General Counsel

The UF Office of Vice President and General Counsel is responsible for advising the University's Institutional Review Boards in legal matters involving the use of human subjects in research.

In addition to federal regulations, investigators are responsible for complying with applicable Florida laws and regulations as they pertain to human subjects research, and the IRB is responsible for ensuring human subjects research is conducted in compliance with applicable Florida laws and regulations. Any legal or ethical ambiguity is to be resolved in favor of providing the highest level of protection for human research subjects. Accordingly, in the event of conflict between state and federal law, the law which provides the greatest degree of subject protection is to be enforced. If there is any question regarding the applicability of federal or state law or regulations to human subjects research, investigators, IRB Members or Administrative Staff, and/or Institutional Officials should contact the Office of the Vice President and General Counsel.

The applicability of state law with regard to human subjects research may be incorporated in Position/Opinion Papers written by UF General Counsel, UF Research Administration, and the IRB Executive Committee. Position/Opinion Papers are reviewed and approved by the IRB and posted through a link on the IRB-01 Website. Additionally, when state law and/or other federal laws and regulations (e.g. VHA) may afford additional human subjects protection and may be applicable to IRB decisions to approve research, the IRB may, as applicable, request additional information from investigators and require the disclosure of additional information during the consent process and in the consent form.

Other Committees

For studies requiring approval by other committees, the PI is responsible for contacting and submitting appropriate paperwork to the applicable committee.

Human Use of Radioisotopes and Radiation Committee (HURRC)

HURRC reviews all full Board projects to determine if the protocol involves the use of radiation or radioisotopes. (Note: HURRC does not review exempt and expedited projects because they should not contain any experimental use of radiation or radioisotopes). HURRC review and approval includes suggested risk language for consent forms. The IRB may use the suggested language or revise it as they deem appropriate.

Investigators may choose to submit to HURRC and the IRB simultaneously for therapeutic research projects with definite investigational use of radiation or radioisotopes. Investigators are not required to submit research projects with no definite involvement of radiation or radioisotopes to HURRC for review. However, a member of HURRC will review all new studies seeking full Board approval in order to determine the absence of experimental radiation/radioisotope usage in the project. This will be accomplished by sending an electronic copy of all full Board meeting materials to the HURRC representative (identical to what is distributed to the full Board) prior to the
meeting. HURRC will notify the IRB, and the investigator, if HURRC approval needs to be obtained but has not been requested by the investigator. In these instances IRB approval will be held until receipt of official written approval from HURRC. Otherwise, without notification from HURRC, the IRB will proceed with review and/or approval as necessary.

For research involving non-therapeutic exposure to radiation the IRB will apply the exposure limits for radiation workers. This limit is a maximum absorbed dose of not more then 5 rem per year or 1.25 rem per calendar quarter. Children may not be involved in this type of research. Consent forms for this type of research should contain a strong statement regarding the cumulative nature of radiation exposure.

Institutional Bio-safety Committee (IBC)

The Institutional Bio-safety Committee (IBC) reviews all projects that involve HUMAN GENE THERAPY (protocols that involve the deliberate transfer of recombinant DNA or DNA of RNA derived from recombinant DNA) into one or more human subjects. All recombinant DNA projects require registration with the UF IBC. Studies that involve Human Gene Therapy should be reviewed and approved by the IBC prior to IRB review. Protocols can be sent to the IRB prior to IBC approval, but IRB approval will not be given until final written IBC approval is provided to the IRB.

Clinical and Translational Science Institute (CTSI) Advisory Committee

Researchers who wish to conduct their studies at the CTSI must submit their project separately to both (1) the IRB and (2) the CTSI Advisory Committee. All CTSI research projects must be reviewed and approved by IRB-01 to ensure protection of the rights and welfare of research subjects and must also be approved by the GAC. Further information on conducting research in the CTSI can be found at https://www.ctsi.ufl.edu/

University of Florida Shands Cancer Center (UFSCC) Multidisciplinary Organ Site Groups (MOSG) and Protocol Review and Resource Utilization Committee (PRRUC)

The UFSCC MOSG and PRRUC evaluate the scientific merit, feasibility and resource requirements of proposed UFSCC clinical trials. In order for a protocol to be conducted by the Clinical Trials Office (CTO), it must receive approval from both the MOSG and PRRUC. After receiving the approval of these groups, the protocol can be submitted to the IRB and other applicable committees.

Research Investigators

Responsibilities

Primary responsibility for assuring that the rights and welfare of human subjects are protected and that human subjects research is conducted ethically and in compliance with applicable regulations rests with principal investigators (PI) conducting the research. This responsibility may not be delegated. Faculty, who assign or supervise research conducted by students or staff, have an obligation to consider carefully whether those individuals are qualified to adequately safeguard the rights and welfare of subjects. If a project involves medically related treatment, the PI must designate a qualified clinician who will be responsible for all study-related healthcare decisions. This clinician must agree to participate prior to the initiation of the research project.
In addition to those in this manual, responsibilities of research investigators are described in “PI Responsibilities” available at http://irb.ufl.edu/researcherresponsibilities.htm, letters sent to the PI from the IRB, and the signed Investigator Assurance submitted to the IRB for each new project.

Additional responsibilities for investigators utilizing FDA-regulated test articles are detailed in 21 CFR parts 50, 56, 312, 812 and FDA Form 1572.

Additional responsibilities for investigators conducting research at the NF/SGVHS are detailed in VHA Handbook 1200.05 and at http://www.northflorida.va.gov/NORTHFLORIDA/Research/SCICOM.asp

Investigators are notified of changes in IRB forms, policies and procedures, information pertaining to human subjects’ protection, federal regulations, and other relevant information through the IRB website, the IRB InvestiGator, IRB Forums, and/or educational events.

Training

All research investigators and staff conducting human subjects research are required to complete the Required Reading (available on the IRB-01 website at http://irb.ufl.edu/education/trainreq.htm), HIPAA training and/or training as prescribed by the IRB and/or the Institution where the research will be conducted. For VA research, the VA Research & Development Committee (R&DC) will not approve human subjects research unless applicable VA training has been completed.

Other Institutions

Shands Teaching Hospitals and Clinics, Inc.

Shands Teaching Hospitals and Clinics, Inc has designated UF IRBs 01 and 03 for the review of human subjects research conducted under FWA00005975.

North Florida/South Georgia Veterans Health System

North Florida/South Georgia Veterans Health System (NF/SGVHS) has designated UF IRB-01 for review of human subject research activities under FWA00002606. IRB membership requirements as described in Veterans Health Administration (VHA) Handbook 1200.05 will be maintained at all times.

Under a Memorandum of Understanding (MOU) between UF and the NF/SGVHS, the UF IRB-01 provides review of human subjects research (a) conducted at the NF/SGVHS, (b) by NF/SGVHS staff, and/or (c) that utilizes NF/SGVHS facilities, resources, or patients. A copy of this document is available upon request from the IRB or NF/SGVHS and online at http://irb.ufl.edu/irb01/othercommittees.htm. Projects reviewed on behalf of the NF/SGVHS receive the same IRB review as those reviewed on behalf of UF and copies of initial and renewed IRB approvals are sent to the NF/SGVHS Research and Development office to be reviewed by the Research and Development Committee (R&DC). Full Board and informational minutes are sent to the NF/SGVHS Research Office who will distribute the minutes for review by the R&DC.
Research to be undertaken by or under the direction of the NF/SGVHS, using VA premises, VA resources, VA staff and/or patients, requires review and approval by the UF IRB-01 and the NF/SGVHS R&DC. R&DC approval is required for any VA-approved research protocol involving human subjects. R&DC approval is contingent upon IRB approvals being in place. The R&DC meets monthly. Notification of VA approval is sent to the PI after documented IRB approval. R&DC review and approval is documented on VA form 10-1223 and a copy is sent to the IRB. It is not a requirement to obtain NF/SGVHS approval prior to final approval by the IRB, but both IRB and R&DC approval must be obtained prior to initiation of a study at a NF/SGVHS facility. Once approved, any revisions to a project must be reviewed and prospectively approved by the IRB and submitted to the NF/SGVHS subcommittees. The PI is responsible for knowing and following VA policy as it relates to human subjects research and protection and training requirements in VA facilities. VA Handbook 1200.05 “Requirements for the Protection of Human Subjects in Research” and other applicable NF/SGVHS Manuals and Forms specific to VA research are available through links at the IRB-01 website.

For research involving the VA, the IRB will review the information present in Addendum V the VA Informed Consent Document (VAF 10-1086), the VA Authorization for Release of Protected Health Information for Research Purposes, and the VA Consent for Use of Picture or Voice (VAF 10-3203) to insure compliance with VA regulations.

**Regulatory Agencies**

UF has filed an FWA with the DHHS Office for Human Research Protections (OHRP) affirming that the University is in compliance with 45 CFR 46. This assurance applies to all research involving human subjects regardless of source of funding.

In studies involving products regulated by the Food and Drug Administration (FDA), UF complies with the requirements set forth in 21 CFR parts 50, 56, 312, and 812.

The VP for Research or designee serves as the communication interface with regulatory agencies such as OHRP and FDA.

**IRB Membership**

**Number of Members**

The UF IRB membership will be consistent with 45 CFR 46.107 and 21 CFR 56.107 and will have at least five members including at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. The IRB membership will include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

**Qualifications of Membership**

IRB members, with varying expertise, experience, education, training, and diversity are selected (1) to promote complete and adequate review of research activities commonly conducted by the institution and (2) to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. CVs for all members are maintained in individual
member files located in the IRB Administrative Office. Potential members must be nominated by their Department Chair and be willing to serve a three-year term.

Diversity of Membership

The IRB membership is monitored to assure diversity of its members, including representation by varying professions and ethnic backgrounds, both genders, individuals knowledgeable about community attitudes and subject populations (i.e., Veterans), and individuals knowledgeable about and experienced working with vulnerable subjects and/or populations. If there is not adequate representation at a given meeting or available on the Board, review may either be deferred or tabled until such representation is available and/or consultation is obtained. Board composition is reviewed and evaluated by the IRB Executive Committee in conjunction with UF Research Administration as changes in membership occur and/or as needed to meet regulatory or organizational requirements. Departments, colleges, and/or others, as applicable, are requested to submit the names of qualified individuals for service when a need is identified.

Appointment of Members

The VP for Research appoints all IRB voting members and alternates for renewable three-year terms upon recommendation of Department Chairs. Prior to appointment as a voting member or alternate, candidates must complete all required training as described in “Training of IRB Chair and Membership.” Once the required training is completed a letter of appointment from the VP for Research will be sent to the appointee and a copy sent to the IRB Chair and member file. Members may be reappointed to a new three-year term without a lapse in service at the end of each term.

Because of its affiliation with the NF/SG VHS, IRB-01 will include at least two appointed VA representatives (salaried for at least 5/8 FTEE) as full voting members (responsible for reviewing any kind of research presented to IRB-01, including research that does not involve the VA). One of these representatives must have scientific expertise. VA representatives to the IRB are selected per VA policy and nominated in writing by the VA Medical Center Director. No VA member of IRB-01 may serve as chair or acting chair of IRB-01. Individuals from VA R & D Administration, including the Associate Chief of Staff for Research and Development and the Administrative Officer for Research and Development, may not serve as voting members of the IRB.

Alternates

Voting members may have an alternate or alternates. To ensure maintaining an appropriate quorum, an alternate’s qualifications should be comparable to the primary member to be replaced. Alternates are nominated and appointed in the same manner as voting members, and provided the same educational materials and training as regular members. Voting and alternate members are listed on the IRB’s membership roster. Ad hoc substitutes are not utilized in the absence of an IRB member or alternate.

Alternate board members replace voting members who are, on occasion, unable to attend convened meetings of the IRB. Alternate members may attend all convened meetings but are non-voting members unless they are attending in the place of the primary voting member, in which case they become voting members. When alternates
substitute for a voting member, the alternate will receive and review the same materials that the full member would have received. The IRB Minutes document when an alternate member replaces a voting member.

Responsibilities

The UF IRB membership is responsible for complying with and ensuring compliance with federal regulations for the protection of human subjects and applying ethical principles in the review of research in order to protect human research subjects. Other responsibilities of members include serving as designated reviewers for assigned protocols, reviewing assigned materials in advance of scheduled meetings, and, presenting their review at the IRB Meeting for which the project was assigned which includes assessment of risk level, recommended action and recommended period of approval. If the IRB Chair or Assistant Director of IRBs determines that a member is not adequately fulfilling his/her responsibilities, the VP for Research may revoke the member’s appointment, alter their appointment (move them to alternate or shorten their appointment period), or ask the reviewer to resign their appointment.

Attendance

Voting members are expected to attend all meetings of the convened Board. If unable to attend a scheduled meeting, the voting member should notify the IRB-01 Administrative Office at the earliest possible time, and arrange for their designated alternate to attend. Any voting member who misses meetings without sending an alternate (and whose absences have not been excused by the Chair) may forfeit membership on the IRB and/or may be removed from the IRB by VP for Research. Members (both voting and alternate) are asked to sign an attendance sheet for each meeting and indicate their anticipated availability for the three subsequent meetings.

Performance Appraisal

The IRB Chair and Executive Committee may consider the following criteria when evaluating IRB Member performance: meeting attendance, pre-meeting preparation, level of participation in meeting discussion, completion and submission of applicable comment sheets, and knowledge of human subjects protection ethical principles and regulations. IRB Membership and Member performance are discussed on the second and fourth Wednesdays of the month at the IRB Executive Committee Meetings and upon reappointment.

Support Staff

The Assistant Director (AD) of IRBs, IRB Coordinators and General Counsel are available at full Board meetings and/or upon request in order to provide clarification as needed on institutional policy, state law, and federal regulatory requirements.

**IRB Management**

**IRB Chair**

The VP for Research is responsible for appointing the IRB Chair, who must have been a member of the IRB for at least two years. The term of appointment for the Chair is
three-years and is renewable. The Chair is charged with the general supervision of the activities of the Health Center IRB-01. The University will provide orientation and training opportunities at the local and/or national level in IRB-01 matters. The Chair provides leadership and promotes activities that protect human subjects who participate in research and fosters an environment conducive to scholarly research.

The duties of the Chair, include, but are not limited to the following: presides at all meetings of the IRB-01; calls special meetings of the IRB-01 as needed; advises and counsels investigators; screens potential IRB-01 Board Members and presents acceptable nominees to the Vice President’s Office for review, selection and appointment; makes decisions on emergency conditions as they relate to the IRB-01’s protection of human subjects in compliance with federal regulations; keeps the IRB-01 informed of developing problems in the area of human research on any project that has been reviewed or is going to be reviewed; communicates regularly and frequently with the IRB-01 staff concerning IRB-01 matters; performs functions delegated to an official of the IRB-01 in accordance with University, state and federal regulations; appoints two or more Vice-Chairs as necessary; designate experienced reviewers from the IRB membership to conduct reviews of research under expedited review procedures (explicit changes); approves Unaffiliated Investigator Agreements with the Vice President; assist with educating the research community; represent the Board at certain institutional meetings; and appoints ad hoc and standing subcommittees as needed. Subcommittees may be chaired by Vice-Chairs or others as designated by the Chair. The IRB Chair does not have any specific pre- or post- full Board meeting duties unless requested by the IRB Administrative staff or others.

Chair performance is evaluated by the VP for Research upon re-appointment. Indicators of Chair/Vice Chair performance (e.g. turnaround time on expedited items) are discussed biweekly at IRB Executive Committee. The Chair and Vice Chairs may be referred to as “Executive Reviewers.”

Vice-Chairs

Two or more Vice-Chairs will be designated by the Chair (from the IRB Membership) and may then serve in this capacity so long as they and the Chair deem appropriate. Vice-Chairs must be experienced voting members, be willing to serve in this capacity, be oriented by the Chair or another experienced Vice Chair, and have the time and support of their respective departments to fulfill this role. Vice-Chairs may serve unlimited terms as determined by the Chair (during the tenure of the Chair) and their particular membership appointment terms. The University will provide orientation and training opportunities at the local and/or national levels in IRB-01 matters. The Vice-Chairs' duties include, but are not limited to, presiding over meetings in the absence of the Chair, conducting expedited reviews and reviews of materials as defined by IRB policy, assisting the Chair in the operation of the IRB-01, and other duties as assigned by the Chair. The Vice Chairs do not have any specific pre- or post- full Board meeting duties unless requested by the IRB Chair, IRB Administrative staff, or others.

Executive Committee

The Chair, Vice-Chairs, Assistant Director for IRBs, and IRB-01, Quality Assurance (QA), and HIPAA Coordinators constitute the Executive Committee of the IRB. The UF Assistant General Counsel serves as the Committee’s advisor and the Director of DSP
may attend as situations warrant. This group meets biweekly and as needed to plan, review and otherwise assist the IRB members and staff, and provides administrative leadership in matters pertaining to the IRB and human subjects’ protection.

Training of IRB Chair and Membership

Each new member of the IRB (including alternates) will be provided orientation and training through:

1. Issuance of an IRB Orientation Manual and Institutional Review Board Member Handbook;
2. Attendance at an IRB orientation and training seminar;
3. Completion of assigned readings which include but are not limited to 45 CFR 46, the Belmont Report, the UF FWA, Chapter 3 of the IRB Guidebook, OHRP Tips on Informed Consent, the IRB website, and the IRB Policy and Procedure Manual;
4. Completion of the NIH web based module (http://69.5.4.33/c01/) and submitting the Certificate of Completion to the IRB office;
5. Viewing OHRP department of education videotapes;
6. Mentorship with experienced IRB member;
7. Initial meeting with the IRB Chair prior to appointment; and
8. Continuing education through review of the IRB Newsletters, periodic material provided at IRB meetings (including, but not limited to, updated OHRP Guidance Documents), attendance at annual retreat/training seminars, and external meeting attendance.

Completion of training will be documented prior to appointment. Documentation of training will be maintained in the Board Member’s file located in the IRB-01 Administrative Office. Experienced members appointed as Vice-Chair will be mentored by the Chair or another experienced Vice-Chair.

Compensation of IRB Members

IRB members do not receive direct monetary compensation above their base University salary for participation on the Board. The Member’s Department may receive compensation for the time commitment of the member from the Individual College represented.

Non-affiliated and non-scientific members may be reimbursed for travel, other expenses, or a nominal amount to compensate for the time spent in the Board meetings.

Member Liability

IRB members function as employees or agents of the University of Florida, and as such are covered by Section 768.28, Florida Statutes. IRB members may not be held personally liable in tort or named as a party defendant in any action for any injury or damage suffered as a result of any act, event, or omission in the scope or his or her function as an IRB member, unless he or she acted in bad faith or with malicious purpose, or in a manner exhibiting wanton and willful disregard for human rights, safety, or property.
Consultants

Members of the IRB are qualified to protect the rights and welfare of research subjects and have the competence and knowledge to review research. Any appointed member of IRB-01, through education, training, and experience, may provide ethical review of projects submitted for consideration by the Board. The IRB may, at its discretion, invite individuals with competence in special areas to assist in the review of complex projects that require expertise beyond or in addition to that available on the Board [45 CFR 46.107 (f)][38 CFR 16.107(f)][21 CFR 56.107(f)]. Projects most likely to require outside consultation may include but are not limited to those that are greater than minimal risk with no direct benefit to subjects or include populations that may be vulnerable to coercion or undue influence. At any time during the review of a protocol, the Executive Reviewer, IRB or Administrative Office (upon consultation with the Chair and/or AD of IRBs) can request consultation. If additional review is deemed necessary, the IRB Chair, IRB Executive Committee, Assistant Director of IRBs, and/or Full Board may select and contact consultants (verbally or in writing), who may or may not be members of the UF Community. Consultants may not have any conflicting interest in the project under review including any of the following items reviewed by the Full Board or outside of Board (e.g. by a Chair): new studies, continuing reviews, revisions, unanticipated problems, adverse events, or noncompliance. As a result consultantssshould complete a Conflict of Interest Disclosure Form that will be maintained with the consultant’s comments in the IRB file.

The IRB will provide the consultant with an electronic and/or paper copy of the submission as well as any supporting documentation that the IRB deems appropriate. The consultant will be asked to provide written comments to the IRB prior to the applicable meeting and consultant comments will be presented by at the convened meeting at which meeting the project is reviewed. If present, consultants may be asked to provide verbal comments during the convened meeting at which the project will be discussed. These individuals may participate in the discussion and deliberation of the submission, but may not vote with the IRB (45 CFR 46.107 (f)). Any written comments will be maintained with the IRB file.

Conflict of Interest

IRB regulations 21 CFR 56.107 and 45 CFR 46.107 state that no IRB may have a member participate in the IRB’s review of any submission in which the member has a conflicting interest, financial or non-financial, except to provide information requested by the IRB. For full board studies, both the electronic and hard copy agenda for each project will indicate if any Board Member has a conflict for any given project. For purposes of this policy, IRB member includes the voting or alternate IRB member or consultant, and the immediate family of the member including spouse and any knowledge of dependent children’s interest.

An IRB Member has a conflict of interest when that individual has any financial interest in which the value could be affected by the outcome of the research, or non-financial interest or any personal or professional relationship or reason, which may make it difficult for the individual to exercise independent judgment in safeguarding the rights and welfare of human research subjects.
An IRB Member may have either a financial conflict of interest, non-financial conflict of interest, or both.

Examples of Financial Interests:

a. Salary or other payments for services (e.g., consulting fees or honoraria);

b. Equity interests (e.g., stocks, stock options, or other ownership interest); and/or

c. Intellectual property rights (e.g., patents, copyrights and royalties from such rights)

d. Research subject to DHHS regulations: financial interests greater than or equal to $10,000.00, even if the value will not be affected by the outcome of the research.

e. Research subject to FDA regulations: financial interests greater than or equal to $50,000.00, even if the value will not be affected by the outcome of the research.

Diversified mutual funds or similar instruments in which the shareholder has no control over the equities held by the fund are not considered to present a conflict of interest.

Non-financial Conflict of Interest

Non-financial conflicts of interest may include, but are not limited to, an IRB Member’s service in any of the following categories with respect to the research protocol under review:

a. Principal Investigator (PI)

b. Co-principal Investigator

c. Investigator receiving funding from the study, as listed in the study budget

d. A supervisory role over the PI of the study

e. Family member of PI

f. Involvement in the design, conduct or reporting of the research

g. Board or executive relationship related to the research regardless of compensation.

Other non-financial conflicts of interest may also arise if an IRB member has an interest that that member believes conflicts with his or her ability to objectively review a protocol.

Business development:

Competing business interests can influence the review process when individuals responsible for business development serve on the IRB or are involved in the day-to-day operations of the IRB. As a result, individuals involved in business development or who own equity in the institution may not serve as a full or alternate member on the IRB or carry out day-to-day operations of the IRB.
Disclosing Conflicts of Interest:

IRB Members shall complete the Health Science Center Institutional Review Board (IRB-01) Disclosure Form (Disclosure Form) upon appointment, and then annually and/or as new reportable interests are obtained. Forms shall be maintained in the IRB Office. Consultants shall complete a Disclosure Form that will be maintained with the consultant’s comments in the applicable IRB file.

IRB Members shall also disclose to the IRB any non-financial conflicts of interest prior to discussion of the protocol under review.

Evaluating Conflicts of Interest:

Each conflict of interest shall be presented to and evaluated by the Assistant Director for Compliance. Completing and/or updating the Disclosure Form shall fulfill this requirement. The Assistant Director for Compliance shall determine whether a conflict exists or can reasonably be construed to exist and communicate this to the IRB Administrative Office for inclusion in the IRB database.

Managing Conflicts of Interest:

If a conflict is deemed to exist, the following procedures shall be followed:

Items reviewed at Full Board and through Expedited Review Procedures

a. IRB members with a known conflict of interest will not be assigned to review submissions in which there is a conflicting interest.

b. The IRB Members with conflicts of interest shall be listed on the Meeting Agenda.

c. The IRB Member shall make prompt, full, and frank disclosure of his or her conflict to the IRB prior to discussion of the research protocol involved.

d. The IRB Member shall not participate in the IRB’s review, discussion, or voting of any research protocol or submission (including but not limited to new studies, continuing reviews, revisions, adverse events, unanticipated problems involving risk to participants, and non-compliance) in which he or she has a conflict, except to provide information requested by the IRB. The IRB Member should leave the room prior to the IRB’s final deliberation and vote.

e. IRB Members and/or Executive Reviewers will be assigned to review submissions in which no conflicting interest has been identified based upon review of the IRB database and/or meeting agenda. If the IRB Member is assigned as a reviewer for a protocol in which the individual has a conflict of interest, the IRB Member shall notify the IRB Office so that the protocol can be reassigned.

f. If a Chair or Vice-Chair receives items for expedited review in which a financial or non-financial conflict of interest exists (i.e. investigator or sub-investigator on the project), the reviewer should:

1. notify the IRB office of the conflict so the item can be reassigned, or
2. refer the item to the full board for review.

g. The IRB may take appropriate disciplinary action against any member who violates this policy.

h. The minutes of the IRB meetings involving conflicts shall include the names of the persons identified as having a conflict, that the conflicted member did not count toward quorum, and that the conflicted member was absent if they left the room. The database shall reflect conflicted members as not voting and/or having left the room.

Note: Florida’s Open Meetings Law (Florida Statute § 286.011) mandates that all meetings of any board or commission be open to the public at all times. As a result, persons with conflicts may not be required to leave the room during the deliberation or vote for any projects in which they have a conflict. While the IRB cannot force individuals with a conflict to leave, the IRB will request it. If the conflicted individual chooses to remain in the room they may not participate in the discussion (except to provide information to the IRB), deliberation, or vote and cannot count towards quorum.

IRB-01 Administrative Staff

The IRB-01 Administrative Staff consists of an Administrative Coordinator and support staff, all of who are employees of the University of Florida and who support the protection of human research subjects and the IRB process. Specifically, the IRB Administrative Staff:

1. complies with applicable federal and state regulations and laws, university policies, and ethical obligations to protect human subjects;
2. assists with the preparation, monitoring, and documentation of IRB Meetings;
3. maintains files on human subjects research;
4. maintains the UF IRB-01 database for tracking studies;
5. receives, reviews, prepares, and distributes submissions for review;
6. prepares, distributes, and maintains the IRB meeting and informational minutes;
7. screens all research submissions (including new applications, continuing review submissions, revisions, tabled items, miscellaneous items, etc) for completeness and compliance with acceptability standards prior to initiating the IRB review process;
8. acts as a resource for investigators and research team members on general regulatory information, guidance with IRB-01 forms, and assistance with the preparation of submissions for IRB review;
9. generates and sends reports of all IRB decisions to Investigators, which include, but are not limited to, notices of approval, study closure, and termination for applicable projects;
10. sends reports of applicable IRB decisions to appropriate Institutional Officials, and VA R&D Committee;
11. interfaces with other offices (e.g. VA, DSP, etc) for research administration;
12. generates and sends reminder notices to investigators of upcoming continuing reviews;
13. corresponds with Principal Investigators to inform them of IRB decisions, required revisions, and requests for additional information/documentation to assist with the IRB decisional process;
14. maintains information on federal regulations relating to human subjects research;
15. provides education regarding the human subjects protection, the IRB process and Federal regulations to the University community;
16. maintains records of IRB membership including appointment letters, CVs, human subjects protection training, contact information, and conflict of interest disclosures;
17. maintains and updates IRB policies and procedures, IRB forms and website; and
18. maintains documentation of IRB activities and retains records in accordance with Federal regulations.

IRB-01 Administrative Staff are employees of the University of Florida and are subject to the policies and procedures of Human Resource Services. Employees are selected based on these policies, a review of their qualifications and final selection by their manager. IRB staff is evaluated annually by their supervisor in compliance with University policy.

Office hours and location

The IRB-01 Administrative Office is located in the J. Hillis Miller Health Science Center. The hours of operation are 8:00 a.m. until 5:00 p.m., Monday through Friday, except during official UF holidays. The mailing address is P O Box 100173, Gainesville FL 32610-0173. The phone number is (352) 273-9600. The fax number is (352) 273-9614. The IRB web page is located at http://irb.ufl.edu/irb01/. The e-mail address for IRB-01 is ufirm-l@lists.ufl.edu, which distributes e-mail to select IRB-01 staff and Executive Committee members.

Resources

The UF IRB-01 will be provided with sufficient resources including, but not limited to, office space, reproduction equipment, filing space, meeting space, and computers including all systems as required for full compliance with applicable regulations.

IRB Functions

Review of Research

General Information

All activities meeting the federal regulatory definitions of human subjects research or clinical investigation (45 CFR 46.102; 21 CFR 56.102), unless exempt under applicable regulations, require prospective IRB review and approval prior to initiation. During the review of research, the IRB assesses the proposed protections of the rights and welfare of human subjects participating in research. Regardless of the type of review (expedited or review at a convened meeting), the investigator is notified in writing of IRB determinations. Information pertaining to the conduct of human subjects research under the oversight of IRB-01, including but not limited to policies and procedures, forms and forms instructions, and informed consent procedures (process and documentation) are available at the IRB-01 website.

Scientific Review of Proposed Research

The IRB conducts scientific and ethical review of all human research under its purview drawing on the knowledge and expertise of the IRB Membership to assess the scientific or scholarly validity of proposed research. Through education, expertise and experience, IRB members are
knowledgeable enough to determine when they do not have the expertise to conduct adequate review. The IRB may, at its discretion, draw on the knowledge and expertise of others (consultants, funding and oversight agencies such as the NIH and FDA, or organizational scientific review committees) to assist in this assessment. If consultants are utilized in the review process, comments are communicated to the Board by a designated reviewer and any written comments are maintained with the IRB file. Reviews by other sources including, but not limited to, the CTSI Advisory Committee, UF Cancer Center Protocol Research Review Committee, and the VA R&D Committees may supplement IRB review. In the event that these outside (of the IRB) committees require the research to be revised to improve scientific/scholarly validity, the investigator must submit these changes to the IRB and the applicable committee (as required by institutional policies) for approval prior to implementation. The IRB remains the final authority in assessing scientific or scholarly validity. Documents relevant to scientific and/or scholarly review are distributed according to IRB policy (see Full Board and Expedited Review) and maintained in the applicable IRB file.

Criteria for approval of Research

Federal regulations [45 CFR 46.111 and 21 CFR 56.111] set forth the criteria for IRB approval of research at initial and continuing review. In order to approve research, the IRB must determine:

- Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

- Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

- Unless appropriately waived by the IRB, informed consent will be sought from each prospective subject or the subject’s legally authorized representative and documented in accordance with and to the extent required by §46.116 and §46.117, respectively.

  - For VA research, legally authorized representatives may only consent for potential subjects who are either incompetent or have impaired decision making capacity. This must be documented in the medical record with a signed and dated progress note.

- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. For protocols that pose greater than minimal risk to subjects, the investigator is asked to provide information on plans for data and safety monitoring.

- When appropriate, the research contains adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
Investigators provide information needed by the IRB to make the determinations required under regulation in the initial submission (protocol, introductory questionnaire and applicable addenda, advertisements) and at continuing review and if research activities change during the conduct of the research. Position/opinion papers (e.g. paying subjects, finder’s fees and advertising), researcher tools (e.g. informed consent checklist), and instructions (e.g. consent process) are available on the IRB-01 website to provide guidance to the research community.

The IRB forms have been designed to elicit information, in sufficient detail, that the IRB needs to review, consider and evaluate in order to make the determinations required under regulation [45 CFR 46.111 and 21 CFR 56.111] and approve research. Additionally, the consent document templates have been formatted in such a manner as to include all of the mandatory elements of consent and additional elements of consent. In addition, other documents that supplement the IRB forms in providing the requisite information for the IRB to make such determinations are required.

The IRB reviews and evaluates research on a protocol by protocol basis to ensure that adequate human subjects’ protections are in place and determines that regulatory criteria for approval have been met during the initial and continuing review of research. The IRB must assess numerous issues including: the purposes of the research, setting in which the protocol will be conducted, procedures for recruiting and enrolling subjects, if potential subjects will be vulnerable to coercion or undue influence, inclusion/exclusion criteria, and influence of reimbursement or compensation to subjects. Reviewer comment sheets guide the IRB in their reviews, determinations, and documentation and tools such as the ICF checklist provide additional guidance. If there is insufficient or incomplete information or if the IRB determines that provisions for protecting subjects are not adequate and criteria for approval are not met based upon information provided, the IRB cannot approve the research and the investigator will be notified and asked to provide additional information as applicable.

Documentation that criteria for approval have been met, will be in the minutes and reviewer comment sheets, and in documents submitted by the PI and reviewed and approved by the Chair and/or Board, including but not limited to, protocol, informed consent forms, introductory questionnaire, waivers of consent and documentation of consent, HIPAA authorizations or waivers, and/or other documents available in the IRB file.

Determination of the CR date

In compliance with the federal regulations, the UF IRB conducts continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. The continuing review date is calculated from the date that the convened IRB or Executive Reviewer (if reviewed under expedited procedures) approved the protocol or approved the protocol with explicit changes for the duration (e.g. 6 or 12 months) approved by the Board. In accordance with regulatory guidance, continuing reviews that are approved within 30 days before the prior IRB approval period expires may retain the anniversary date as the date by which the next continuing review must occur.

Management of Protocols with Lapsed Approval

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. As a result, investigators
are required to submit a copy of the UF Continuing Review/Study Closure Report (CRR) (available at http://irb.ufl.edu/irb01/forms.htm) on all Expedited and Full Board projects prior to the expiration date, even if the study is completed or the investigator has no intention of continuing the project. Both initial approval and re-approval letters sent to the PI detail their responsibilities in timely continuing review and implications of study expiration. The “expiration date” that appears on correspondence from the IRB (e.g. approval and re-approval letters, expiration notices and expiration letter) is the first date that the research is no longer approved. Investigators can view project expiration dates at any time via the IRB-01 Web Functions located at: https://shands.org/cgi/irb/secure/login_irb.asp.

As a service to Investigators, IRB-01 Administrative Office sends out first and second Expiration notices (generated by the IRB database) 90 and 45 days prior to a study’s expiration. Instructions for submitting continuing review paperwork are included in hard copy with the 90 day notice and are available on the IRB website and on the CRR. Upon expiration of approval, the study status in the IRB database indicates study expiration. Once a study expires, the IRB Administrative Office sends an expiration notice indicating that all research activities must stop and none of the following activities can occur: (1) collection, use, or reporting of any data; (2) performance of any study interventions, unless the IRB finds that it is in the best interests of individual subjects to continue participating in research interventions or interactions; (3) enrollment or screening of any new subjects; and/or (4) receiving any study funding. If a study expires and enrolled subjects are undergoing study interventions, the PI must contact the IRB who will determine if it is in the best interest of the subject to continue participation. For VA research the PI and IRB will follow the guidelines as outlined in VHA Handbook 1200.05 and the NF/SGVHS Human Research Protection Program Procedures for the Protection of Human Subjects in Research. There is no grace period extending approval for the conduct of research beyond the expiration date. Once a project expires, IRB review and re-approval must occur before re-initiation of research occurs. The Principal Investigator is given an additional 30 days from the expiration date to submit the Continuing Review/Study Closure Report. For any project that is allowed to expire and for which a Continuing Review or Study Closure is not received within 30 days of expiration, the project may be moved from “expired” status to “expired non-renewable” status. To conduct further research on a project that has been moved to “expired non-renewable, the PI must re-submit the project according to the guidelines for new project submissions.

For protocols with lapsed approval, a deviation comment sheet will be included along with the submission to the Executive Reviewer and/or Board. Expiration of IRB approval will be evaluated by the Executive Reviewer and/or IRB in accordance with the IRB’s non-compliance policy (page 53) and determinations will be documented on the applicable deviation reviewer comment sheet. (For expired full board studies, a second line will have to be entered into the database indicating a deviation thus generating a deviation comment sheet. For expired expedited studies, a deviation/non-compliance comment sheet will be attached. The Executive Reviewer can determine that the non-compliance is neither serious nor continuing or refer to full board for further determination. Expirations are noted in the Compliance section of the Project History which is included with all continuing reviews) The Executive Reviewer/Board will determine on a protocol by protocol basis whether the expiration is serious and/or continuing and the determination will be documented on the applicable RCS and/or in the IRB minutes. The PI will be notified in writing of the IRB determination. Expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under DHHS regulations.
Re-activating a Closed Research Protocol

If a Principal Investigator, in good faith, closes a protocol which he or she believes is completed, but then wishes to re-activate the research due to a request by the sponsor, or another reason deemed appropriate by the IRB Chair or designee, then the Principal Investigator must submit a letter requesting that the study be re-opened along with the reason(s) for re-activating the research protocol. In addition, the P.I. must submit a new fully completed continuing review form. Only protocols that have not met their last continuing review expiration date can qualify for a re-activation. Re-activation of Full Board protocols must be done by the Full Board. The re-approval date for the re-activated research protocol will be determined by the Executive reviewer or Full Board, but will not exceed one year.

Temporarily re-opening a Closed Study for Administrative, Data Collection, or Data Analysis reasons:

If a Principal Investigator, in good faith, closes a protocol which he or she believes is completed, but then wishes to temporarily re-open the study for administrative, data collection, or data analysis reasons, or another reason deemed appropriate by the IRB Chair or designee, then the Principal Investigator must submit a letter requesting that the study be re-opened along with the request(s) for temporarily re-opening the research protocol. The executive reviewer will evaluate the request; insure that it is minimal risk, and that the request is in the spirit of the consent form signed by study subjects (when applicable).

If the temporary re-opening of the study is allowed, the study will be approved as a “Longitudinal Status” and remain open per current UF IRB-01 policy.

Reviving a Research Protocol that has been moved to “Longitudinal Review” or otherwise is closed to enrollment and all study interventions are complete on all study subjects.

The IRB will move a protocol to “Longitudinal Review” status, based on information provided by the Principal Investigator who indicates that recruitment is complete and that all research activities have been completed on all study subjects, and only follow-up activities remain. If the P.I. wishes to revive the research due to either enrolling additional study subjects or initiating study related activities, then the Principal Investigator must submit a letter requesting that the study be revived along with the reason(s) for re-activating the research protocol. In addition, the P.I. must submit a new fully completed continuing review form. Reviving of Full Board protocols must be done by the Full Board. The re-approval date for the revived research protocol will be determined by the Executive reviewer or Full Board, but will not exceed one year.

Grant Review

Department of Health and Human Services (HHS) regulations [45 CFR 46.103(f)] require that each application or proposal for HHS-supported human subject research be reviewed by the IRB to ensure that all research described in the IRB Protocol is consistent with the application or proposal. The requirement for IRB review of each application or proposal for HHS-support applies only to the awardee institution; therefore, for DHHS funded research in which UF is the awardee institution, a full copy of the HHS grant application, excluding appendices, must be provided by the investigator to the IRB for review and approval at the time funding is obtained. If an applicable grant proposal is not submitted or if the protocol is not consistent, investigators
will be contacted by the IRB. Documentation of grant review is noted in the IRB-01 database and in the project file.

Review of Research

In its review of research, the IRB has the authority to approve, require modification (to secure approval), or disapprove proposed research involving human subjects. Following its consideration of a proposed project, the IRB will notify investigators and the institution of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity.

Full Board Review

The UF IRB is required to conduct initial and continuing reviews of all non-exempt research at convened meetings at which a majority of the members are present, unless the research falls into one or more categories appropriate for expedited review.

A majority of voting members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present to conduct a convened meeting. For research to be approved, it must receive the approval of a majority of those members present at a meeting where a quorum is present.

Guidelines and instructions for completing and submitting paperwork to the IRB are available on the IRB website at http://irb.ufl.edu/irb01/forms.htm or in the IRB-01 Administrative Office. Protocols must be submitted to the IRB-01 Administrative Office prior to a meeting’s deadline in order to have it prepared and reviewed at a given meeting. Information pertaining to Full Board Meetings (http://irb.ufl.edu/irb01/fullboardmeetings.htm) and Deadlines for IRB Meetings (http://irb.ufl.edu/irb01/deadlines.htm) are posted on the IRB-01 Website.

For submissions requiring consideration by the Full Board, the submission is logged into the tracking log, entered into the database by experienced IRB staff, pre-reviewed as applicable, assigned a meeting date, copied, prepped and scanned according to IRB-01 administrative procedures, entered into the agenda, and forwarded for reviewer assignment (see Reviewer Assignment).

IRB-01 uses a modified primary reviewer system for actions requiring review by the convened IRB. This “modified” system provides that all IRB members, not just the designated reviewers, receive an electronic copy of all full board submissions including all documents submitted by the PI (except the Investigator’s Brochure, HHS grant applications, and extensive survey instruments) rather than only a protocol summary and consent form. Designated reviewers (in the case of new studies, three reviewers; in the case of all other submissions, two reviewers), receive hard and electronic copies of all materials submitted by the PI and are considered the lead reviewers for the assigned project. Designated reviewers are responsible for: Conducting an in-depth review of submitted materials and documenting this review using the applicable IRB-01 Reviewer Comment Sheets, contacting the Investigator prior to the assigned meeting, when possible, to resolve outstanding issues and leading the discussion of the assigned project. Investigators, or a designee of the Investigator, are encouraged to attend Full Board Meetings to provide information as requested by the IRB. In all cases, assigned reviewers and all other members of the IRB will be asked for any comments or recommendations. Prior to the final deliberation and vote, investigators and/or IRB Members with conflicts of interest are asked to leave the room. Florida State law permits conflicted individuals to remain present, although they
may not participate in the deliberations or vote. Prior to each vote, a quorum is verified by IRB administrative and support staff. Final deliberations will occur, including a recommendation for action (which will include appropriate information to comply with regulations such as assessing a risk level, approval period, etc), and a final vote is taken and recorded.

Any IRB member, upon request, can have access to the complete IRB protocol file. All IRB members have full opportunity to discuss each research proposal during the convened meeting.

Reviewer Comment Sheets are attached, as applicable, to each hard copy of submissions assigned for review. Reviewer Comment Sheets serve as guidance in determining whether the protocol meets criteria for approval and/or other regulatory requirements and help document project review. Unassigned reviewer comment sheets are available to the entire IRB membership for any protocol undergoing review. Designated reviewers (and any unassigned reviewer with written comments) should fully complete and submit all applicable Reviewer Comment Sheets to the IRB administrative staff during or immediately following the meeting. Additional comments made by the reviewers in the form of narrative notes, annotations to any documents (e.g. consent form), and/or e-mail correspondence between the IRB and investigator, should be submitted to the IRB Office along with the Reviewer’s Comment Sheet, for maintenance in the IRB project file per the Record Retention Policy. Documentation of applicable protocol specific findings required under regulation will be in relevant documents submitted by the investigator and reviewed and approved by the IRB, minutes, and/or reviewer comment sheets.

Initial Review

Initial review of research must be conducted at a convened meeting except where expedited review is allowable under the Federal regulations. In order for a project to be approved, it must receive the approval of a majority of the quorum and meet the regulatory criteria for approval as described above.

Definition: New protocols submitted for Full Board review include those that are first time submissions, those that have been expired greater than 30 days (“expired/non-renewable”), or those that have been closed and that the investigator wishes to re-activate, and which do not meet the criteria for expedited review or exempt status. New protocols may be submitted at any time but must meet the published IRB deadline to be placed on the agenda of a particular meeting and must meet submission acceptability guidelines as described on the IRB-01 website. The approval period for a protocol starts on the date of the convened meeting at which the IRB approved the protocol or approved the protocol with explicit changes. The approval period can be no longer than 12 months and is based on the information provided to the IRB and the perceived risk to the subjects.

Investigator Responsibilities: The Principal Investigator must submit the following documents to the IRB for review and consideration at the time of initial review: Introductory Questionnaire (IQ) including any applicable addenda (including Addendum V for research involving the VA) and supplementary information as requested, protocol (either sponsor’s protocol or investigator-initiated protocol written in IRB required format available on the IRB-01 website), informed consent form written in IRB required format (unless a waiver or waiver of documentation of consent is requested as described in “Informed Consent Instructions”), any relevant merit review or grant application (if applicable), Investigator’s Brochure or equivalent material (if applicable), copies of applicable subcommittee approvals (e.g. HURRC, IBC), advertisements (or other materials intended to be seen or heard by subjects; must include all actual print, audio, and/or
video advertisements – See IRB Position Paper on Advertisements That Directly Recruit Subjects), subject surveys and/or questionnaires, and any other information that the Investigator deems pertinent to review of the project. For DHHS-supported multi-center clinical trials, any DHHS-approved protocol and sample informed consent documents should be submitted.

Investigators enrolling subjects who do not speak or read English should see the Informed Consent Instructions and applicable position paper on the IRB-01 website.

**Office Responsibilities:** New protocols received by the IRB Administrative Office, are assigned a new protocol number, entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Investigators or their designee are contacted as appropriate to provide clarification and/or documentation prior to Board Review. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at http://irb.ufl.edu/irb01/forms.htm) will be scheduled for the meeting. Once complete, as determined by the Administrative Office, the submission, including all documents submitted by the PI and applicable IRB forms, including but not limited to Informed Consent Checklist and/or HIPAA Review Sheet (“Green Sheet”) is forwarded for inclusion on the applicable Full Board meeting agenda and for reviewer assignment. Once assigned, Reviewer Comment Sheets are attached to each hard copy. All documents listed on the agenda and those provided by the IRB Office are distributed to designated reviewers in hard copy and to the entire membership on CD.

**Reviewer Responsibilities:** During the week prior to the meeting (whenever possible), all board members will receive an electronic copy of all documents submitted by the Investigator for each new protocol.

Three specific designated reviewers are assigned to review initial submissions; one of which is considered the lead reviewer. All of the designated reviewers will receive a hard copy of all supporting documents in addition to the electronic copy. HHS grant applications and if available, DHHS-approved protocol, DHHS-approved sample consent, and/or investigator brochures must be reviewed by at least one of the designated reviewers. Any IRB member may contact the IRB office if more information is needed. Investigators may be contacted as appropriate to provide clarification and/or documentation prior to Board Review. Copies of e-mail correspondence with Investigators should be submitted to the Administrative Office with continuing review paperwork for maintenance in the IRB file.

The discussion of new submissions is led by the assigned designated reviewers and directed by the Chair. As part of the review process the assigned reviewers evaluate the scientific and/or scholarly merit of the proposed study, risks to subjects, anticipated benefits, risk/benefit ratio, consent procedures (including the general requirements for obtaining legally effective informed consent and documenting informed consent as described in “Informed Consent Instructions”), recruitment of subjects (including the specific content/language of the advertisements, medium the ads are being presented to specific subjects, etc. See IRB Position Paper on Advertisements That Directly Recruit Subjects), equitable selection of subjects, and provisions for data and safety monitoring and the protection of subject privacy and confidentiality. When following DHHS or FDA regulations the reviewers must determine that all required and appropriate additional elements of disclosure are made in the informed consent process. The assigned reviewers present pertinent information to the Board for discussion. For VA research the IRB will refer to the applicable requirements as outlined in VHA Handbook 1200.05. The entire membership is expected to participate in the review of all protocols, not just the protocols.
assigned to them. In order to approve research, the IRB must determine that the criteria for approval (as described above) are met. At the end of the discussion, based on the information reviewed, presented and discussed, the reviewer and/or Chair make a recommendation for action, risk level and approval period. A vote is taken on each action and recorded in the database.

Waiver of Consent/Waiver of Documentation of Consent: For projects requesting alteration in consenting or documentation procedures (e.g. waiver of consent or waiver of documentation) the IRB can waive consent or documentation of consent in accordance with applicable federal regulations as described in “Informed Consent Instructions”. If requested by the investigator, the IRB will determine if Waiver of Consent, or Waiver of Documentation of Consent is approvable based upon protocol specific information provided by the PI. The required findings for a waiver of consent or waiver of documentation of consent will be documented on the applicable comment sheet and/or in the IRB minutes.

Continuing Review

Continuing review of research must be substantive and meaningful. In accordance with HHS regulations at 45 CFR 46.108(b) and at 46.115(a)(2), continuing review by the convened IRB is required unless the research is otherwise appropriate for expedited review as described in OHRP Guidance on Categories of Research That May Be Reviewed by the IRB Through an Expedited Review Procedure http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm. Therefore, if research was initially approved by the convened Board, continuing review will normally be considered by the convened Board.

IRB-01 is responsible for conducting continuing review of ongoing 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. Most protocols undergo continuing review annually, but the IRB has discretion to require protocols to undergo continuing review more frequently as warranted by such factors as the nature of the study; the degree of risk involved; and the vulnerability of the study subject population. In specifying an approval period for studies of less than 12 months, i.e., those deemed by the IRB to pose higher risk to subjects, the IRB may, at its discretion, define the continuing review period with either a time interval (e.g. 3 or 6 months), or a maximum number of subjects (e.g. after 3 subjects). If a continuing review period is defined by a maximum number of subjects the IRB must also list a maximum time interval. The minutes and/or comment sheets for such projects should reflect these determinations regarding risk and approval period.

Continuing to conduct research after expiration of IRB approval is a violation of the Federal Regulations. If IRB approval expires, research activities including (1) the collection, use, or reporting of any data; (2) the performance of any study interventions, unless the IRB finds that it is in the best interests of individual subjects to continue participating in research interventions or
interactions; (3) the enrollment or screening of any new subjects; and/or (4) receipt of any study funding must stop. For further information, see the section of this manual entitled “Management of Protocols with Lapsed Approval.”

The Continuing Review/Study Closure Report submitted by Investigators and considered by the IRB provides a status report on the progress of the research. Additionally, investigators must submit a Cumulative Adverse Event and Unanticipated Problems Table with the Continuing Review Report and any other applicable paperwork as outlined. In addition to this manual, information pertaining to continuing review is included in, but not limited to, IRB letters to investigators (approval, re-approval, expiration notices) and in the document entitled “Continuing Review Requirements” sent to the PI (with the first expiration notice) and posted on the IRB-01 website.

The IRB may, at its discretion, require verification from sources other than the investigator that no material changes have occurred in the research since the previous IRB review. Protocols that may require verification include, but are not limited to, those projects conducted by investigators who previously have failed to comply with the requirements or determinations of the IRB or Federal regulations and projects where concern about possible material changes occurring without IRB approval have been raised based upon information provided in continuing review reports or from other sources. The investigator may be required to submit additional information as determined by the IRB, or may be subject to research monitoring as described below in the Quality Assurance section of this manual.

**Definition:** All non-exempt protocols, including HDEs, approved by the IRB are subject to continuing review. When a protocol is first approved, the IRB determines the appropriate approval period. The approval period can be no more than 12 months and is based on the information available and the perceived risk to the subject. Full Board continuing review reports will be sent to two designated reviewers. If reviewed and approved within 30 days prior to the project’s most recent expiration date, the new approval period will extend after the current period (as described in OHRP’s guidance titled “How is the Continuing Review Date Determined?” at [http://www.hhs.gov/ohrp/humansubjects/guidance/contrev0107.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/contrev0107.htm)

**Investigator Responsibilities:** Investigators must submit typed answers to the Continuing Review/Study Closure Report, the most recent version of the complete protocol, a completed Cumulative Adverse Event and Unanticipated Problems reporting table, a clean copy of the currently approved informed consent (if new subject enrollment continues), and the last signed copy of the informed consent. Any revisions must be submitted according to the revision guidelines. If available and applicable, DSMB reports, Audit Reports, publications or meeting proceedings, and/or any other new findings/publications that relate to the risk/benefit ratio of the study should be submitted. Investigators are encouraged to submit Continuing Review Reports a minimum of two meetings in advance of the expiration to avoid lapses in approval and potential interruption of funding.

**Office Responsibilities:** Continuing Review submissions received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Investigators or their designee are contacted as appropriate to provide clarification and/or documentation prior to Board Review. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at [http://irb.ufl.edu/irb01/forms.htm](http://irb.ufl.edu/irb01/forms.htm)) will be scheduled for the meeting. Once complete, the submission, including all of the documents provided by the PI and
those provided by the IRB Administrative Office including a Project History (comprehensive history of all actions taken by the Full Board and through expedited review procedures including, but not limited to, information captured in meeting minutes and correspondence from the IRB to Investigators and protocol specific and PI specific compliance history), the last IRB-approved informed consent, the previous years’ continuing review application, and Introductory Questionnaire, is forwarded on for inclusion on the applicable meeting agenda and reviewer assignment. Once assigned, Reviewer Comment Sheets are attached to each hard copy. For protocols with lapsed approval, a deviation comment sheet will be included along with the submission. All documents listed on the agenda and those provided by the IRB Office are distributed to designated reviewers in hard copy and to the entire membership on CD.

Reviewer Responsibilities: During the week prior to the meeting (whenever possible), all board members will receive an electronic copy of all documents as described above.

Two specific designated reviewers are assigned; one of which is considered the lead reviewer. The two designated reviewers receive a hard copy of all supporting documents in addition to the electronic copy. Reviewers are responsible for considering and evaluating the responses provided by the Investigator on the Continuing Review/Study Closure Report, for ensuring that answers are complete and not in conflict with information provided previously, and for presenting this information to the convened Board. Additionally, the Reviewers should ensure that the currently approved or proposed consent document is accurate and complete. Investigators may be contacted as appropriate to provide clarification and/or documentation prior to Board Review. Copies of e-mail correspondence with Investigators should be submitted to the Administrative Office with continuing review paperwork for maintenance in the IRB file.

The designated Reviewer should present a brief review of the protocol and information provided in the Continuing Review Report to the Board and should make a recommendation regarding the acceptability of granting the renewal. In this assessment, the reviewer should ensure that the criteria for approval continue to be satisfied including consideration of the risks and benefits and current safeguards for human subjects and determine whether any new information has emerged that might affect the risk/benefit ratio. The IRB should ensure that new information or findings, which may relate to the subjects’ willingness to continue participation is provided to study subjects. Applicable Reviewer Comment Sheets are provided and should be completed and submitted as described in Review of Research. The discussion of the continuing review application is led by the designated assigned reviewers and directed by the Chair. The entire membership is expected to participate in the review of all protocols, not just the protocols assigned to them. At the end of the discussion, based on the information reviewed, presented and discussed, the primary reviewer and/or Chair make a recommendation for action, risk level and approval period (continuing review interval based upon risk to subjects). A vote is taken on each action and recorded in the database.

Longitudinal Review

As described above, protocols originally involving greater than minimal risk to subjects and approved by the full Board must obtain continuing review approval by the full Board. However, continuing review for these projects can be changed by the full Board to an expedited process (Longitudinal Review) if all of the following are true:

1. the research is permanently closed to the enrollment of new subjects;
2. all subjects have completed all research-related interventions; and
3. the research remains active only for long-term follow-up of subjects.
Additionally, projects where the remaining research activities are limited to data analysis may be appropriate for continuing review via this mechanism as determined by the convened Board.

If the above conditions are met Longitudinal Review for all subsequent continuing reviews for the protocol may be recommended by the IRB reviewer or requested by the investigator. However, only the full Board may change the status of a project from full Board Review to Longitudinal Review. If the Investigator requests that a protocol be moved to longitudinal status, a Project Revision Form and all supporting documents must be completed and submitted for consideration. Meeting minutes and/or reviewer comment sheets will document decisions pertaining to change of protocols to longitudinal status.

Investigators are responsible for continuing review of projects as prescribed by the IRB but not less than once per year, even for projects considered in longitudinal status. If the project expires, all research activities, including data analysis must stop. For projects approved as “longitudinal,” see “Expedited Review Process: Continuing Review” for Investigator, Office, and Reviewer responsibilities.

Revisions

Investigators are responsible for reporting proposed changes in research activity to the IRB, and for ensuring that changes in IRB approved research are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject. Investigators are informed of this requirement in their initial and continuing review approval letters as well as in their Required Reading (under Researcher Responsibilities, item #4, http://irb.ufl.edu/researcherresponsibilities.htm). When a proposed change in an approved research study is not minor, that is, the revision involves greater than minimal risk to subjects, the revision must be reviewed at a convened meeting of the IRB before the change can be implemented. Minor changes in previously approved research may be reviewed utilizing an expedited process (See Expedited Review Process: Revisions).

The IRB must consider and approve all changes to previously approved research, no matter how minor, before they are implemented. Proposed changes may affect, but are not limited to, the protocol, informed consent form, and the Introductory Questionnaire. Investigators are responsible for submitting proposed changes in research activity to the IRB, and for ensuring that changes in IRB-approved research are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject. If changes to the protocol are implemented for the safety of the subject prior to IRB review and approval, such changes must be reported to the IRB within 5 days, with any supporting documentation necessary for the IRB to make a determination that the change was consistent with ensuring the subjects’ continued welfare. Information relating to protocol changes will be provided to subjects when such information may relate to the subjects willingness to continue to take part in the research.

MAJOR revisions usually involve greater than minimal risk to subjects and include, but are not limited to, a change in PI for Full Board studies and/or anything that would increase potential risk or decrease potential benefits to subjects. Major revisions are reviewed by the full Board and will be scheduled for an IRB meeting according to the IRB meeting deadlines. These revisions are placed on the IRB agenda and are assigned to two designated reviewers to present to the full Board for action. The request must be reviewed with the same criteria for concern for human subjects as used in the review of a new protocol.
Investigator Responsibilities: The preliminary determination of revision type is the responsibility of the investigator. Investigators must submit a completed Project Revision Form and, if necessary, a cover letter, explaining the revisions, any affected pages of the Introductory Questionnaire, protocol, Informed Consent Form and/or other forms, and any information to be provided to the subject to the IRB Office. Changes to the protocol, consent, IRB forms, or other documents must be indicated by strike-through when words are removed and underlining when words are added. In addition, "clean" copies of affected documents must be submitted if revisions were made.

Office Responsibilities: Major revisions received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) by administrative staff. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at http://irb.ufl.edu/irb01/forms.htm) will be forwarded for review. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation. Once complete the submission, including all of the supporting documents provided by the PI and those provided by the IRB Administrative Office including a Project History, the last IRB-approved informed consent, and the current protocol and Introductory Questionnaire, is forwarded on for inclusion on the applicable meeting agenda and reviewer assignment. Once assigned, Reviewer Comment Sheets are attached to each hard copy. All documents listed on the agenda and those provided by the IRB Office are distributed to designated reviewers in hard copy and to the entire membership on CD.

Reviewer Responsibilities: During the week prior to the meeting (whenever possible), all board members will receive an electronic copy of all documents as described above.

Two designated reviewers are assigned; one of which is considered the lead reviewer. Designated reviewers receive a hard copy of all supporting documents in addition to the electronic copy. Any member may contact the IRB office if more information is needed. Reviewers are responsible for considering and evaluating the information provided by the Investigator and for presenting this information to the convened Board. Investigators may be contacted as appropriate to provide clarification and/or documentation prior to Board Review. Copies of e-mail correspondence with Investigators should be submitted to the Administrative Office. Any IRB member, upon request, can have access to the complete IRB protocol file.

The lead Reviewer should present a brief overview of the revision. As part of the review process, the assigned reviewers should ensure, given the proposed revision that applicable criteria for approval of the research continue to be satisfied. The assigned reviewers present pertinent information to the Board for discussion. The discussion of any revision is led by the designated assigned reviewers and directed by the Chair. The entire membership is expected to participate in the review of all protocols, not just the protocols assigned to them. At the end of the discussion, based on the information reviewed, presented and discussed, the primary reviewer and/or Chair make a recommendation for action which may include, but is not limited to, the need to re-consent and/or provide information (by letter) to enrolled subjects. The need to re-consent subjects using the revised version of the Informed Consent Form will be determined by the board when such information may relate to the subjects continued willingness. A vote is taken on each action and recorded in the database. Applicable Reviewer Comment Sheets are provided and should be completed and submitted as described in Review of Research.
Minor Changes in Enrollment Criteria:

Any variation or exception to the inclusion or exclusion criteria is considered a change to the research project (note: project includes not only the protocol but everything else considered by the Board when reviewing the research). Both sets of federal regulations (OHRP and FDA) require that any change in research may not be initiated without prior IRB review and approval. IRB-01’s Policies and Procedures mirror this requirement by requiring prior approval for any change no matter how minor it is. An investigator may face a situation where a prospective research subject may not exactly meet the entrance criteria specified in the protocol. When the sponsor is notified, the sponsor indicates they will accept that subject into the protocol. However, the IRB considers enrolling a subject that does not meet entrance criteria into a research protocol as a protocol violation.

The following are steps the investigator must take to avoid being out of compliance with Federal regulations on Human Subjects Research.

If the project is sponsored and if the sponsor approves the enrollment of a subject that does not meet the IRB-approved eligibility criteria as a single patient exception/variation rather than a revision to the overall project, the investigator must obtain written confirmation from the sponsor that an exception to the eligibility criteria has been granted. While obtaining the sponsor’s permission is definitely required, it is NOT the only thing you must do; once the sponsor’s permission has been received in writing, IRB approval must be obtained PRIOR to enrolling the subject. In order to enroll a subject that does not meet the IRB-approved eligibility criteria, the PI must:

Obtain written permission (e-mail or letter) from the sponsor for the exception/variance. This documentation should provide specific details about the exception such as the specific enrollment criteria values that are not met (i.e. what the protocol requires and the subject’s status/values), explaining/justifying potential risk to this subject, and discussing the potential effect (if any) on the research as a whole. We also ask that the sponsor discuss whether or not the enrollment criteria should be permanently adapted to match this exception (if the altered values are ok for one subject, why not everyone?).

Complete an IRB-01 Project Revision form (http://irb.ufl.edu/docs/frm-rev.doc) requesting that the IRB approve the exception/variance to the previously approved inclusion exclusion criteria. You must provide specific details on what the criteria are, what the potential subject’s actual values/status are, discuss potential risk to the subject, and discuss the potential effect (if any) on the research as a whole (you may refer to the sponsor’s letter if the information is present there).

Submit both of the above to the IRB-01 office and receive IRB approval BEFORE enrolling the potential subject.

Thoroughly review the inclusion and exclusion criteria for your research protocol. If you feel they are too restrictive, address this with the sponsor or appropriate individual.

1) If the protocol has already been submitted or approved by the IRB, submit a revision to the IRB.

2) You must receive approval for this revision prior to enrolling subjects under the new criteria.
If, during the course of the protocol, a potential research subject does not meet the exact inclusion/exclusion criteria, then before the subject can be enrolled, a revision must be submitted to the IRB office, with a letter from the sponsor indicating the approval of the change. This revision will be reviewed by the Chair or Vice Chair that day (if needed):

1) If the change is no more than minimal risk to the subject, it may be approvable that day through expedited review.

2) If the change poses more than a minimal risk to the subject, it must go to the full Board for review.

If, during the course of a return visit by an already enrolled subject, a laboratory parameter or some other inclusion/exclusion criteria is not strictly met, then:

1) If the change is no more than minimal risk to the subject, the investigator must receive written notice from the sponsor that they approve the modification, and can continue with the protocol, informing the IRB within 5 working days of the particulars of this event.

2) If the change poses more than a minimal risk to the subject, it must go to the full Board for review before the protocol can continue, unless not implementing the change would adversely affect the health of the study subject. In this case, the investigator can continue with the protocol, informing the IRB within 5 working days of the particulars of this event.

Tabled Response

Definition: Once an investigator responds in writing to issues raised by the IRB, the response and the original submission must be returned to the convened full Board for review. Whenever possible, this investigator’s tabled response will be assigned to the same Members who reviewed the previously tabled submission.

Investigator Responsibilities: When responding to a “Tabled Letter,” Investigators must submit a cover letter or completed Tabled Submission Response Form responding to the issues raised by the Board. In addition, if any protocol documents need to be revised by the investigator in order to address issues raised by the Board, the investigator must also submit a copy of all affected pages with changes indicated by strike through when words are removed and underlining when words are added. In addition, a “clean” copy (with the changes executed) of any affected pages must be enclosed, as well as a complete “clean” of any altered Informed Consent Forms. Any other documentation requested by the Board should also be attached.

Office Responsibilities: Tabled Responses received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) by administrative staff. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation prior to Board Review. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at http://irb.ufl.edu/irb01/forms.htm) will be scheduled referred for inclusion on the applicable meeting agenda. Once complete, the submission, including all of the supporting documents provided by the PI and those provided by the IRB Administrative Office including the Project History and the applicable original submission and any subsequent correspondence is
forwarded on for inclusion on the applicable meeting agenda and reviewer assignment. Once assigned, Reviewer Comment Sheets are attached to each hard copy. All documents listed on the agenda and those provided by the IRB Office are distributed to designated reviewers in hard copy and to the entire membership on CD.

**Reviewer Responsibilities:** During the week prior to the meeting (whenever possible), all board members will receive an electronic copy of information submitted for tabled studies.

Two designated reviewers are assigned one of which is considered the lead reviewer, unless the tabled project is new, in which case three designated reviewers will be assigned. Designated reviewers receive a hard copy of all supporting documents in addition to the electronic copy. Any member may contact the IRB office if more information is needed. Reviewers are responsible for considering and evaluating the information provided by the Investigator and for presenting this information to the convened Board. Investigators may be contacted as appropriate to provide clarification and/or documentation prior to Board Review. Copies of e-mail correspondence with Investigators should be submitted to the Administrative Office. Any IRB member, upon request, can have access to the complete IRB protocol file.

The lead Reviewer should present a brief overview of the tabled response and any other pertinent information to the Board for discussion. As part of the review process, the assigned reviewers should ensure that applicable criteria for approval of the research are satisfied. The discussion of any tabled response is led by the designated assigned reviewers and directed by the Chair. The entire membership is expected to participate in the review of all protocols, not just the protocols assigned to them. At the end of the discussion, based on the information reviewed, presented and discussed, the primary reviewer and/or Chair make a recommendation for action. Additional elements may be required in the action, depending on what category the original submission fit (e.g. if a new project is tabled, the action to approve a tabled new protocol must include risk assignment, etc). A vote is taken on each action and recorded in the database. Applicable Reviewer Comment Sheets are provided and should be completed and submitted as described in Review of Research.

**Unanticipated Problems and Serious Adverse Events:** See “Reportable Events”

“Other” (Miscellaneous)

**See Expedited Review Process: Other (Miscellaneous)**

**Expedited Review Process**

Federal regulations establish expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research. Federal regulations define *minimal risk* as 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.

Review of research by an expedited procedure is an alternative to review by the convened IRB for a defined class of research. Under an expedited review procedure, the review of research (including research subject to DHHS and FDA regulations) may be carried out by an IRB Executive Reviewer, or by an experienced IRB member, designated by the Chair. Experienced members can be selected based on 1) at least six months of IRB experience, research
experience, any life experiences or background applicable to human subject research, and 2) any other qualification the IRB Chair deems appropriate. The person(s) conducting the expedited review may either approve, require modifications (to secure approval) or refer the research to the convened IRB for review in accordance with the non-expedited review procedures. In conducting expedited review, the IRB reviewers may exercise all of the authorities of the IRB except that they may not disapprove the research. A research activity may only be disapproved after review by the convened IRB. Decisions regarding review by an expedited procedure are communicated to the investigator and the institution in writing.

DHHS and FDA have published identical lists of categories of research that may be reviewed by the IRB through an expedited review procedure. Human subjects research may qualify for consideration under an expedited review process if the research meets certain applicability criteria and falls into the at least one of the permissible categories of research as described below.

There are no deadlines for submitting paperwork for Expedited Review. Submissions that fit expedited criteria will be processed and sent as quickly as possible to a designated Executive Reviewer. Expedited Review may take up to four weeks or longer (if the submission has issues that the Reviewer attempts to resolve with the PI) to review and approve, although the average time is between three and four weeks. Investigators submitting protocols requiring more immediate review and turnaround, should complete an Urgent Request Form available in the IRB-01 Administrative Office to accompany the submission.

If needed, the Executive Reviewer can request additional information from the PI prior to approving an expedited submission by (1) contacting the PI directly or (2) returning the paperwork, including the comment sheet detailing clarifications back to the IRB Administrative Office so that an official letter (e.g. “needs reply”) can be generated. If official correspondence is generated, the response from the PI will be forwarded back to the requesting reviewer, when possible. If the Executive Reviewer is unable to approve the project under expedited review procedures, the Reviewer should indicate on comment sheet that the submission be referred to Full Board. Upon receipt, the IRB Administrative Office will include the submission on the next applicable agenda and notify the investigator in writing that the submission has been forwarded to the Full Board for review. Any expedited submission found to have issues of noncompliance (e.g. over-enrollment, failure to maintain consent forms, etc) at the time of review by the Office Staff or the designated Executive Reviewer will be referred to the Full Board for review and action.

For projects undergoing expedited review, the applicable Reviewer Comment Sheet serves as guidance in determining whether the protocol meets criteria for approval and/or other regulatory requirements and serves as documentation of the review including a description of the review, actions taken by the reviewer and that, in the reviewer’s opinion, the research meets the conditions for approval under expedited review procedures, involves only procedures in one or more of the specific permissible expedited categories and meets the criteria for approval under the applicable regulations. Documentation of applicable protocol specific findings required under regulation will be in relevant documents submitted by the investigator and reviewed and approved by the IRB/Executive Reviewer.

Information pertaining to submissions reviewed via an expedited review process will be communicated to the full Board via Informational Minutes.

Initial Review
Human subjects research may qualify for consideration under an expedited review process if the research meets certain applicability criteria and falls into the at least one of the permissible categories of research (as defined by the FDA and DHHS) that may be reviewed by the IRB through an expedited review procedure. Criteria require that the research that presents no more than minimal risk to human subjects and that an expedited procedure not be used when the proposed research is classified or when the identification of the subjects and/or their responses would reasonable place them at risk of criminal or civil liability or be damaging to the subjects and (2) involve only procedures listed in one or more of the following categories:

1) Research on drugs for which an investigational new drug application is not required or research on medical devices for which a) an investigational device exemption application is not required or b) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2) Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows: (a) from healthy, nonpregnant adults, who weigh at least 110 pounds. For these subjects amounts drawn may not exceed 550 ml in an 8 week period and no more than 2 times per week; or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml/kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at the time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electrotetinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

6) Collection of data from voice, video, digital, or image recordings made for research purposes.
7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Categories 1-7 pertain to both initial and continuing review.

**Investigator Responsibilities:** The Principal Investigator must submit the following documents to the IRB for review and consideration at the time of initial review: Introductory Questionnaire including any applicable addenda and supplementary information as requested, protocol (either sponsor’s protocol or investigator-initiated protocol written in IRB required format available on the IRB-01 website), informed consent form written in IRB required format (unless a waiver or waiver of documentation of consent is requested as described in “Informed Consent Instructions”), any relevant merit review or grant application (if applicable), advertisements (or other materials intended to be seen or heard by subjects), subject surveys and/or questionnaires, and any other information that the Investigator deems pertinent to review of the project. Guidelines for Expedited Submissions and for completing paperwork are available on the IRB website or in the IRB-01 Administrative Office.

Investigators enrolling subjects who do not speak or read English should see the Informed Consent Instructions available at the IRB-01 website.

**Office Responsibilities:** New protocols received by the IRB Administrative Office, are assigned a new protocol number, entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Investigators or their designee are contacted as appropriate to provide clarification and/or documentation before sending to an Executive Reviewer. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at http://irb.ufl.edu/irb01/forms.htm) will be forwarded for review. Once complete, the submission, including documents submitted by the PI and any applicable IRB forms, including but not limited to the Informed Consent Checklist and/or HIPAA Review Sheet (“Green Sheet”), along with the applicable Reviewer Comment Sheet(s) is forwarded to an Executive Reviewer. The Office is expected to forward submissions to the designated Executive Reviewer at least twice but preferably three times during the week. Urgent Items can be forwarded to any Executive Reviewer at any time for review.

**Reviewer Responsibilities:** Each week Executive Reviewers will alternate responsibility for reviewing all submissions categorized as meeting Expedited Review criteria. Each Reviewer is responsible for coordinating with the Office receipt of new submissions and return of those submissions that have been reviewed. For new submissions the Reviewer will receive a copy of all of the material submitted by the investigator along with the applicable Reviewer Comment Sheet(s). As part of the review process the Executive Reviewer evaluates the scientific and/or scholarly validity of the proposed study, any risks to subjects, anticipated benefits, risk/benefit ratio, consent procedures (including the general requirements for and documentation of informed consent as described in “Informed Consent Instructions”), equitable selection of subjects, and provisions for data and safety monitoring and the protection of subject privacy and confidentiality. For projects undergoing expedited review, the Comment Sheet serves as documentation of the review and that, in the reviewer’s opinion, the research meets the conditions for approval under expedited review procedures, involves only procedures in one or
more of the specific permissible expedited categories and meets the criteria for approval under the applicable regulations. The Comment Sheet must be completed, signed, and dated by the reviewer. If not otherwise noted, the approval period for studies meeting the criteria for expedited review is 12 months.

Waiver of Consent/Waiver of Documentation of Consent: For projects requesting alteration in consenting or documentation procedures (e.g. waiver of consent or waiver of documentation) the Executive Reviewer can waive consent or documentation of consent in accordance with applicable federal regulations. If requested by the investigator, the reviewer will determine if Waiver of Consent, or Waiver of Documentation of Consent can be granted based upon protocol specific information provided by the PI. The required findings for a waiver of consent or waiver of documentation of consent will be documented on the appropriate comment sheet, and signed and dated by the reviewer and/or in the IRB minutes.

The specific permissible expedited review category is included in the Approval Letter and is communicated to the Board via Informational Minutes.

Continuing Review

DHHS and FDA define criteria for the conduct of continuing review utilizing an expedited review process. To be eligible for expedited continuing review, research cannot be classified and must meet one or more of the following categories:

Category 1 through 7 as defined above.

Category 8: Continuing review of research previously approved by the convened IRB (a) where the research is permanently closed to the enrollment of new subjects, and all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.

Category 9: Continuing review of research, not conducted under an investigational new drug application or an investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Investigator Responsibilities: Investigators must submit typed answers to the Continuing Review/Study Closure Report, the most recent version of the complete protocol, a completed Cumulative Adverse Event and Unanticipated Problem Reporting table, clean copy of the currently approved informed consent (if new subject enrollment continues), and the last signed copy of the informed consent, if applicable. Any revisions must be submitted according to the revision guidelines. In addition and if applicable, any other information including, but not limited to Audit Reports, publications or meeting proceedings, and/or any other new findings/publications or information that relate to the risk/benefit ratio of the study should be submitted.

Office Responsibilities: Continuing Review submissions received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Continuing review submission will be forwarded to an Executive Reviewer if (1) the protocol was initially approved as expedited as indicated in the IRB database; (2) if the
IRB database indicates “longitudinal” status; or (3) if previously approved by the Board, the investigator indicates that no subjects have been enrolled. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation before sending for review. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at http://irb.ufl.edu/irb01/forms.htm) will be forwarded for review. Once complete, the submission, including all of the supporting documents submitted by the PI and those provided by the IRB Administrative Office including the Project History, the last IRB-approved informed consent, the previous years’ continuing review application, and Introductory Questionnaire, along with the applicable Comment Sheet, is forwarded to an Executive Reviewer. The Office is expected to forward submissions to the Chair of the week at least twice but preferably three times during the week. Urgent Items can be forwarded to any Chair at any time for review.

Reviewer Responsibilities: Reviewers are responsible for considering and evaluating the responses provided by the Investigator on the Continuing Review/Study Closure Report and in any other documents provided by the PI and for ensuring that answers are not in conflict with information provided at previous continuing reviews and that all answers are consistent with the protocol. Additionally, the Reviewer should ensure that the currently approved or proposed consent document is accurate and complete. Investigators may be contacted as appropriate to provide clarification and/or documentation prior to Board Review. Copies of e-mail correspondence with Investigators should be submitted to the Administrative Office with continuing review paperwork for maintenance in the IRB file. For projects undergoing expedited review continuing review, the Comment Sheet serves as documentation of the review and includes risk level, approvable permissible expedited category, action taken by the reviewer, any comments of the Reviewer and that the information provided for review meets criteria for re-approval under the applicable regulations. The Comment Sheet must be completed, signed, and dated by the reviewer. Reviewers must complete and return the Reviewer Comment Sheet to the Administrative Office with the submission.

The specific permissible expedited review category is documented on the Reviewer Comment Sheet and conveyed to the Board via Informational Minutes.

Revisions

As described earlier, investigators are responsible for reporting proposed changes in research activity to the IRB, and for ensuring that changes in IRB approved research are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject. Minor changes in previously approved research during the period for which the protocol is approved, involving minimal risk to subjects, including but not limited to, a change in PI of a study approved under expedited review procedures, change in sub-Investigator (for any IRB approved study), change in project title, and/or administrative changes to the protocol, may be reviewed under expedited review procedures. Changes in previously approved research involving greater than minimal risk to subjects (major revisions), must be reviewed at a convened meeting of the IRB as described under Full Board Review: Revisions.

Investigator Responsibilities: See Full Board Review: Revisions

Office Responsibilities: Minor revisions received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) by administrative staff. Only submissions fulfilling all IRB-01
administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at [http://irb.ufl.edu/irb01/forms.htm](http://irb.ufl.edu/irb01/forms.htm)) will be forwarded for review. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation before sending for review. Once complete, the submission, including all of the supporting documents provided by the PI and the Administrative Office including the Project History, the last IRB-approved informed consent and the applicable Comment Sheet is forwarded to an Executive Reviewer for consideration and action. The Office is expected to forward submissions to the designated Executive Reviewer at least twice but preferably three times during the week. Urgent Items can be forwarded to any Chair at any time for review.

**Reviewer Responsibilities:** The Executive Reviewer reviewing the submission is expected to:

1. evaluate the revision,
2. determine if the changes (1) are greater than minimal risk or (b) impact the risk/benefit ratio of the study, and therefore whether or not the submission requires full Board review,
3. determine if subjects already enrolled in the project need to be re-consented (if applicable);
4. complete and sign and date the Reviewer Comment Sheet; and
5. return all applicable paperwork to the IRB Office for processing.

The Comment Sheet serves as guidance in determining whether, in the reviewer's opinion, the submission can be approved via an expedited review process or must be forwarded for consideration by the Full Board. The Executive Reviewer may request additional information from the IRB Office or the PI as needed to evaluate the revision and refer any revision to the full board as deemed necessary for further consideration.

**Unanticipated Problems and Serious Adverse Events:** See “Reportable Events”

**Other (Miscellaneous)**

Definition: Occasionally investigators will submit information that does not fit into any of the categories described above. All miscellaneous submissions will initially be sent to an Executive Reviewer for review under expedited procedures.

**Investigator Responsibilities:** Investigators should submit a cover letter describing the information and a copy of any supporting documentation (e.g. information from the sponsor) for consideration. If any protocol documents need to be revised by the investigator as a result of this information, the item should be submitted as a revision.

**Office Responsibilities:** “Other” items received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) by administrative staff. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at [http://irb.ufl.edu/irb01/forms.htm](http://irb.ufl.edu/irb01/forms.htm)) will be forwarded for review. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation before sending for review. Once complete, the submission, including all of the supporting documents provided by the PI and the Administrative Office including the Project History, the last IRB-approved informed consent and the Miscellaneous Comment Sheet is forwarded to an Executive Reviewer for consideration and action. The Office is expected to forward submissions to designated Executive Reviewer at least twice but preferably three times during the week. Urgent Items can be forwarded to any Chair at any time for review.
**Reviewer Responsibilities:** The Executive Reviewer reviewing the submission is expected to:

1. evaluate the submission per the Miscellaneous Comment Sheet, including assessing whether the submission represents noncompliance or an unanticipated problem involving risk to subjects or others,
2. determine if the information (1) is greater than minimal risk or (b) impacts the risk/benefit ratio of the study, and therefore whether or not the submission requires full Board review;
3. complete and sign and date the Reviewer Comment Sheet; and
4. return all applicable paperwork to the IRB Office for processing.

The submission may be forwarded to the full board for review and consideration, either as directed by the Comment Sheet or at the Executive Reviewer’s discretion, as described under Full Board Review Procedures. If the Executive Reviewer or Board find that the Miscellaneous item is noncompliance then the Non-Compliance Pertaining to Human Subjects Research policy (page 53) will be followed. If the Executive Reviewer or Board find that the Miscellaneous item is an unanticipated problem then the Unanticipated Problems Involving Risk to Subjects or Others and Adverse Events policy (page 58) will be followed.

**Study Closures:**

Federal regulations require prompt reporting to the IRB of proposed changes in a research activity. The UF IRB requires that Investigators submit a Study Closure Report when study activities including enrollment, interventions/interactions, and/or data analysis of personally identifiable information have been completed (including premature completion of the research). Analysis of de-identified research data may continue after study closure. Study closures are initially conducted under expedited review procedures (as a minor change in previously approved research), but the Executive Reviewer can refer the closure for consideration by the Full Board as deemed necessary.

**Investigator Responsibilities:** Investigators must submit typed answers to the Continuing Review/Study Closure Report, a completed Adverse Event Reporting table, and the last signed copy of the informed consent. If available, any other new findings/publications that relate to the study should be submitted.

**Office Responsibilities:** Study Closures received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at [http://irb.ufl.edu/irb01/forms.htm](http://irb.ufl.edu/irb01/forms.htm)) will be forwarded for review. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation before sending for review. Once complete, the submission, including all of the supporting documents submitted by the PI and those provided by the IRB Administrative Office including the Project History the last IRB-approved informed consent, and applicable Reviewer Comment Sheet, is forwarded to an Executive Reviewer for review and action. The Office is expected to forward submissions to the designated Executive Reviewer at least twice but preferably three times during the week. Study Closures found to have issues of noncompliance (e.g. over-enrollment, failure to maintain consent forms, etc) at the time of review by the Office Staff or the designated Executive Reviewer will be referred to the Full Board for review and action.
**Reviewer Responsibilities**: Reviewers are responsible for evaluating the responses provided by the Investigator on the Study Closure Report and for ensuring that answers are not in conflict with information provided at previous continuing reviews. Investigators may be contacted as appropriate to provide clarification and/or documentation. Copies of e-mail correspondence with Investigators should be submitted to the Administrative Office with continuing review paperwork for maintenance in the IRB file. Reviewers must complete and return the Reviewer Comment Sheet to the Administrative Office with the submission. The Investigator will be notified in writing when the study has been closed.

Closed projects will be maintained onsite, in the IRB Administrative Office, for three months after closure. After this time the project will be moved to long term storage and maintained according to the Record Retention Policy.

**Review of Exempt/Non-Human Research**

HHS Regulations (§ 46.101(b)) define categories of human subjects research that are exempt from IRB review. See Section entitled “Human Subjects Research Exempt from IRB Review.” All nonexempt research will be reviewed in accordance with 45 CFR 46.

Research investigators who intend to involve human subjects in research will not make the final determination of exemption from applicable Federal regulations; rather IRB Exempt Reviewers (IRB Chair, Vice Chair or designated IRB Administrative Staff) are responsible for reviewing the preliminary determinations of exemption made by investigators and their supervisors. Only the IRB may make the final determination that proposed research meets the regulatory criteria for exemption. For VA research, the IRB will defer to the requirements for Exempt research as outlined in VHA Handbook 1200.05 handbook. If there is any question as to whether proposed research meets the criteria for exemption or if the proposed research poses ethical questions or concerns relating to human subjects protection, the IRB Administrative Exempt Reviewer will refer the submission for evaluation by the Chair/Vice-Chair. Chairs/Vice-Chairs may not only request changes or determine the research meets exempt criteria, but also disapprove the study if the study does not meet exempt criteria or refer the study for more stringent review (within Expedited or Full Board categories/requirements)

There are no deadlines for submission of exempt protocols. Projects approved as exempt research do not require continuing review by the IRB, unless changes in the research are such that the research no longer qualifies for exempt status. Changes in research activities must be reported to the IRB prior to initiation, and the IRB may, depending upon information submitted, change protocol status depending upon the proposed changes in the research activities. VA approved exempt protocols require continuing review by the VA R&DC as outlined in VHA Handbook 1200.05.

**Investigator Responsibilities**: Research investigators requesting exempt review of a project must submit: Introductory Questionnaire for Exempt Studies (indicating which exempt criterion the proposed research meets), and any data collection forms, questionnaires or interview questions to be used in the study, and/or any other forms that may be relevant to the determination of exemption.

**Office Responsibilities**: New protocols received by the IRB Administrative Office are assigned a new protocol number, entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Investigators or their designee are contacted as
appropriate to provide clarification and/or documentation before sending to an Exempt Reviewer. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at http://irb.ufl.edu/irb01/forms.htm) will be forwarded for review. Once complete, the submission, including documents submitted by the PI and any applicable IRB forms, including but not limited to HIPAA Review Sheet (“Green Sheet”) and the applicable Reviewer Comment Sheet(s) is forwarded to an Exempt Reviewer. The Office forwards submissions as they are received.

**Reviewer Responsibilities**: Exempt Reviewers are responsible for considering and evaluating the responses provided by the Investigator on the Exempt IQ, for contacting the investigator as needed to provide clarification and/or additional documentation and for determining if the research activity meets the defined criteria for exemption. The Exempt Reviewer will document the basis for exemption on the “Request for Exempt Review” Comment Sheet. The completed comment sheet, along with other applicable documents, will be retained in accordance with the IRB Record Retention Policy.

If there is question whether a protocol qualifies for exempt status, the Exempt Reviewer can contact the investigator for further clarification, or return the protocol packet and completed Exempt Review Comment Sheet to the IRB Administrative Office for generation of a letter requesting clarification of issues raised by the reviewer. Additionally, the Exempt Reviewer may determine that the protocol should be reviewed under expedited or Full Board procedures. Should this occur, the investigator will be notified by either the Reviewer or Administrative Office regarding the status change of the protocol. Any status change will be reflected in the IRB database.

If there are interactions with participants, the Exempt Reviewer can decide if an informed consent process is required, disclosing such information as: that the activity involves research, a description of the procedures, that participation is voluntary, name and contact information for researcher, adequate provisions for maintaining privacy and confidentiality, and/or possibly other elements of consent as described in the Informed Consent Checklist.

The PI will be notified in writing of the determination of exemption, including the applicable exempt category and information pertaining to these studies will be communicated to the full Board via informational minutes.

**Non-Human Subject Research/Indefinite Plans**

Some types of research may be undertaken without definite plans to include human subjects (as defined in 45 CFR 46.102(f)). In the event that the research does not include human subjects, federal regulations do not apply and IRB review may not be required (this determination however may only be made by the IRB). Examples of non-human subject research may include:

- tissue obtained from another source (not directly from the patient) that is either:
  - totally anonymous and unlinkable to the person who it was obtained from, or
  - is coded such that the researcher obtaining the sample does not know who it belongs to, AND a confidentiality agreement assures the researcher cannot learn the identity of the person who the sample was obtained from.
• data obtained from another source (not directly from the patient or their records) that is either:
  o totally anonymous and unlinkable to the person who it was obtained from, or
  o is coded such that the researcher obtaining the data does not know who it belongs to, AND a confidentiality agreement assures the researcher cannot learn the identity of the person who the data was obtained from.

• data or tissue obtained directly from individuals who are deceased prior to their involvement in the study.

**Investigator Responsibilities:** Research investigators requesting review of non-human subjects research must submit: Introductory Questionnaire for Exempt Studies (indicating that the research meets the criteria for non-human subjects research), Confidentiality Agreements (as applicable) and any data collection forms, to be used in the study, and/or any other forms that may be relevant to the determination of non-human status.

**Office Responsibilities:** New protocols received by the IRB Administrative Office are assigned a new protocol number, entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) and accuracy by experienced IRB administrative staff. Investigators are contacted as appropriate to provide clarification and/or additional documentation. Only submissions meeting IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at [http://irb.ufl.edu/irb01/forms.htm](http://irb.ufl.edu/irb01/forms.htm)) will be forwarded for review. Once complete, the submission, including all of the supporting documents, is forwarded to the Exempt Reviewer. The Office forwards non-human submissions as they are received.

**Reviewer Responsibilities:** Activities that do not meet the definition of “human subjects’ research” (“Non-human”) can be reviewed and approved by an Exempt Reviewer. The basis for the determination will be documented on the applicable Comment Sheet and the completed sheet, along with other applicable documents, will be retained in accordance with the IRB Record Retention Policy. The PI will be notified in writing of the determination of “non-human” status.

If there is question whether a protocol qualifies for non-human status, the Exempt Reviewer can contact the investigator for further clarification, or return the protocol packet and completed “Non-Human” Comment Sheet to the IRB Administrative Office for generation of a letter requesting clarification of issues raised by the reviewer. Additionally, the Exempt Reviewer may determine that the protocol does not meet the definition of non-human research and should be reviewed as exempt or under expedited or Full Board procedures. Should this occur the investigator will be notified by either the Reviewer or Administrative Office of this change in status. Any status change will be reflected in the IRB database.

**Reportable Events**

Federal regulations require prompt reporting to the IRB, appropriate institutional officials, the head of the sponsoring Federal department or agency, if any, and OHRP and/or FDA:

• Any serious or continuing non-compliance with the Federal Regulations, or requirements, determinations, or policies and procedures of the IRB,

• Any unanticipated problems involving risks to subjects or others, and

• Any suspension or termination of IRB approval.
Non-Compliance Pertaining to Human Subjects Research

The federal regulations require that serious or continuing non-compliance be reported promptly to the IRB, appropriate institutional officials, the head of the sponsoring Federal department or agency, if any, and OHRP and/or FDA. Investigators are required to comply with the Federal Regulations, state law, University policies and/or requirements, determinations, and/or policies and procedures of the IRB pertaining to research involving human subjects. For VA approved research, investigators are also required to comply with VA reporting requirements.

Non-compliance is any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with the Federal Regulations, state law, University Policies and/or requirements, determinations, and/or policies and procedures of the IRB. Non-compliance may range from minor to serious, be unintentional or willful, and may occur once or several times. The seriousness of non-compliance will be evaluated on a case-by-case basis. For VA research the IRB will defer to the requirements outlined in VHA Handbook 1058.01.

Serious non-compliance is any action or omission in the conduct or oversight of research involving human subjects that may affect the rights, safety and/or welfare of research participants, increase risk or decrease benefits to subjects, and/or compromise the integrity or validity of the research (VA research refer to VHA Handbook 1058.01).

Continuing non-compliance is a pattern of failing to follow Federal Regulations, state law, University Policies, and/or requirements, determinations, and/or policies and procedures of the IRB. Continuing non-compliance is assessed by the number of incidents during the course of a given protocol or across a number of protocols (for the same investigator) and whether the same non-compliant action or activity was repeated or a variety of noncompliant actions or activities occurred (VA research refer to VHA Handbook 1058.01).

Reporting Suspected Non-Compliance

Reports of suspected non-compliance can be made to the IRB Chair, Vice-Chairs, or any IRB Member and/or the IRB Administrative Staff from anyone inside or outside of the UF Community who has reason to believe that noncompliance has occurred. Complaints may be verbal or via written correspondence and should be reported as soon as possible upon discovery. Reports (verbal or written) should include: title of the applicable research project; name of the principal investigator; IRB Number, if known; and a detailed description of the suspected noncompliance. The recipient at the IRB should document these issues in writing. Upon receipt of reports of alleged noncompliance, the Assistant Director (AD) of IRBs and/or the IRB Chair should be notified. For VA Research, reports of suspected non-compliance will be reported as outlined in VHA Handbook 1058.01. All reports of suspected noncompliance will be investigated/evaluated (see below).

Investigators must report all alleged incidents of noncompliance. Events that must be reported within 5 working days of discovery are unexpected, related/possibly related, and (a) continuing non-compliance (as defined above), or (b) serious noncompliance (as defined above). All other alleged incidents should be reported at Continuing Review. Deviations and regulatory non-compliance should be reported per the IRB-01 Definitions and Reporting Guide: Deviations and Regulatory Non-Compliance found at http://irb.ufl.edu/docs/guide-dev.doc. VA approved research will comply with requirements outlined in VHA Handbook 1058.01. Others making reports are encouraged to provide as much information as possible including, but not limited to:
• Title of the research project in which the noncompliance occurred
• Name of the principal investigator;
• IRB Project Number, if known; and
• A detailed description of the suspected noncompliance.

If subject safety is at risk the IRB recommends notifying the Chair or IRB office immediately.

Evaluating Suspected Non-Compliance (Initial Investigation-Response)

The IRB AD and/or the IRB Chair may initiate an investigation into allegations of suspected noncompliance. If there is any question that the potential noncompliance could be serious and/or continuing, the IRB Chair may suspend the study. The IRB AD and/or IRB chair will direct any preliminary investigation and designate individuals to assist in any investigation. A preliminary investigation may include but is not limited to any or all of the following: an interview with the complainant or others; inquiries via telephone or email; and/or a Quality Assurance Review of the applicable projects’ research data; informed consent/assent documents; medical records; inclusion/exclusion criteria; IRB records; and any other relevant information. The extent of the preliminary investigation will be based on the type of information needed to determine the truth of the allegation, and whether the allegation represents potential serious or continuing noncompliance. A summary of allegations and preliminary findings will be prepared and submitted to IRB AD and/or Chair for assessment and determination. The IRB AD may determine that the allegation was not substantiated based upon the preliminary investigation and determine that no further action is needed. If the preliminary investigation reveals evidence of non-compliance, the matter, including all supporting documentation, will be referred to the IRB Chair for review and determination.

Noncompliance that is not serious and/or not continuing

If it is determined by the IRB Chair that there is evidence of noncompliance that is neither serious nor continuing, the Chair may determine that no further action is needed, that remedial action is needed or that the matter should be forwarded to the full board for consideration and determination. For Non-Compliance involving research at the VA, the IRB will refer to the applicable requirements outlined in VHA Handbook 1058.01.

Handling of Noncompliance that is serious and/or continuing

If it is determined by the IRB Chair that there is evidence of noncompliance that is serious or continuing, the IRB Chair may suspend any or all activities related to (a) a particular research project and/or (b) any other activities that the investigator(s) is associated with. All serious and/or continuing noncompliance will be forwarded to the full Board for consideration along with any summary of allegations and findings, if available.

IRB Responsibilities for Handling Reports of suspected Non-compliance or Non-Compliance in fact

The convened IRB reviews preliminary reports of non-compliance that is serious or continuing, or that has been forwarded for review by an Executive Reviewer. IRB Administrative Staff assign two designated reviewers, one of which is considered the lead reviewer. All members of
the IRB will receive the following materials for review: Report of allegation or summary of allegation; summary of investigational findings (previously reviewed by the Assistant Director and/or Chair) including any information or documentation offered by the complainant and/or respondent; and any supplemental information relevant to the non-compliance. Designated reviewers are expected to conduct an in-depth review of all materials and present the review before the convened board. If the Chair has suspended the research because of concerns related to subject safety, the IRB will vote to confirm or reverse that decision. The IRB may make a final determination based upon the information reviewed (presented) or may require further information before making a final determination. If the IRB determines non-compliance in fact that is neither serious nor continuing, the IRB may require remedial action as described below. IRB Reviewers will complete the applicable reviewer comment sheet and the IRB staff will record in the meeting minutes deliberations and determinations made by the IRB. Notification of the determinations of the IRB and any corrective actions will be sent to the Principal Investigator.

If the Board determines: 1) noncompliance in-fact, 2) that the noncompliance was serious and/or continuing, and/or 3) that the event was an unanticipated problem involving risk to subjects or others (page 58), the Board will determine on a case-by-case basis, what actions, if any, will be taken. IRB Reviewers will complete the applicable reviewer comment sheet and the IRB staff will record in the meeting minutes deliberations and determinations made by the IRB. Information on serious and/or continuing non-compliance determinations will be entered into the IRB Database. Notifications will be made per the Reporting Policy. For VA approved research, notifications will be made per requirements outlined in VHA Handbook 1058.01.

For the Investigation of Complaints and Allegations of Serious or Continuing Non-Compliance some or all of the following steps may be taken:

1. The Chair and/or IRB may at any time designate, verbally or in writing, a Designated Reviewer or an advisory committee to review the allegations, reports, or findings.
2. The Chair, IRB, Designated Reviewer and/or Advisory Committee may, upon receipt of notice of any serious or continuing non-compliance confirm, verify, or gather more the information. This may entail any type of communication including a face-to-face meeting, telephone conference, email, or written correspondence. If the source is not reasonably available, is unwilling to communicate, or the Chair, IRB Executive Committee, and or Designated Reviewer determines that the source should not be contacted, the Chair, IRB Executive Committee, and/or Designated Reviewer may take other action, as appropriate, to confirm the information.
3. The Chair and/or IRB may at any time suspend protocols or restrict study activities (such as enrollment) in any protocols that are related to the issue. This includes but is not limited to those protocols related solely by virtue of having the same principal investigator, sub-investigator, or research staff. Before protocols are suspended, any risks to human subjects that will result from suspensions shall be considered. If the Chair suspends any protocol, the Chair shall, within a reasonable time, afford the IRB the opportunity to review and approve, disapprove or revise the suspension.
4. The Chair, IRB Executive Committee, Designated Reviewer and/or Advisory Committee may notify the investigator that allegations, reports, or findings of serious or continuing noncompliance or unanticipated problems involving risk to subjects exist and are under review. This notification may be verbal, via email, or in writing. The Chair, IRB Executive Committee, IRB and/or Designated Reviewer may make this notification whenever it is reasonable to do so, given the nature of the issue. The Chair, IRB Executive Committee,
IRB and/or Designated Reviewer may, if appropriate, reveal the source of allegation to the investigator.

5. The Chair, IRB Executive Committee, IRB, Designated Reviewer and/or Advisory Committee may obtain an initial verbal or written response from the investigator whose study is being reviewed.

6. The Chair, IRB Executive Committee, IRB, Designated Reviewer, and/or Advisory Committee may interview the investigator or witnesses, review records, search existing literature or take other actions as appropriate to evaluate the issues.

7. The Chair, IRB Executive Committee, Designated Reviewer, and/or Advisory Committee may obtain an initial verbal or written response from the investigator whose study is being reviewed.

8. The Chair, IRB Executive Committee, Designated Reviewer and/or Advisory Committee shall, within a reasonable time after concluding its review, make a verbal or written report to the full Board of the receipt of the initial information, the investigator's response, if any, and the investigation.

9. If the IRB determines non-compliance in fact, the Board shall determine whether the non-compliance is serious or continuing.

10. The IRB may make whatever final findings and take whatever final actions it deems appropriate after the IRB is satisfied in its sole judgment, that the investigation is complete. Such final actions may include but are not limited to: closing the matter with no further action, taking any one or combination of the final actions listed below. The IRB shall not, however, take any final remedial action until the investigator has been given at least one opportunity to respond.

11. The IRB shall, within a reasonable period of time, in writing, notify the investigator, of the IRB's final findings and actions. The Institution and other applicable individuals and/or entities will be notified as appropriate of findings of serious or continuing noncompliance, suspension or termination of IRB approval, or unanticipated problems involving risk to subjects or others.

12. The investigator may, within a reasonable period of time, request that the IRB reconsider its final findings and/or final remedial actions. This request for reconsideration shall be in writing and shall adequately describe the basis for the investigator's request.

13. The IRB shall, in its sole discretion, determine whether, when and how, if at all, to reconsider its final findings or actions in response to the investigator's request for reconsideration.

14. The IRB shall advise the investigator and the Institution, as appropriate, in writing, of its final determination and/or disposition regarding the investigator's request for reconsideration.

15. For VA approved research additional steps may be required as outlined in VHA Handbook 1058.01.

Remedial Actions for Non-Compliance

The range of IRB actions for non-compliance in fact include, but are not limited to:

a. Closing the matter with no additional action;
b. Obtaining more information prior to making a final determination;
c. Modifying the research protocol, procedures and/or information disclosed during the consent process;
d. Monitoring of the research;
e. Monitoring of the consent process;
f. Suspension and/or termination of the research;
g. Referral to other organizational entities (e.g., legal counsel, risk management, institutional official);
h. Requiring an investigator to submit a written corrective action plan addressing any identified issues. The IRB may suspend an investigator until the corrective plan has been submitted, approved by the IRB, and fully implemented by the investigator.

i. Requiring more frequent IRB continuing review of relevant protocols;

j. Limiting the numbers or types of studies for which an individual may be principal investigator;

k. Suspending an investigator from conducting human subjects’ research in any capacity at the Institution until the investigator and/or his/her research team undergoes specified training and/or education. The IRB may require follow-up testing to demonstrate the training and education was effective;

l. Requiring an investigator to take any action appropriate to remedy the non-compliance. This may include re-contacting prior subjects and/or re-consenting current subjects (required when such information may relate to participants’ willingness to continue to take part in the research);

m. Suspending an investigator from conducting human subjects research at the Institution except under appropriate additional mentoring/oversight by the investigator’s department chair or other appropriate individual or group of individuals, possibly to include a Data Safety Monitoring Board;

n. Making appropriate reports to Institutional officials and/or outside individuals, institutions, entities and/or governmental agencies, as required;

o. Making a recommendation to the Institutional Official to disallow or qualify the use for publication, or otherwise, of any data collected on the non-compliant protocol or by the non-compliant investigator;

p. Making a recommendation to the Institutional Official that the investigator's access to any research accounts be frozen;

q. Disapproving continuation of the study in question and/or other studies involving the PI;

r. Permanently terminating the investigator’s involvement in some or all of the protocol;

s. Recommendation to UF Administration that further action be taken; and/or

t. Any other action the IRB, in its sole judgment, deems appropriate.

Documenting Non-Compliance

The investigator will be notified in writing of the findings and determinations of the board. Documentation pertaining to non-compliance is maintained in the IRB file and entered into the IRB database. A copy of a PI specific Compliance Report is provided in hard copy with each project history that goes to an Executive Reviewer or before the convened IRB.

Non-Compliance Issues with an Investigator that Involve More Than One Study

When the IRB finds that a Principal Investigator has non-compliance issues that involve more than one of their research protocols, the IRB AD and/or IRB Chair may initiate a “Non-Compliance Protocol” in the IRB Database. Global issues dealing with the identified non-compliance will be communicated back and forth using this “Non-Compliance Protocol.” Once a “Non-Compliance Protocol” has been initiated on an investigator, it will remain active until all issues are resolved. Once resolved, it will be “suspended” so that it will remain with the investigator. The Non-Compliance Database report for an investigator will indicate whether a “Non-Compliance” protocol exists for that individual.

IRB Non-compliance
Reports and/or allegations of IRB noncompliance will be directed to the Assistant Director (AD) of IRBs who will direct any investigation needed to substantiate the allegation which may include, but is not limited to: review of the IRB hardcopy file, database, and/or minutes. A summary of findings will be submitted to the Assistant Director for determination of action which may include: notification of the applicable IRB Chair and/or notification of General Counsel, Director of Sponsored Research, and any applicable Institutional Official. The AD can request a response from the IRB/IRB Chair to any findings of noncompliance prior to IO notification.

Unanticipated Problems Involving Risk to Subjects or Others and Adverse Events

Federal Regulations [46.103(b)(5)(i) and 56.108(b)(1)] require that unanticipated problems involving risk to subjects or others be promptly reported to the IRB, appropriate institutional officials, and any supporting department or agency head and OHRP and/or FDA. Although the regulations do not define unanticipated problems, OHRP (2007) published guidance on unanticipated problems. Reportable events under FDA regulations include a subset of unanticipated problems (serious, unexpected and related adverse events).

For Unanticipated problems involving risk to subjects or others and adverse events involving research at the VA, the IRB will refer to the applicable requirements outlined in VHA Handbook 1058.01.

Definitions

Unanticipated problem (UPR): any incident, experience, or outcome that meets all of the following criteria:

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

(2) related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

(3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. Events that do not cause detectable harm or adverse effects to subjects or others may still represent unanticipated problems (OHRP Guidance, 2007).

Both risks to subjects and risks to other individuals (e.g., research personnel, subjects’ family members) are included in the concept of UPRs. Risks may reflect any type of potential harm (e.g., physical, psychological, social, economic). Other problems that are unanticipated and indicate that subjects or other are at increased risk, but that are not caused by research procedures may also be considered UPR. Examples of UPRs can be found at http://irb.ufl.edu/docs/UPRDef.doc. Additional information regarding UPRs for VA research can be found in VHA Handbook 1058.01.

Adverse event: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or
disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

Unexpected Adverse Event: Any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with either:

(1) the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

(2) the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

Expected Adverse Event: Any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is consistent with:

(1) the known toxicities and side effects of the research procedures;
(2) the expected natural progression of subjects’ underlying diseases, disorders, and conditions; and
(3) subjects’ predisposing risk factor profiles for the adverse events.

Possibly related to participation in research: Any reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research.

Serious Adverse Event: Any adverse event that results in death for all local subjects and non-local deaths (considered by the local PI or project Study Chair to be related or possibly related to study participation), is life-threatening, results in inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, or based upon appropriate medical judgment, may jeopardize the patient or subject and/or may require medical or surgical intervention to prevent one of the outcomes listed in the definition above.

Unexpected Adverse Drug Experience (21 CFR 312): any adverse event, the specificity or severity of which is not consistent with the current investigator brochure or the investigational plan (protocol, consent form). In addition, known adverse events may occur more frequently than expected.

Unanticipated Adverse Device Effects (21 CFR 812): any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Internal Adverse Event: adverse events experienced by subjects enrolled by the investigator(s) at that institution

External Adverse Event: adverse events experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial.
OHRP (2005) considers a subset of adverse events to represent unanticipated problems that would need to be reported under HHS regulations including: 1) Adverse events that are serious, unexpected, and related or possibly related to participation in the research; 2) Serious adverse events that are expected in some subjects, but are determined to be occurring at a significantly higher frequency or severity than expected; and 3) Other unexpected adverse events, regardless of severity, that may alter the IRB’s analysis of the risk benefit ratio of the research, and warrant consideration of substantive changes in the research protocol or informed consent process/document.

Events That Require Reporting to the IRB

DHHS (45 CFR 46) and VA (38 CFR 16) human subjects protection regulations, and FDA (21 CFR 56) IRB regulations require that unanticipated problems involving risk to subjects or others, including a subset of adverse events, be promptly reported to the IRB.

By definition the following unanticipated problems involving risks to subjects or others must be reported to the IRB and may require reporting to FDA, OHRP/DHHS and/or other entities under the Reporting Policy:

1. Incidents, experiences, or outcomes that are unexpected, related or possibly related to participation in the research, and suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. For unanticipated problems, the IRB is responsible for determining whether the research places subjects or others.
2. Adverse events that are: serious, unexpected, and related or possibly related to participation in the research. For adverse events, the UF IRB determines relatedness.
3. Unexpected and related adverse events; the IRB determines seriousness.
4. Information security incidents involving any unauthorized use, disclosure, transmission, removal, theft, loss or destruction of research-related protected health information.

Reporting Requirements of IRB-01

Investigators are required to and ultimately responsible for promptly reporting unanticipated problems to subjects or others to the IRB regardless of funding source, study sponsor or type of study. Adverse events should be reported per the IRB-01 Adverse Event Evaluation and Reporting Guide found at: http://irb.ufl.edu/docs/AEGuide.pdf. Deviations and regulatory non-compliance should be reported per the IRB-01 Definitions and Reporting Guide: Deviations and Regulatory Non-Compliance found at http://irb.ufl.edu/docs/guide-dev.doc

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/irb01/formsinstruct.htm. Each category has an established time frame for reporting to the IRB that include:

Non-adverse events meeting the definition of an unanticipated problem involving risk to subjects or others and/or serious and unexpected adverse events that meet the IRB-01 criteria for
expedited reporting must be reported by the Principal Investigator, in writing, within five working days of discovery (five working days from notification for off-site adverse events) of the event.

Reporting requirements outlined in VHA Handbook 1058.01 will be followed for VA approved research.

**Investigator Responsibilities:** The Principal Investigator is responsible for reviewing the IRB-01 Definitions and following the IRB-01 Reporting Guides for unanticipated problems, deviations/regulatory non-compliance, and/or adverse events, complying with expedited reporting and for completing the applicable reporting forms (available at the IRB-01 website). Where appropriate the Principal Investigator is responsible for submitting reporting forms and any other supporting documentation to the IRB Administrative Office within 5 working days of discovery. If an event, incident, experience, or outcome is life-threatening or fatal, the IRB must be notified by phone within 24 hours.

**Office Responsibilities:** Reportable events (deviations/regulatory non-compliance, serious and unexpected adverse events and/or unanticipated problems) received by the IRB Administrative Office are entered into the database and reviewed for completeness (which includes the use of current forms and inclusion of all required paperwork) by administrative staff. Only submissions fulfilling all IRB-01 administrative requirements (as outlined in Guidelines and Procedures for Submitting Research to the IRB for Review available at [http://irb.ufl.edu/irb01/forms.htm](http://irb.ufl.edu/irb01/forms.htm)) will be forwarded for review. If issues are found with a submission, the PI or designee will be contacted to provide clarification and/or documentation. Once complete the submission, including all of the supporting documents provided by the PI and those provided by the IRB office including the Project History, the last IRB-approved informed consent form, and the applicable Reviewer Comment Sheet, is forwarded to an Executive Reviewer for review and action.

**Chair Responsibilities:** The IRB Chair or Vice Chair will review any reports to determine if the research has been associated with unexpected serious harm to subjects and/or if there is any immediate risk to subjects participating in the protocol. In such a case, the Chair may immediately suspend the study or enrollment in the study and refer the issue to the next full board meeting for discussion. The Chair or designee will notify the Investigator and appropriate Institutional officials of the suspension (See IRB Actions/Decisions: Project Suspensions/Terminations). Deaths that are unexpected and related or possibly related to study interventions, or where a relationship cannot be ruled out, will be referred from the Chair to the full Board for review. For VA approved research the Chair will review reports as specified in VHA Handbook 1058.01.

If no immediate risk to human subjects exists, and in the opinion of the Chair the event(s), incident(s), experience(s), or outcome(s) represent an UPR, including but not limited to AEs or serious/continuing noncompliance (page 53), the Chair will complete the applicable Reviewer Comment Sheet and request the event be added to the agenda for the next applicable full board meeting. If the event is clearly not unexpected (event is expected), does not suggest that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) and/or is not serious (for adverse events) and is not related to or possibly related to participation in the study than was previously known or recognized, the Chair may determine that no further action is needed. At the discretion of the Chair, any event, incident, experience, or outcome can be forwarded to the Board for consideration and determination. If the Executive Reviewer refers the submission, the Reviewer should indicate on comment sheet that the submission be referred to Full Board. Upon receipt, the IRB
Administrative Office will forward the submission, including all documents submitted by the PI, the completed Executive Reviewer Comment Sheet, the project history, last approved consent, Introductory Questionnaire, and protocol, for inclusion on the next applicable agenda and reviewer assignment. The investigator will be notified in writing that the submission has been forwarded to the Full Board for review. Once assigned, Reviewer Comment Sheets are attached to each hard copy. All documents listed on the agenda and those provided by the IRB Office are distributed to designated reviewers in hard copy and to the entire membership on CD.

**Reviewer Responsibilities:** At least one week prior to the convened meeting, assigned reviewers will receive a hard copy of the information provided by the investigator and office (including a project history, last approved consent form, and executive reviewer comments, as applicable). Reviewers are responsible for considering and evaluating the information provided by the Investigator on the Adverse Event or Unanticipated Problem Reporting Form, for ensuring that answers are complete and for presenting this information to the convened Board.

Reportable events will be assigned to two designated reviewers one of which is considered the lead reviewer. These reviewers present the event at a full board meeting and both receive a hard copy of all supporting documents in addition to the electronic copy. Any member may contact the IRB office if more information is needed. A Reviewer Comment Sheet will be attached to each submission assigned for review. The designated reviewers lead discussion of adverse events and/or unanticipated problems. If the Chair suspended the research because of concerns related to subject safety, the IRB will vote to confirm or reverse that decision. The IRB may make a final determination based upon the information reviewed (presented) or may require further information before making a final determination.

Upon making a determination that an event, outcome, experience, or incident represents an unanticipated problem, the IRB may determine that further action is required. Potential actions may include, but are not limited to:

1. A request for clarification of previously submitted information or for additional information from the investigator,
2. Revision(s) to the protocol, (e.g., additional tests or visits to detect similar events in a timely way or modification of inclusion or exclusion criteria to mitigate the newly identified risks),
3. Modification of informed consent documents to include a description of newly recognized risks and, if necessary, seek re-consent from current participants,
4. A requirement to inform enrolled subjects about newly recognized risks (e.g. re-consent) or otherwise inform current or past participants,
5. A change in the continuing review interval,
6. Suspension of new subject enrollment,
7. Implementation of additional procedures for monitoring the research or consenting of subjects (by the IRB or designation of a Safety Monitoring Committee),
8. Further inquiry into other protocols utilizing the particular drug/device/procedure in question, and/or
9. Suspension of research procedures in currently enrolled subjects or termination of the study.

Upon making a determination that an event, outcome, experience, or incident represents an unanticipated problem and recommendation for action as applicable, the Board will provide
prompt written notification to the Investigator and applicable Institutional Official per the Reporting Policy (for VA research, requirements outlined in VHA Handbook 1058.01 will be followed).

**Minimal Risk Studies:** For currently approved studies, if a protocol involves minimal risk interventions (e.g., certain surveys), the PI may report only those adverse events or unanticipated problems that the investigator considers Serious (or that may increase risk to subjects or others), unexpected, and related or possibly related to participation in the protocol. Events, experiences, incidents and/or outcomes meeting these criteria must be reported to the IRB (1) within 5 working days of discovery of the event and (2) on the Cumulative Adverse Event Table required at Continuing Review. Effective May 3, 2006: The Board voted to approve a change that allows PIs to report only those events considered serious, unexpected and related to the study or study interventions for exempt and expedited studies approved by the IRB. All studies are still required to report unanticipated problems involving risk to subjects or others.

**Off-Site, Off-Protocol Adverse Events:** PIs do not have to report adverse events that occur to individuals who are NOT enrolled on the study approved by IRB-01 (e.g., subjects enrolled on a different study that utilizes the same investigational drug). The IRB will not accept, process or review off-protocol events like this unless the PI determines that the event unexpectedly increases risk to past, present, or future subjects. If the event unexpected increases the risk to subjects the PI should submit the Adverse Event Reporting form available at: [http://irb.ufl.edu/docs/AESnU.doc](http://irb.ufl.edu/docs/AESnU.doc).

**Adverse Event Reporting for Studies involving HUMAN GENE THERAPY** require special reporting in accordance with NIH Guidelines (Appendix M). In addition to the local IRB, Investigators must report to NIH Office of Biotechnology Activities (OBA), UF Institutional Bio-Safety Committee (IBC), FDA (if the Investigator is Sponsor-Investigator), and the Sponsor (if other than the PI), in the manner described in Appendix M.

**NOTE:**

If no adverse events or unanticipated problems have occurred, the Cumulative Table must still be completed and submitted at continuing review.

**Data Safety Monitoring Reports/Adverse Event Summary Reports**

The PI, upon receipt, should submit copies of Data Safety Monitoring Reports and/or Adverse Event Summary Reports to the IRB within 5 business days if unexpected and related/possibly related problems are identified (see IRB-01 Reporting Guide: Unanticipated Problems (That are not Adverse Events) to Subjects or Others; otherwise, these reports can be submitted at the time of continuing review. The IRB Chair or Vice Chair will review any reports to determine if there is any immediate risk to subjects participating in the protocol. In such a case, the Chair may immediately suspend the study or enrollment in the study and bring the issue to the next full board meeting for discussion. The Chair or designee will notify the Investigator and appropriate Institutional officials of the action, as required under Federal Regulations.

The Chair will complete a Miscellaneous Comment Sheet and if appropriate request the information be added to the agenda for the next applicable full board meeting. If the information does not alter the risk benefit ratio of the study, the Chair may determine and document that no further action is needed.
Project Suspension/Termination

Suspension: An action taken by the IRB Chair, Vice Chair, convened IRB, or the Institutional Official or his representatives to temporarily stop some or all previously approved research activities (recruitment, enrollment, or specific procedures) typically taken “for cause.” Any “hold” placed on any research activity will be considered a suspension. Situations where an investigator voluntarily stops research activities will not be considered a suspension and as such will not be reported to oversight agencies.

Termination: An action taken by the convened IRB to permanently stop all activities in an IRB-approved research protocol. Terminated protocols are considered closed and will require a final review report. A protocol in which IRB approval has been terminated requires the Principal Investigator to provide the IRB with a list of participants for whom termination of research activities would increase risks or cause harm and justification for why this harm would occur. It will be the determination of the IRB whether the justification is valid and research activities can continue for these participants. Additional actions for VA research may be required as outlined in VHA Handbook 1200.05 and VHA Handbook 1058.01.

The IRB has the authority to suspend or terminate approval of research not being conducted in accordance with Federal Regulations, requirements or determinations of the IRB, or that has been associated with unexpected serious harm to subjects. The IRB Chair may also urgently suspend research that has been approved by the IRB upon receipt of information from any source verbally or in writing, of any alleged non-compliance with requirements, determinations, or policies and procedures of the IRB or of any reports of unanticipated problems involving risks to subjects or others. If the Chair suspends research activity because of concerns related to subject safety, the IRB will vote to confirm or reverse that decision. If the Chair or Board suspends any research activity on a protocol, the Chair or designee will promptly notify the Investigator and applicable IO or designee immediately by phone, with subsequent notification in writing that includes a statement of the reasons for the IRB's action. While suspended, all study interventions must stop, except those immediately necessary to protect subjects’ well being, as determined by the Chair or IRB. Enrollment of new subjects will not be permitted. If a study is suspended and enrolled subjects are undergoing study interventions, the PI must contact the IRB (and for VA Research, the VA Chief of Staff) who will determine if it is in the best interest of the subject to participate. All adverse events must continue to be reported. Suspended protocols are subject to the same continuing review and adverse event reporting requirements of active protocols. Protocols may be suspended for

1. Non-Compliance: See non-compliance policy.
2. Unanticipated Problems Involving Risks to Subjects or Others: See Unanticipated Problems Policy.
3. Expiration: When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically and a project's approval is suspended. Such expiration of IRB approval does not need to be
4. By request: Investigators and sponsors may at times need to temporarily suspend a protocol for a variety of other reasons not related to noncompliance or risk to subjects. In these cases, the IRB will suspend the study until the investigator requests in writing that the suspension be lifted. Such suspensions may need to be reported to the Institution as deemed necessary by the Chair or IRB.
If a project is suspended by an entity other than the IRB, the IRB should be notified within 5 working days. Any suspension or termination of a protocol by the IRB will be promptly reported in accordance with the Reporting Policy.

If study approval is terminated by the IRB:

1. Current participants must be notified that the study has been terminated (unless the IRB determines notification is not required);
2. Procedures for withdrawal of enrolled subjects will consider the rights and welfare of subjects;
3. When follow-up of subjects for safety reasons is permitted/required by the IRB, the subject should be informed; and
4. When follow-up of subjects for safety reasons is permitted/required by the IRB, any adverse events or outcomes should be reported to the IRB and sponsor.

Specific actions will be considered by the IRB on a protocol-by-protocol basis.

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

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 following individuals will be notified, in writing, within 7 business days of the convened IRB decision/determination:

Principal Investigator

Applicable Institutional Official (IO) (UF, Shands) or designee.

UF General Counsel

The IRB letter will describe the IRB action and the reason for the action.

For VA approved research any termination or suspension of research will be reported directly to the NF/SGVHS facility Director and ACOS of Research within 5 business days after the termination or suspension occurs. The IRB will follow all reporting procedures as outlined in VHA Handbook 1058.01.

Following notification of a reportable event, UF General Counsel in conjunction with the IRB Chair, UF Director of Sponsored Research and Compliance, Assistant Director of IRBs, and/or other individuals as applicable, will draft a report to be sent to applicable individuals and agencies containing the following information:

- Title of the research project and/or grant proposal in which the problem occurred
- Name of the principal investigator on the project
- Number of the research project assigned by the IRB and the number of any applicable federal awards
- The nature of the reportable event
  - Unanticipated problem involving risks to subjects or others, or
  - Serious or continuing non-compliance, or
  - Suspension or termination of approval of research
- Brief description of protocol (which may include information relevant to IRB determination)
- A detailed description of the problem including the findings of the IRB and the reasons for the IRB decision
- Actions taken by the IRB/Institution to address the problem,
- Plans, if any, to send a follow-up or final report by the earlier of:
  - A specific date
  - When an investigation has been completed or a corrective action plan implemented

The draft report is sent to the UF IO for review and modification as needed. The final report is approved and signed by the UF IO and distributed by the UF IO or designee to the following, as appropriate, within 30 days of the final IRB determination:

IRB-01, 02, 03, WIRB Chairs (whichever IRBs are involved or potentially impacted by the issue)
FDA, if the study is subject to FDA Regulations
OHRP, if the study is subject to DHHS Regulations
NF/SGVHS Facility Director, if the study involves VA Research
NF/SGVHS ACOS-R, if the study involves VA Research
NF/SGVHS RCO, if the study involves VA Research
General Counsel, Shands Healthcare Inc., if the study involves Shands
Any “Common Rule” Federal Agency that is supporting the research
Principal Investigator
UF General Counsel
Assistant Director IRBs
Director, Sponsored Research and Compliance

Notes:

For research that involves the VA, the VA IO or designee is responsible for reporting to applicable VA individuals, entities and VA regulatory agencies.

For research that involves Shands, the Shands IO or designee is responsible for reporting to applicable oversight agencies.

For research that involves both UF and another entity (VA and/or Shands), a decision may be made by the respective IOs that a joint report be 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.

Expiration of IRB approval, although referred to as “suspended” in the expiration letter, does not need to be reported to OHRP as a suspension of IRB approval under DHHS regulations.

**IRB Actions and Decisions**

Any action taken by the Board must receive the approval of a majority of those present at a convened meeting. The range of possible actions taken by the IRB is applicable to any type of submission reviewed by the Board.
**Item Approved as Submitted**

When a submission is approved by the IRB, the investigator is notified, in writing. Additional information conveyed in the Approval Letter for new studies includes: consent mechanism (waiver, waiver of documentation, or stamped and dated approved consent), Investigator responsibilities, record retention requirements, and category of approval for exempt or expedited protocols. Along with the written notification of approval, a copy of the IRB-approved consent document with the dates of approval is sent to the PI and a copy maintained in the IRB file. Copies of approval letters for new studies are sent to the VA Research Office and Clinical Research Center.

**Item Approvable Subject to Contingencies**

In the course of initial or continuing review of research, or review of proposed changes to previously approved research, the IRB may approve a research protocol with contingencies. IRB approval with contingencies means that at the time when the IRB reviews and approves a research study (or proposed changes to a previously approved research study), the IRB requires as a condition of approval that the investigator (a) make specified changes to the research protocol or informed consent document(s), (b) confirm specific assumptions or understandings on the part of the IRB regarding how the research will be conducted, or (c) submit additional documents, such that, based on the assumption that the conditions are satisfied, the IRB is able to make all of the determinations required for approval under the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. With respect to research reviewed and approved with Contingencies by the IRB at a convened meeting, the IRB may designate the primary reviewer, the IRB chairperson (and/or other individual(s) with appropriate expertise or qualifications) to review responsive materials from the investigator and determine that the Contingencies have been satisfied, and further review by the IRB at a subsequent convened meeting would not be necessary. The IRB may require the following as conditions of approval of research:

1. Confirmation of specific assumptions or understandings on the part of the IRB regarding how the research will be conducted (e.g., confirmation that the research excludes children, clarification of subject numbers);
2. Submission of additional documentation (e.g., certificate of ethics training, ancillary committee reviews, etc.);
3. Precise language changes to protocol or informed consent documents; or
4. Substantive changes to protocol or informed consent documents along with clearly stated parameters that the changes must satisfy (e.g. Confirmation that consent form is in eighth grade language).

When the contingencies approved by the convened IRB stipulates that the investigator must make specified changes to the research protocol or informed consent document(s) (including but not limited to new studies, continuing reviews, major revisions, etc), an IRB Administrative Reviewer (who is an IRB Member) will verify that the changes made were the changes requested, and approve the submission.

When the contingencies approved by the convened IRB stipulates that the investigator must confirm specific assumptions or understandings on the part of the IRB regarding how the research will be conducted, or must submit additional documents, such that, based on the assumption that the conditions are satisfied, the IRB is able to make all of the determinations required for approval. In these cases, the primary reviewer, the IRB Chair or another
experienced IRB member will verify that the changes made were the changes requested and that all contingencies were met, and will approve the submission.

In either of the above cases, the effective date of the initial approval is the date on which the IRB chairperson (or any other individual(s) designated by the IRB) has reviewed and accepted as satisfactory any revised protocol or informed consent documents or any other responsive materials required by the IRB from the investigator.

Reviewers are asked to clearly specify the modifications required to secure approval on the reviewer comment sheet or on the documents submitted by the investigator (e.g. consent form) so that IRB Administrative Staff preparing the Approval with Contingencies Letter have the language determined approvable by the convened Board.

There are two mechanisms by which approval with contingencies can occur: (1) The Investigator is notified by e-mail and hard copy letter of specific changes that must be made in the submission in order to be approvable via this mechanism. The investigator is asked to complete and submit an Approval with Contingencies Response Form along with a copy of the Approval with Contingencies change letter and any other applicable documents to the IRB for further action. When received by the IRB Administrative Office, the Approval with Contingencies change response is entered into the database and is sent for review by an experienced IRB member. If the changes approved by the convened Board were explicit and the PI makes the requested changes exactly as requested; however, if the PI fails to make all of the requested changes, or makes any additional changes (no matter how minor), the submission will be forwarded to an Executive Reviewer for determination. If the changes fall under the criteria for a minor revision and are not directly relevant to the determinations required by the IRB, the Executive Reviewer can approve the submission; otherwise, the submission is forwarded back to the convened Board for consideration. (2) At the time of a convened meeting at which the changes are requested, the IRB Administrative Office can make the stipulated changes to an electronic version of the submission. Once the changes have been made, both clean and strikeout versions are returned to a Board for approval. The investigator is notified in writing that the submission has been approved. Copies of both clean and modified documents are sent and the PI notified that if he/she is not in agreement with the changes, that a revision must be submitted. The date of approval of the project (from which the approval period is calculated) is the date the convened Board approved the research or approved the research with explicit changes rather than the date the explicit changes were approved by the Chair or designee. Information pertaining to Explicit Changes approved via an expedited review process will be communicated to the full Board via Informational Minutes.

If the investigator does not agree with any of the contingencies requested by the Board, the investigator should submit a cover letter with the rationale for the non-concurrence and the supporting paperwork for reconsideration by the Board. If the Investigator agrees with the changes, but there is minor modification in the language, this may be reviewed and approved by a Chair.

Item Tabled
When the convened IRB requests substantive clarifications, modifications, explanations, or additional information regarding the protocol or informed consent documents that are directly relevant to the determinations required by the IRB under the regulations, the protocol will be tabled and approval deferred pending subsequent review of the tabled response at a subsequent Full Board meeting. The Investigator will be notified by e-mail and hard copy letter of the Board determinations and actions. The PI is asked to complete and submit a Tabled Submission Response along with any applicable documents to the IRB for further review and action. See Full Board Review: Tabled Response.

No Action/Further Action Needed

When the Chair or Board reviews information from the Investigator, and the issue is resolved by information submitted, there may be a determination that no action or no further action is needed on behalf of the investigator.

Item Disapproved

Only the convened IRB may disapprove non-exempt research. If the IRB decides to disapprove a research activity, the principal investigator will be sent a letter from the Board detailing the reasons for disapproval and give the investigator an opportunity to respond in person, writing or both. PIs or their designee are invited to attend meetings at which submission are reviewed. If the item disapproved is a new protocol, the protocol may be resubmitted with corrections and/or clarifications under the original project number. Alternatively, the investigator may submit the project as new with a cover letter specifically addressing the reasons for disapproval and the concerns of the Board, and how those issues were resolved. A copy of the letter from the IRB that outlined the Board's reason for disapproval, the investigator's summary letter, and the new protocol will be distributed to all IRB members for reconsideration at a full Board meeting.

Administrative Withdraw

If the IRB requests additional information (as is the case when your submission is Tabled, requires Explicit Changes, or has other kinds of "Needs Reply" letters generated), researchers have 30 days from the date of our letter to submit some form of a response (even if only to request another 30 days). If the IRB-01 office does not receive an official written response in 30 days the database will automatically execute one of two options:

1. **Automatic action if a PI fails to reply within 30 days - New studies and Revisions:**

   The database will automatically withdraw your submission. If you wish to have this submission reconsidered you must not only resubmit it in its entirety but also be sure to address the issues identified by the IRB.

2. **Automatic action if a PI fails to reply within 30 days - Continuing Reviews, Adverse Events, Miscellaneous items, etc:**

   Since the review and approval of these items could impact the safety to subjects already enrolled in the trial they will be forwarded to a Chair for review. If the Chair determines there are no safety concerns, the submission will be withdrawn. If this occurs and you wish to have this submission reconsidered you must not only resubmit it in its entirety but also be sure to address the issues identified by the IRB. Conversely, if the Chair determines there
are potential risks to subjects then the submission along with your failure to respond will be forwarded to the full Board for consideration.

**Reporting IRB Findings and Actions** (procedures for reporting to Investigators and Institution)

The IRB notifies investigators, and the institution, in writing, of its decisions to approve or disapprove the research activity, or of modification required to secure approval of the research activity. The IRB-01 Administrative Office promptly generates IRB correspondence through the database and distributes these official hard copies to the pertinent parties (e.g. the principal investigator and, if appropriate, DSP, CTSI, VA, etc.) via the mail system. If an investigator prefers to send a representative to our office to obtain a particular piece of correspondence, he/she may contact us and ask us to hold it for retrieval. Groups of investigators may also request a “pick up folder” in which IRB-01 will place correspondence for retrieval rather than sending it via the mail system. Note: while the IRB-01 Administrative Office strives to fulfill requests for document retrieval rather than mailing, the standard policy is to send correspondence via the mail system and occasionally correspondence may be mailed despite a researcher’s request for retrieval. IRB-01 can provide copies of correspondence on request.

As a courtesy to investigators, the IRB-01 Administrative Office also strives to send any correspondence that requires an investigator response (e.g. tabled, explicit changes, disapproval, needs reply, suspension, etc.) via e-mail to the principal investigator and, if listed, a secondary contact. This e-mail is intended to enable the PI to reply more quickly to our correspondence and does not substitute for the official hard copy of the correspondence. Investigator responses to requests of the IRB will be reviewed according to Tabled Response or Explicit Change procedures outlined in this manual or for other correspondence that “needs reply,” the investigator should submit a the appropriate response form or cover letter responding to the requests of the applicable reviewer and the IRB Administrative Office will forward to the Board if the Board requested the information or the applicable Executive Reviewer if the submission was reviewed under expedited procedures.

The IO, through the Division of Sponsored Programs has access to the decisions of the IRB through the IRB database and the Director of Compliance is sent copies of Full Board and Informational minutes. DSP administrative personnel including the Institutional Compliance Officer and/or the Assistant Director of IRBs are sent the Full Board meeting agenda in advance of meeting. The IRB notifies DSP of the decision to approve, disapprove, or require modifications to secure IRB approval of research activities by sending electronic versions of IRB approved minutes and informational minutes.

**VA Notification of IRB Actions**

The IRB notifies the NFSG VHS of its decision to approve, disapprove, or require modifications to secure approval of research. The VA RCO and Research Service personnel have real-time access to the IRB database and myIRB to review information (including both draft and final Full Board and informational minutes) pertaining to VA research. In addition, copies of approval and renewal letters are sent to the Research Service; IRB full board and informational minutes are sent to the VA RCO Research Office who will distribute the minutes to the R&D Committee for review.

**Reviews Requiring Special Consideration**
Vulnerable Subjects

Federal regulations acknowledge the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The IRB also considers UF Students, UF and VA staff, terminally ill patients, and institutional residents as potentially vulnerable. When investigators propose the inclusion of some or all subjects who are likely to be vulnerable to coercion or undue influence, the Investigator and IRB should consider additional safeguards, as necessary, to protect the rights and welfare of these subjects. Projects conducted or supported by DHHS or that involve FDA-regulated test articles will be reviewed in accordance with the applicable Subparts.

Review Process

Investigators wishing to include potentially vulnerable populations as either the “targeted” population or in the demographics of the potential subject pool must provide information relevant to their inclusion in the applicable paperwork (protocol, IQ, IQ Addenda) for consideration by the IRB. Information including but not limited to subject selection, recruitment and consenting procedures, and justification for the inclusion of vulnerable subjects and any additional safeguards should be included. IRB forms and form instructions have been designed to elicit information that the IRB needs to review, consider and evaluate in order to make the determinations required under regulation and approve research.

When reviewing projects involving vulnerable or potentially vulnerable subjects, the IRB follows Full Board or Expedited Review Procedures (described earlier) as applicable and (1) should be sufficiently qualified to review such projects either through representation of individuals knowledgeable about working with vulnerable populations on the Board or (2) will rely on consultants to provide additional expertise as needed. In its review, the IRB will consider information provided by the PI and may request additional information or clarification as needed before approving the research. The IRB systematically evaluates research and the protocol submission and considers the inclusion of vulnerable subjects on a protocol by protocol basis including the justification for the inclusion of vulnerable subjects or populations in the study and any additional safeguards that may be needed to protect the rights and welfare of these subjects and minimize risks. Additional safeguards may include, but are not limited to:

- Requiring someone not involved in the research to seek informed consent
- The inclusion of a consent monitor or subject advocate
- A waiting period between initial contact, consent discussion and enrollment to allow time for family discussion and questions; and/or
- Provisions for additional consent protections such as obtaining consent from a legally authorized representative (LAR) and/or assent from subjects with limited autonomy.

In addition to the regulatory criteria set forth for the approval of research, in the absence of additional codified protections, when reviewing projects that may involve vulnerable populations, the IRB may consider approving research that involves vulnerable subjects if at least one of the following conditions is met: a) the research does not involve more than minimal risk to the subject; b) the research is likely to benefit the subject directly, even if the risks are considered to be more than minimal; or c) the research involves greater than minimal risk with no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition.
For all research involving vulnerable or potentially vulnerable subjects, IRB records, including but not limited to, documents submitted by the PI and reviewed and approved by the IRB or Executive Reviewer, minutes and/or comment sheets (for projects undergoing full board or expedited review) will document the inclusion of vulnerable subjects, and protocol specific findings, additional safeguards and determinations of the IRB for research involving pregnant women, human fetuses, neonates, prisoners, children and/or other vulnerable populations.

The IRB must approve a protocol for the enrollment of potentially vulnerable subjects prior to their inclusion in the protocol. If the IRB does not approve a project for the inclusion of vulnerable subjects, the Investigator must revise the project prior to the inclusion of any individual or class of individuals deemed vulnerable or potentially vulnerable. Any subject who may be considered vulnerable enrolled in a project without prior IRB approval should be reported in writing to the IRB within 5 business days of discovery.

VA Policy on the Inclusion of Certain Vulnerable Populations

VHA Handbook 1200.05 describes additional protections (and restrictions) for vulnerable subjects participating in VA Research. Specifically:

1. 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 in accordance with VHA Handbook 1200.05.

2. 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 in accordance with VHA Handbook 1200.05.

3. Research involving children and/or prisoners shall not be conducted by VA investigators while on official duty or at VA facilities or approved off-site facilities. Investigators should contact the NF/SGVHS Research Service Office for further information.

4. Research involving pregnant women as subjects will be reviewed and documented in accordance with the provisions of VHA Handbook 1200.05 and 45 CFR 46 Subpart B.

5. IRB Review and documentation of research involving “mentally disabled persons” or those “persons with impaired decision making capacity” shall be in accordance with provisions of VHA Handbook 1200.05.

The 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 IRB submission forms.

Children and Minors

Children are recognized as vulnerable under the federal regulations and as such have additional protections codified under Subpart D to 45 CFR 46 and 21 CFR 50 (for FDA-regulated research).

Federal Regulations (both 45 CFR 46 and 21 CFR 50) define children as 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.

Florida law defines “minor” as any person who has not attained the age of 18 years. (§ 1.01, Florida Statutes). Under Florida law, 18 is the age of majority and is, therefore, the usual age at which people can consent to treatments or procedures.
Children and minors can be considered synonymous for purposes of this policy unless the minor status is removed upon the occurrence of any of the following events:

1. Attaining the age of 18 years. (§743.07, Florida Statutes)
2. Emancipation by order of the circuit court. (§743.015, Florida Statutes)
3. Marriage (the minor status is not reinstated upon the dissolution of the marriage). (§743.01, Florida Statutes)

Under Florida law (§744.3215, Florida Statutes), a minor is presumed to be legally incompetent as a result of his or her age or presumed immaturity of judgment and therefore are presumed to not have the capacity to care for his or her person or property, including the capacity to consent to medical and mental health treatment. Biological or adoptive parents are the minor’s natural guardians. A natural guardian is a guardian who can exercise all the legal rights and powers for the minor/ward that can be delegated.

In Florida, a patient has the right to know if medical treatment is for purposes of experimental research and to consent prior to participation in such experimental research (§381.026, Florida Statutes). Since the parent/natural guardian can exercise all of the legal rights and powers of the minor, the parent/natural guardian can consent to the minor’s participation in experimental research. In the absence of a natural guardian, due to death, incapacity, removal of parental rights or other permanent absence, a minor will normally have a court-appointed guardian or will be a ward of the state.

A court-appointed guardian of a minor is usually a plenary guardian who is authorized to exercise all the legal rights and powers for the minor/ward that can be delegated. If the guardianship is limited, then the restrictions on the guardianship will be specified in the letters of guardianship issued to the guardian by the court (§§744.361 and 744.345, Florida Statutes). A plenary guardian is a guardian who can exercise all the legal rights and powers for the minor/ward that can be delegated. A plenary guardian can give consent to medical and mental health treatment (§744.102(8)(b); §744.301; §743.0645(1)(c), Florida Statutes); however, unless specifically authorized by the court, a plenary guardian cannot give legal right to consent to participation in research (§§744.3215(a)(b) and 744.3725, Florida Statutes).

There are some situations, under Florida law where minors may consent for themselves including:

1. medical examination and/or treatment for STDs including HIV Testing (§§384.30(1) and 381.004(3)(b)(2), Florida Statutes)
2. termination of a pregnancy of a minor; however, notice must be provided to the parent at least 48 hours prior to performing or inducing the termination of the pregnancy (§390.01115, Florida Statutes);
3. voluntary admission to a substance abuse treatment facility (§397.601, Florida Statutes); and
4. donating blood without compensation (§743.06, Florida Statutes)

Additionally, pregnant unwed minors may consent to medical treatment or procedures relating to their pregnancy and minor unwed mothers can consent to medical treatment or procedures for her child. (§§743.065(1) and (2), Florida Statutes)

Minors may also make their own decisions regarding contraception.
The protections under Subpart D apply to persons who are “children” under the federal regulations. If investigators have questions regarding the inclusion of children in research, they should contact the IRB Administrative Office.

UF IRB requirements for the inclusion of children in research are consistent with the additional protections described in the Subpart D to the Federal Regulations. Investigators who propose to include children in research must complete the applicable Addendum to the Introductory Questionnaire that addresses the regulatory requirements for the inclusion of children in the proposed research. The risk/benefit ratio will determine the acceptability and approvability of the research and the requirements for parental/guardian permission and assent of the child.

Assent means a child’s affirmative agreement to participate in research and permission means the agreement of parent(s) or guardian to the participation of their child or ward in research. Federal Regulation defines a parent as a child’s biological or adoptive parent and a guardian as an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care (Florida law described above).

Provisions for soliciting and documenting the assent of the children and permission of parents or guardians, unless appropriately waived in accordance with applicable regulations, will be addressed by the IRB on a protocol-by-protocol basis in accordance with the provisions set forth in 45 CFR 46.408.

Further information on enrolling children in research at UF is available at http://irb.ufl.edu/irb01/tools.htm.

Related topic: See IRB Opinion Paper entitled Research Involving (1) Unmarried Minors (< 18 Years Of Age) Who Are Pregnant or Mothers, or (2) Babies of Unmarried Minor Parents.

Pregnant Women, Fetuses, Neonates, or In Vitro Fertilization

Pregnant women, fetuses and neonates are recognized as vulnerable populations under the federal regulations and as such have additional protections codified under Subpart B of the Federal Regulations (45 CFR 46). These regulations also cover research using human in vitro fertilization as well as human fetal tissue, placenta or post-delivery fetal material.

UF IRB requirements for the inclusion of pregnant women, fetuses, or neonates in research are consistent with regulations (45 CFR 46 Subpart B). For research that involves or may involve pregnant women, fetuses or neonates, Investigators must complete the applicable IRB addenda (W) to the Introductory Questionnaire. To approve research that involves or may involve pregnant women, fetuses or neonates the IRB must find and document, in addition to the requirements of Subpart A, the determinations under Subpart B. The risk benefit ratio will determine the acceptability of the research and the requirements for consent.

Research involving Prisoners as Subjects

Federal Regulation

Definitions
“Prisoner” means 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 which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing (45 CFR 46.303(c)).

Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted.

Individuals who would be considered prisoners include but are not limited to:
1. Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration;
2. Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration; and
3. Parolees who are detained in a treatment center as a condition of parole.

Individuals who would not be considered prisoners include but are not limited to:
1. Individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community;
2. Individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to nonpenal institutions for treatment because their illness makes them a danger to themselves or others;
3. Persons living in the community and sentenced to community-supervised monitoring, including parolees; and
4. Probationers and individuals wearing monitoring devices; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population.

Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of **healthy persons (45 CFR 46.303(d))**

** OHRP interprets the term “healthy persons” in this definition as referring to healthy persons who are not prisoners.

Research conducted or supported by HHS:

No research involving prisoners is exempt from the regulations outlined in 45 CFR 46 and thus must be reviewed under an expedited review procedure (if the research meets the criteria for expedited review [http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm)) or by the convened IRB. Regardless of the review mechanism (expedited or full board) a prisoner representative will be included in the review.

Research supported or conducted by HHS that involves or may involve prisoners is permissible only if the research involves one or more of four permissible categories outlined in Subpart C of the regulations. Permissible categories include:
I. the study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

II. the study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

III. research on conditions particularly affecting prisoners as a class; the regulations list as examples vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere, and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults;

IV. research on practices, either innovative or accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. If the IRB-approved proposal is a study in which some prisoners will be assigned to a control group and these prisoners may not benefit from their participation in research, such research may proceed only after the HHS Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of his or her intent to approve the research (45 CFR 46.306(a)(2)). Control groups which may not benefit from research include a control group receiving standard of care that the prisoners would otherwise receive, services as usual, or a placebo.

A fifth category of permissible research for certain epidemiological research conducted or supported by HHS may be appropriate for a Secretarial waiver. To qualify under this category, the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease.

For research supported or conducted by HHS that involves or may involve prisoners, Investigators must complete the applicable IRB addenda to the Introductory Questionnaire. To approve research that involves or may involve prisoners, the IRB must review and find, in addition to the requirements of Subpart A, that:

1. The research under review represents one of the permissible categories of research;

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

5. The information is presented in language which is understandable to the subject population;

6. Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is
clearly informed in advance that participation in the research will have no effect on his or her parole; and

7. Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

In addition to satisfying the membership requirements of 45 CFR 46.107, when an IRB reviews a proposal that involves or may involve prisoners as subjects, the composition of the IRB must satisfy the following additional regulatory requirements at 45 CFR 46.304(a) and (b):

A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB.

At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research proposal is reviewed by more than one IRB, only one IRB need satisfy this requirement.

Research involving prisoners may be approved with a waiver or alteration of informed consent as long as an appropriately constituted IRB reviews the research and makes the appropriate findings regarding the waiver or alteration of informed consent requirements (45 CFR 46.116). Even if informed consent is waived or altered, subpart C of 45 CFR part 46 still requires that the subjects be clearly informed in advance that participation in the research will have no effect on their parole, if such notification is relevant.

Regardless of which permissible category is selected, for any HHS-conducted or -supported research involving prisoners, the institution(s) engaged in the research must certify to the Secretary (through OHRP) that the IRB reviewed the research and made the seven required findings as required by the regulations (45 CFR 46.305(c) and 46.306(a) (1)) and receive OHRP authorization prior to initiating any research involving prisoners if OHRP determines that the research involves one of the permissible categories. If OHRP determines that the proposed research does not involve one of the permissible categories, it will state in the letter to the institution that such research involving prisoners cannot proceed.

Requirements for Institutional Certification to OHRP

The institution’s certification must indicate that the IRB reviewed the research under subpart C and made the seven findings as required by the regulations (45 CFR 46.305(a)). In addition, the institution must provide OHRP with a copy of the relevant research proposal includes:

- the IRB-approved protocol; any relevant HHS grant application or proposal;
- any IRB application forms required by the IRB;
- and any other information requested or required by the IRB to be considered during initial

The following information should be included in the institutional prisoner research certification letter to facilitate processing:
- the OHRP Federalwide Assurance (FWA) number;
- the IRB registration number for the designated IRB; and
- the date(s) of IRB meeting(s) in which the protocol was considered, including a brief chronology that encompasses:
  - the date of initial IRB review; and
  - the date of subpart C review, if not done at the time of initial IRB review.

If an enrolled subject becomes a prisoner

If a human subject involved in ongoing research becomes a prisoner during the course of the study and the research is HHS-supported or funded and the relevant research proposal was not reviewed and approved by the IRB in accordance with subpart C of 45 CFR part 46, the investigator must promptly notify the IRB. All research interactions and interventions (including obtaining identifiable private information) with the now-incarcerated prisoner-subject must be suspended immediately (unless the investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated until the requirements of subpart C are satisfied). If the investigator wishes to have the prisoner subject continue to participate in the research, the IRB must promptly re-review the project in accordance with the requirements of Subpart C, and the institution(s) engaged in the research involving the prisoner subject must send a certification to OHRP and wait for a letter of authorization in reply. Otherwise, the prisoner subject must stop participating in the research, except as noted below.

Prisoner Research not conducted or supported by HHS

If research is not HHS-conducted or -supported, the IRB will review the research in accordance with Subpart A and the institution does not need to submit any certification to OHRP, regardless of whether the institution has chosen to extend the applicability of its FWA and subpart C to all research. Additionally research proposals in category (iii) or (iv) that are not conducted or supported by HHS do not require a Secretarial consultation.

Research Involving Incapacitated/Incompetent/Decisionally Impaired Adults Unable to Provide Consent

To approve research under the federal regulations, the IRB should determine that subject selection is equitable and be “particularly cognizant” of the special problems of research involving vulnerable populations including “mentally disabled persons”. This includes determining that additional safeguards have been included in the study to protect the rights and welfare of these subjects [45 CFR 46.111]. There is no definition of “mentally disabled persons” nor are there additional safeguards codified in regulation.

Both HHS and FDA Regulations require the investigator to obtain the legally effective informed consent of the subject or the subject’s legally authorized representative before involving the subject in research [45 CFR §46.116 and 21 CFR §50.20]. Further, informed consent must be documented by the use of a written consent form approved by the IRB and signed (and dated) by the subject or the subject’s LAR [45 CFR 46.112 and 21 CFR 50.27]. Under certain situations, consent and/or documentation of consent may be waived (see “Informed Consent Instructions” for further information). Obtaining surrogate consent may be appropriate, when specifically approved for such circumstances by the IRB in advance of implementation. Florida statute and VA regulation define who can consent for incapacitated/incompetent/decisionally impaired adults. Even with this in mind, investigators proposing to include decisionally impaired
adults in research should include provisions for subject assent when the subject is able to express assent or dissent.

State Law

The subject’s legally authorized representative is defined under state law. Guidance on how to obtain valid informed consent from a surrogate decision maker for an adult subject who is cognitively impaired and lacks decisional capacity is available in the IRB Position Paper What Happens When the Subject Cannot Consent? At http://irb.ufl.edu/docs/op-legal%20consent.doc

IRB Responsibilities

See “Vulnerable Subjects: Review Process” described above. For research that involves incapacitated, incompetent, or decisionally impaired subjects, the IRB draws on the knowledge, education and experience of the membership or consultants to provide scientific and ethical review of proposed research. To approve research that involves incapacitated, incompetent, or decisionally impaired subjects, the IRB should find and document that the requirements of Subpart A are satisfied and consider the risk benefit ratio to determine the acceptability of the research and the requirements for consent of the subject or subjects LAR and assent of the subject as applicable.

VA Policy

The IRB will refer to the applicable guidelines outlined in VHA Handbook 1200.05 for research involving incapacitated, incompetent, or decisionally impaired subjects.

Employees and Students

In order to minimize any potential coercion involving someone being asked to be a study subject by his or her supervisor, the IRB-01’s policy is that:

- A supervisor may not target their employees or their students as study subjects.
- An employee or student may be enrolled into a protocol in which their supervisor is an investigator, provided the employee or student became aware of said protocol via a non-targeted ad for said protocol (i.e: the ad is located in a public place and not solely in the employee’s work area).
  - If the protocol is a therapeutic protocol, the supervisor may obtain informed consent
  - If the protocol is non-therapeutic, the supervisor may not obtain informed consent.

*Note, a supervisor is defined as someone that has direct or indirect administrative or decision-making authority over the person in question.

Research Involving FDA-Regulated Test Articles

Devices

FDA Regulations (21 CFR 812.2) provide criteria for determining the level of device risk.
Investigational devices are categorized as either "significant risk" (SR) or "non-significant risk" (NSR), unless qualifies for an abbreviated IDE or exempt from IDE regulations as follows:

Qualifying for Abbreviated IDEs

(1) An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:
   (i) Labels the device in accordance with 21 CFR 812.5;
   (ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
   (iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under 21 CFR 50 and documents it, unless documentation is waived by an IRB under 21 CFR 56.109(c).
   (iv) Complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
   (v) Maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
   (vi) Ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7); and
   (vii) Complies with the prohibitions in 812.7 against promotion and other practices.

(2) An investigation of a device other than one subject to paragraph (e) of this section, if the investigation was begun on or before July 16, 1980, and to be completed, and is completed, on or before January 19, 1981.

Exempted from IDE regulations

(1) A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.

(2) A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

(3) A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
   (i) Is noninvasive,
   (ii) Does not require an invasive sampling procedure that presents significant risk,
   (iii) Does not by design or intention introduce energy into a subject, and
   (iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
(4) A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

(5) A device intended solely for veterinary use.

(6) A device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c).

(7) A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

A SR device is defined by the regulations as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and

(1) Is an implant; or
(2) Is used in supporting or sustaining human life; or
(3) Is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise prevents impairment of human health; or

Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

A NSR device investigation is one that does not meet the definition for a significant risk study.

Investigator Responsibilities: In addition to the responsibilities for full board or expedited studies (as noted above), Investigators are responsible for including the sponsor’s (including the investigator on investigator-initiated studies) assessment of device risk and any other pertinent information that may help the IRB in evaluating the risk of the study. Such information may include a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures; whether other IRBs have reviewed the proposed study and what determination was made; and the FDA’s assessment of the device’s risk, if such an assessment has been made. Investigators are asked to provide the IDE number for SR devices on the IQ.

IRB Responsibilities: Under some circumstances, an IRB must determine whether a device involves significant risk (SR) or non-significant risk (NSR) to subjects. A sponsor’s preliminary determination that a medical device study presents an NSR is subject to IRB approval. The IRB is responsible for making an independent risk determination based on the proposed use of the investigational device in a study and not on the device alone. However, if the study sponsor or FDA has determined a device to be SR in its IDE application approval, the IRB must consider the device to be SR during review. Full Board review is required for all studies involving SR devices. If the IRB makes an independent determination that a device poses SR, the investigator will be notified, in writing, of this decision, who, in turn, must notify the sponsor. Prior to final IRB approval of a project involving a SR device, an IDE number must be obtained from the FDA by the investigator or the sponsor (if not already obtained) and provided to the IRB.

If a device is considered to be NSR by the sponsor and the IRB reviews and concurs, an IDE is not required, and the study may begin after all applicable approvals have been obtained. The sponsor should provide the IRB with a risk assessment and the rationale used in making its NSR risk determination for its review.
Once a risk determination has been made, the IRB will consider whether the study meets the criteria for approval. IRB minutes for studies involving investigational devices should include, in addition to other regulatory requirements, risk determination and rationale for the determination.

If the NF/SG VHS is involved the IRB will adhere to guidelines outlined in VHA Handbook 1200.05.

Investigational Drugs

The FDA (21 CFR 312.3) defines a clinical investigation as any experiment in which a drug is administered or dispensed to or used involving one or more human subjects outside the course of medical practice. Clinical investigations involving investigational new drugs, marketed drugs or other chemicals for challenges in human subjects may require the submission of an investigational new drug application (IND) to the FDA. An IND application provides the FDA with information such as the rationale and design of the study, safety data, manufacturing process, and investigator qualifications that is relevant for the protection of human research participants. Current Federal law requires that a drug or biologic be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA. Compliance with FDA IND regulations mitigates risk to subjects, investigators and the institution.

Whenever a UF investigator intends to administer, dispense or use a drug in a clinical investigation, an IND is needed unless the clinical investigation meets FDA criteria for IND exemption. FDA Regulation 21 CFR 312.2(b) stipulates that the clinical investigation of a drug product that is lawfully marketed in the U.S. is exempt from the IND regulations if all of the following apply:

1. (i) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

2. (ii) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

3. (iii) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

4. (iv) The investigation is conducted in compliance with the requirements for institutional review set forth in part 21 CFR 56 and with the requirements for informed consent set forth in part 21 CFR 50; and

5. (v) The investigation is conducted in compliance with the requirements of 21 CFR 312.7.
(2) (i) A clinical investigation involving an in vitro diagnostic biological product listed in paragraph (2)(ii) of this section is exempt from the requirements of this part if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and (b) it is shipped in compliance with 21 CFR 312.160.

(ii) In accordance with paragraph (2)(i) of this section, the following products are exempt from the requirements of this part: (a) blood grouping serum; (b) reagent red blood cells; and (c) anti-human globulin.

(3) A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of this part if shipped in accordance with 21 CFR 312.160.

(4) FDA will not accept an application for an investigation that is exempt under the provisions of paragraph (1) of this section.

(5) A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

**Investigator Responsibilities:** Since the assessment of IND applicability can be difficult, UF has developed guidance for conducting research that exposes humans to drugs, biologics, chemicals, and/or any other food substance that can be accessed at [http://irb.ufl.edu/irb01/drugstudy.htm](http://irb.ufl.edu/irb01/drugstudy.htm). When using an drug during the course of a clinical investigation, the investigator must complete the Drug Addenda to the Introductory Questionnaire.

The IND Application (FDA Form 1571), Statement of the Investigator (FDA Form 1572) and other applicable forms are available at: [http://www.fda.gov/cder/about/smallbiz/Forms.htm](http://www.fda.gov/cder/about/smallbiz/Forms.htm). Any correspondence between the FDA and the investigator (including, but not limited to IND exemption or IND number) must be submitted to the IRB prior to final approval. When proposing the use of an investigational drug in a clinical investigation, the Investigator’s Brochure and the FDA Form 1572 must be submitted to the IRB. When proposing the use of a marketed drug in a clinical investigation, the FDA-approved package insert must accompany the IRB submission. Sponsor-investigators initiating and conducting a clinical investigation are required to meet the obligations of both sponsor and investigator. The IRB Administrative Staff and/or IRB must be able to verify that the IND supplied by the investigator on the IQ/IQ addenda is valid. The IND number provided by the PI should match the IND number in a sponsor’s protocol or in a letter from the FDA or sponsor. If the IND number provided by the PI in the submission is not valid, the PI will be notified by the IRB Administrative Staff via written correspondence (e-mail or letter).

If the clinical investigation is clearly IND exempt, the investigator must provide protocol specific evidence that each criterion has been met.

**IRB Responsibilities:** To determine the validity of the IND number provided by the investigator, the IRB Administrative Staff and/or the IRB reviewers will review documentation (materials) from the sponsor (protocol, correspondence) or the FDA (letter). The IRB will review research studies involving investigational new drugs or marketed drugs, but will not grant final approval until an IND or letter of exemption has been obtained from the study sponsor or FDA.
The IRB and/or UF Administration retain the right to have investigators contact the FDA if there is any question regarding IND applicability.

If the NF/SG VHS is involved the IRB will not approve the study to be conducted at the VA until after receiving and considering the VA’s assessment on the investigator’s use of the test article.

Expanded Access to Investigational Drugs

Information on expanded access to investigational drugs can be accessed at [http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#treatment](http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#treatment) These situations are different from "Emergency Use" (described below) in that the Treatment IND or Treatment Protocol is always a planned use and thus sufficient time is available to obtain prior IRB review and approval.

Emergency Use of a Test Article without IRB Review

Federal regulations for the protection of human subjects do not permit research activities to be started without prior IRB review and approval. These regulations, however, do not limit or interfere with the authority of a physician to provide emergency medical treatment for patients, subject to FDA requirements for release and emergency use of an unapproved drug, biologic, or device on a single patient. The FDA regulations do not provide for expedited IRB approval in emergency situations. An IRB must either: (a) convene and give “full board” approval of the emergency use or (b) if the conditions of 21 CFR 56.102(d) are met and it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval.

FDA defines emergency use as the use of an investigational drug or biological product in a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. The emergency use provision in the FDA regulations [21 CFR 56.104 (c)] is an exemption from prior review and approval by the IRB of a single patient use of a drug, device, or biologic considered to be investigational; however, reporting the use to the IRB is required by the FDA, and UF requires consultation with the IRB Chair, Vice-Chair or, if the Chair or Vice-Chair is unavailable, an experienced IRB Member prior to use. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval, although the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had time to convene a meeting to review the use. The emergency use exemption of an investigational drug, biologic or device requires that all of the following conditions be met:

1. The test article is used one time per institution to treat a single patient; and
2. The Patient has a life-threatening condition necessitating use of test article (Note that having an ultimately fatal condition does not constitute a life-threatening emergency);
3. No standard acceptable treatment is available; and
4. There is not sufficient time to obtain full IRB approval.

Life-threatening, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined below.

“Life-threatening” means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life threatening do not require the condition to be immediately life threatening or to immediately result in death.
Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

*Severely debilitating* means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Emergency use is emergency clinical care and does not meet the DHHS definition of research [45 CFR 46.102(d)]. The FDA considers it research but allows an exemption from IRB review. IRB acknowledgement that a particular case meets FDA criteria for emergency use applies to the treatment of one patient only and is not the same as IRB approval to conduct a research study under DHHS rules. Since prior IRB approval is not obtained, the patient may not be considered a research subject and data regarding care may not be included in any report of prospectively conceived research activity. Any subsequent use of the test article at UF would require prospective IRB approval.

**Investigator Responsibilities:** A physician planning to use an unapproved drug, device or biologic to treat a patient should contact the IRB Chair or Vice Chair (by calling the IRB Office) prior to the emergency use of the test article to discuss whether the case meets FDA criteria for emergency use. If the treating physician attests that the situation is life-threatening and that no standard acceptable treatment is available, the IRB Chair, Vice Chair, or an experienced IRB member (“Reviewer”), grants clearance to proceed with the emergency use. If the Reviewer determines that the request meets the regulatory criteria for emergency use, the reviewer communicates this to the IRB Administrative Office. The IRB will send the physician a letter that the IRB is aware of the proposed use and considers its use to meet the requirements of 21 CFR 56.104(c). Sponsors often require a copy of this letter before they will ship or release the test article.

If the investigator cannot attest that the situation is life-threatening, that there is no adequate alternative treatment available, and there is not sufficient time for full IRB approval, the Reviewer cannot grant clearance to proceed with the emergency use.

Although emergency use of a test article is exempt from IRB review, it is not exempt from the FDA regulatory requirements to obtain and document informed consent of the subject or the subject’s LAR; therefore, written informed consent, signed by the subject or the subject’s LAR is required. Obtaining of informed consent is deemed feasible unless certain criteria are met and then there are special provisions for the emergency use of a test article without informed consent (see below).

In addition, the FDA must be notified of the emergency use by the holder of the IND/IDE. If the treating physician is not the IND/IDE holder, he/she must notify the sponsor about the emergency use so that the sponsor can notify the FDA.

For tracking purposes, the treating physician must document the emergency use of a test article, in writing, and report the use to the IRB on the UF Report of Emergency Use of Investigational or Unapproved Item within 5 working days of its use. This report must be accompanied by a signed informed consent and any pertinent information pertaining to the test article. Adverse events should be reported in compliance with UF IRB Adverse Event Reporting Policy.
Office Responsibilities: If contacted regarding emergency use of a test article, the IRB Office will direct the treating physician to the appropriate Reviewer and will prepare the written statement, at the direction of the Reviewer certifying that the requirements for emergency use have been met. Alternatively, the Reviewer may generate the written statement and provide a copy to the IRB Office.

The written statement will notify the treating physician that the Emergent Use 5-day follow-up form is required to be submitted to the IRB office within 5 days after the test article has been used on the subject (along with the protocol and a copy of informed consent signed by the subject/legally authorized representative). Once these documents are submitted to the IRB, it will be entered in the database. When entering the title, insert the words “Emergent Use” at the beginning, select “Emergent Use” for the status, and schedule the submission for the next full board meeting. An IRB number will be assigned at this time for tracking.

Reviewer Responsibilities: The Reviewer will review the UF Report of Emergency Use, consent form and other accompanying documentation to confirm that the use of the investigational test article met the criteria for emergency use, complete the applicable reviewer comment sheet, and return to the IRB Office so that a follow-up letter to the PI can be generated. If the test article use did not meet the emergency use criteria, the Reviewer may forward to the full board for review. In the case of noncompliance, the IRB will determine whether the noncompliance is a serious or continuing requiring additional action. If the Reviewer has any other concerns regarding the emergency use, the Reviewer may forward on to the Board for review at his/her discretion.

Emergency Use of a Test Article without Informed Consent

Under FDA regulations [21 CFR 50.23] the obtaining of informed consent from the subject or the subject’s LAR shall be deemed feasible unless, before the use of a test article both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

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

Investigator Responsibilities: The Investigator must complete and submit an Independent Physician's Certification of Emergency Use of Investigational or Unapproved Item without Informed Consent to the IRB within 5 working days after the use of the test article.

If, in the investigator’s opinion, immediate use of a test article is required to preserve the subject's life, and time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the Investigator may make the determinations (1-4) listed above and, within 5 working days after the use of the test article, have the determination reviewed and evaluated, in writing, by a physician who is not participating in the clinical investigation [21 CFR 50.23(b)]. The IRB must be notified within 5 working days after the use of the test article.
Planned Emergency Research

IRB-01 does not make exceptions to informed consent requirements for planned emergency research subject to FDA or HHS Regulation and thus will not review requests for waivers of consent for planned emergency research. For research conducted at the VA, refer to the VA SOP for Emergency Use of a Test Article on Human Subjects.

Humanitarian Use Device (HUD) with Humanitarian Device Exemption (HDE)

A HUD is a device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or is manifested in fewer than 4,000 individuals in the United States per year, rather than to generate data to support a finding of effectiveness. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD). The statute and the implementing regulation (see 21 CFR 814.124(a)) require prospective IRB review (that the HUD is used within its approved labeling) and approval before a HUD is used, except in emergency use situations as described in the section entitled Emergency Use of a Test Article Without IRB Review.

The IRB is responsible for initial and continuing review of the HUD and the healthcare provider (ie, physician) is responsible for obtaining IRB approval before the HUD is administered to or implanted in a patient.

Investigator Responsibilities: The investigator is responsible for completing and submitting the HDE Introductory Questionnaire for initial use and the HDE Continuing Review Report for continued use. If the HUD is being used as part of a clinical investigation (ie. safety and efficacy data will be collected in support of a pre-market approval application (PMA)), the Investigator must submit an Introductory Questionnaire, Protocol, Informed Consent, and any other applicable information pertinent to IRB review.

Office Responsibilities: New submissions requesting IRB review of an HUD/HDE are assigned a new protocol number, entered into the database and reviewed for completeness (which would include inclusion of all pertinent documents listed above) by administrative staff. Investigators are contacted as appropriate to provide clarification and/or documentation prior to IRB Review. Once complete, the submission, including all of the supporting documents, is forwarded on to the Full Board for review. Continuing review may be conducted by an Executive Reviewer.

Research Conducted Off-site or at Multiple Sites

When an IRB reviews research conducted off site or at multiple sites, there may be multiple IRBs involved. For example, an IRB may review research to be conducted at a nursing home, school, or company where the nursing home, school, or company has its own IRB. In such an event, affiliated (UF/Shands/VA) researchers must obtain appropriate approval from a UF IRB unless the Institutional Official grants a special exception to rely upon the review of another qualified IRB.

In the event IRB-01 reviews a multi-site project, the following rules will apply:

1. Any information (including but not limited to protocol modifications, interim results, adverse events, and unanticipated problems involving risk to subjects or others) from
any site that directly impacts the rights or welfare of subjects participating in research approved by IRB-01 must be reported to IRB-01 per the appropriate reporting policy.

2. The local investigator is responsible for complying with the reporting requirements of any outside entities associated with the research (sponsor, any other IRBs with jurisdiction over the research, etc). This includes forwarding appropriate IRB-01 correspondence as needed.

3. IRB-01 only processes/reviews protocol specific correspondence submitted directly by our local investigators. Unless an emergency exists, IRB-01 does not consider information sent directly from sponsors, outside investigators, etc.

4. IRB-01 will communicate and collaborate with outside IRBs as needed to protect the rights and welfare of subjects as well as to insure compliance will all appropriate requirements, laws, and regulations.

5. Unless otherwise specified by the Institutional Official, IRB-01 remains the final authority in relation to the conduct of research submitted by local investigators.

6. Research where the local investigator is a sub-contractor who is enrolling subjects and reporting results to an outside entity: IRB-01 does not have to communicate with any of the outside IRBs. It is the sponsor’s responsibility to insure all of the involved sites have appropriate IRB approval. Any (a) serious, unexpected, and related adverse events, and (b) unanticipated problems involving risk to subjects/others, occurring on this project at any involved site must be reported to IRB-01 per IRB-01’s current reporting policies.

7. Research where the local investigator sub-contracts work out to investigators at the other sites: outside investigators (at other sites) are responsible for obtaining approval from their local IRB. However, since our local investigator is relying on the outside investigator, IRB-01 needs to receive copies of correspondence from the outside IRB approving (initial and continuing review) each outside investigator’s/site’s participation in the research. Any (a) serious, unexpected, and related adverse events, and (b) unanticipated problems involving risk to subjects/others, occurring on this project at any involved site must be reported to IRB-01 per IRB-01’s current reporting policies.

8. Outside sites send identifiable information to local investigator who is not performing any study interventions/interactions: outside investigators are responsible for obtaining approval from their local IRB. However, since our local investigator is relying on the outside investigator, IRB-01 needs to receive copies of correspondence from the outside IRB approving (initial and continuing review) each outside investigator’s/site’s participation in the research. In particular, IRB-01 must also receive a copy of the informed consent approved by the outside IRB that authorizes the disclosure of identifiable information to our local investigator. Any unanticipated problems involving risk to others occurring on this project at any involved site must be reported to IRB-01 per IRB-01’s current reporting policies.

9. When the local investigator/institution is serving as the central/lead/coordinating site on a multi-site study, the Introductory Questionnaire submitted to the IRB must describe the plans for communicating information relevant to the protection of participants among the participating sites and institutions, including communications of adverse events, unanticipated problems, protocol modifications, and interim results. The IRB in turn must assess if the communication plan is adequate to the protection of subjects.

10. Local investigator conducts research at outside facility with its own IRB: local investigator must obtain IRB-01 approval and provide documentation showing they have permission to conduct research at outside facility in compliance with their requirements (outside facility determines if project must also be reviewed by their IRB). If outside IRB approval is required, IRB-01 must receive copies of initial and continuing review. Any (a)
serious, unexpected, and related adverse events, and (b) unanticipated problems involving risk to subjects/others, occurring on this project at any involved site must be reported to IRB-01 per IRB-01’s current reporting policies.

11. Local investigator conducts research at outside facility without IRB: local investigator must obtain IRB-01 approval and provide documentation showing they have permission to conduct research at outside facility. If the outside facility is considered engaged in research (per OHRP guidance on Engagement http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm) with our investigators, the outside facility must submit an FWA and name an IRB to review their involvement in the project. UF IRB-01 may enter into an IRB Authorization Agreement and serve as the IRB for either a specific project or preferably for any research conducted by UF/Shands/VA faculty, staff, or students. The IRB Authorization Agreement must be signed by the University of Florida Institutional Official/designee. Outside institutions may not name IRB-01 on an FWA without prior approval of the University and a fully authorized IRB Authorization Agreement. Any (a) serious, unexpected, and related adverse events, and (b) unanticipated problems involving risk to subjects/others, occurring on this project at any involved site must be reported to IRB-01 per IRB-01’s current reporting policies.

12. Outside sites send de-identified (either (a) no links or (b) links but there is a confidentiality agreement) information to local investigator: IRB does not need to receive copies of correspondence from outside IRBs. No adverse events or unanticipated problems at other sites need to be reported to IRB-01.

IRB Operations

Meetings

Meeting Time, Place and Location

Unless otherwise noted, IRB meetings are held in Room 10-214 of Shands at UF Hospital, from 8:30 a.m. until 2:00 p.m. on the first and third Wednesdays of every month. Additional meetings may be called by the Chair to complete unfinished business or resolve emergency situations, or at the Chair’s discretion.

IRB Meeting Convened via Telephone Conference Call

In the event that a single or small number of urgent issues exist that require full Board review, and it is not practical to convene a meeting where a majority of members are present, the IRB Chair may call for a meeting of the convened board via telephone conference call. Alternatively, one or more members may conference call in to a regular full Board meeting if unable to attend in person. All members participating in a full Board meeting via conference call will receive all pertinent material prior to the meeting and will be able to actively and equally participate in the discussion. A verbal vote will be called for rather than a show of hands. The minutes of a any meeting that allows full Board members to participate via conference call will show that the two criteria above, in addition to the usual regulatory requirement, have been met.
**Deadlines for Meeting Agendas**

The IRB Administrative Office has set deadlines for items requiring Full Board Review in order to inspect, process and distribute information to reviewers so that meaningful review may take place. Items received in the IRB office prior to the posted deadline, will be placed on the agenda for the applicable meeting. Items that are on the agenda and not addressed at the current meeting will roll over to the next meeting. Deadlines are posted on the IRB website. Deadlines may be revised as necessary in order to facilitate processing, review and distribution.

**Attendance**

Members are expected to attend meetings of the convened Board for which they have indicated availability, and if unable, should notify the IRB-01 Administrative Office at the earliest possible time, as well as arrange to have their designated alternate attend in their place. Any member who misses three consecutive meetings without sending an alternate (and whose absences have not been excused by the Chair) or who misses half or more of the meetings in a year, whether sending an alternate or not, may forfeit membership on the IRB and be removed from the IRB by the Chair or VP for Research. The unaffiliated member must be present at the majority of the meetings in a given year. If the unaffiliated member is unable to make at least 70% of the meetings an alternate may be required, the member may forfeit their membership, or the member may be removed from the IRB by the Chair or VP for Research.

**Reviewer Assignment**

IRB members are assigned to review projects by experienced IRB administrative personnel. Every effort will be made to assign designated reviewers of full board agenda items, where there is no conflicting interest (see Board Member conflict of interest) that is consistent with protocol specific information (content) and reviewer expertise (scientific or scholarly), education, training, experience, and/or representative capacity. Members of the IRB are qualified to protect the rights and welfare of research subjects and have the competence and knowledge to review research. Any appointed member of IRB-01, through education, training, and experience, may provide ethical review of projects submitted for consideration by the Board. Occasionally the IRB Administrative staff (during pre-review), designated reviewers (during review), or Full Board may determine that additional appropriate expertise is needed to review a specific submission. The Assistant Director and/or the IRB Chair may be contacted verbally or by e-mail to discuss the need for consultant review (see Consultants).

Consideration may be given to a reviewer’s workload for any given meeting. Tabled projects will be assigned the same reviewers as the previous meeting, if possible, for consistency.

Experienced IRB Administrative Staff assign reviewers for expedited items on a protocol-by-protocol basis to designated Executive Reviewers. Executive Reviewers are encouraged to contact the IRB Office or other Executive Reviewers if there are questions or concerns regarding a specific submission and may, at their discretion, forward any submission to the convened Board for consideration.

**Joint Gainesville/Jacksonville Review of Projects**

Projects conducted in both Gainesville and Jacksonville may be reviewed and approved by a convened meeting of either IRB-01 or IRB-03. This review may be accomplished by having a member of the secondary IRB participate in the review process by either attending the meeting.
(teleconference allowed), or by submitting written comments prior to review at the scheduled meeting.

Exempt or expedited projects will be sent from the primary to the secondary IRB for review. The secondary site reviewers' comment sheet will be maintained in the IRB file in addition to the comment sheet from the primary reviewer.

The primary site for new projects requiring full Board review will assign a project number, review the submission for completeness, correspond as necessary with the investigator, and place on the agenda for review according to the deadlines for that IRB. The secondary site (e.g. Gainesville or Jacksonville) will be noted in the IRB database. The IRB Coordinator for the primary IRB will send all applicable materials for review to the secondary IRB Coordinator, in advance of the scheduled meeting for reviewer assignment and comment. Both primary and secondary IRB reviewers are provided the same review materials (as discussed in Full Board Initial Review) and both should complete a reviewer comment sheet. The secondary site reviewer may participate in the discussion of the project via telephone, teleconference, or in person, if available, but may not vote. Upon IRB approval, the primary IRB will generate the approval letter for distribution to the Principal Investigator. All subsequent submissions (e.g. revisions, adverse events, continuing review) and correspondence should be sent to the primary IRB for consideration; paperwork should not be sent to both IRBs for review.

When Gainesville or Jacksonville sites are added after a project has been approved, the alternate IRB may review the project utilizing an expedited process. As with initial review, the IRB Coordinator for the primary site will send all applicable material (including the original application and all supporting documents) for review to the secondary IRB Coordinator for reviewer assignment and comment sheet completion. The assigned reviewer at the primary site will consider all of the issues raised in reviewing the addition of the alternate site and, when necessary, all concerns will be communicated to the principal investigator.

Consent forms for joint projects should have contact information for both sites/investigators included.

Pre-meeting distribution to members

Assigned reviewers will receive a packet containing an agenda, all applicable assigned review materials and corresponding comment sheets, and meeting CD during the week prior to the scheduled IRB-01 meeting. Designated reviewers receive materials as described in the “Office Responsibilities” Section under Full Board Review. All materials pertaining to full board projects (regardless of submission type), are scanned and electronically transferred to disk for distribution to Board members. Members can review the meeting CD with either their own computers or with a laptop provided by the IRB which they may retain so long as they are a member of the IRB.

Review and presentation of materials during IRB-01 Meetings

Assigned reviewers are expected to bring the hard copy materials and comment sheets to the meeting. IRB staff will provide meeting CDs and laptops if needed. The meeting CD is projected onto a screen. A board member, typically the IRB Chair or Vice Chair, will use the projected agenda to keep track of what items have been reviewed previously and which one is currently being discussed. The IRB may choose to project particular studies from the CD in order to assist with the review of the item.
Any items not already on the agenda and distributed to all members via the Meeting CD must be photocopied and distributed hard copy to all members. The minutes must reflect the addition of any items not previously listed on the agenda.

**Meeting Management**

IRB meetings are run by the IRB Chair (or Vice Chair, in the event the Chair is absent or unavailable). The Chair starts and ends the meeting. During the meeting, the Chair decides which submission will be reviewed next. Typically agenda order will be followed, but the Chair may choose to take items out of order (such as in the event that a board member or principal investigator is only available at a certain time). The Chair can call for a motion or vote, or choose to delay a vote (such as in the event additional information is pending from the investigator) and proceed to the next submission. The Chair typically identifies conflicted individuals and asks them to leave the room before final deliberations and voting. The Chair should audio record (using a tape or digital recorder) the motion prior to the vote. The Chair and Vice Chairs count to quorum and participate in the vote.

**Principal Investigator’s Participation during IRB-01 Meetings**

Research Investigators (or a designee) are encouraged to attend IRB-01 Meetings to provide information, clarify issues or answer questions pertaining to projects under review. Investigators (designee) are asked to sign the IRB Meeting Log and are called prior to review of their project. The principal investigator (designee), if present, will be introduced to the IRB members and may be present to respond to questions and provide information to the IRB. Any investigator or sub-investigators will be asked to leave the meeting during the final discussion, deliberation and voting phase of the review process. PI representation will be noted in the meeting minutes.

**Investigator Conflict of Interest**

**Disclosing Conflicts of Interest**

The UF IRBs consider appropriate disclosure to be an important step in managing potential conflicts of interest. Investigators are responsible for disclosure to a sponsor and the IRB of financial holdings, relationships, and other interests (financial and non-financial) which might constitute a conflict of interest for the researcher as an investigator.


Additionally, all Investigators shall complete the applicable sections of Introductory Questionnaire, Protocol, and ICF pertaining to conflict of interest. Investigator includes the principal investigator and any other person who is responsible for the design, conduct, or reporting of the research and includes the Investigator’s spouse and dependent children. Investigators shall disclose financial interests that they, their spouse or their dependent children have. Investigators with an individual conflict of interest are identified on Addendum A: Assurance and subsequently document the conflict on Addendum L: Conflict of Interest, both of which must be reviewed and approved by the IRB.
Reviewing Protocols with a Conflict of Interest

When the study documents, Protocol, and/or proposed consent document identify a potential conflict of interest, the IRB Administrative Staff sends an electronic copy of the submission via e-mail to the Assistant Director (AD) for Compliance (for UF-only or joint UF-VA appointed investigators) who will conduct an evaluation of the conflict in accordance with institutional policy and if indicated, institutes the Institutional Conflict of Interest (COI) process. The Assistant Director will notify the IRB staff and IRB reviewers via e-mail suggestions for disclosure language in the consent form if the investigator has any financial interest. Additionally, if the investigator with the conflict has a management position with an outside entity or a Significant Financial Interest that may adversely affect the protection of subjects and/or the integrity of the research, the applicable COI Administrator may recommend that someone other than the conflicted investigator consent potential subjects and/or evaluate adverse events. The UF COI Administrator communicates the conflict evaluation and recommendations to the IRB via e-mail. The IRB considers the conflict and recommendations and implements a management plan for the study that takes into consideration whether the financial interest will adversely affect the protection of subjects in terms of the criteria for IRB approval, including but not limited to, risks, benefits, subject selection, consent process and/or whether the financial interest may adversely affect the integrity of the research. The IRB makes the final determination of any management plan and may at its discretion institute additional human subjects protection measures (other than disclosure) when the conflict may affect the protection of subjects or integrity of the research. Additional protection measures may include, but are not limited to: provisions for monitoring the collection or analysis of data, not allowing an investigator to consent or to participate in all or a portion of the study, or not approving the study. Any real or potential financial or non-financial interests must be evaluated and managed prior to final IRB approval. Evaluation and management of any COI will be documented in the IRB record which includes minutes, comment sheets, and/or copies of e-mail correspondence.

If the VA is involved with a COI, the IRB will refer to the NF/SGVHS Research Office and applicable VHA handbooks for guidance.

Investigators must notify the IRB Office of any changes during the course of the research protocol which might create a conflict of interest, including the addition of any new investigators. Any conflict of interest arising after initial IRB approval shall be reported yearly (at the time of CR) and/or as new interests arise.

At a minimum, all Informed Consent Forms shall contain the following language:

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator may benefit if the results of this study are presented at scientific meetings or in scientific journals.

Institution

An institutional COI exists when the financial interests of the institution or the institutional officials might affect institutional processes including the review or oversight of research. The University of Florida policy on institutional conflicts of interest is available at [http://www.generalcounsel.ufl.edu/downloads/Appendices/AppendixA4.pdf](http://www.generalcounsel.ufl.edu/downloads/Appendices/AppendixA4.pdf). The above procedure to evaluate the conflict is followed and institutional conflicts are disclosed to subjects in the consent form.
Voting Requirements

Meeting Quorum

An IRB meeting will be called to order provided a quorum exists. A quorum is defined as a majority of the voting members (or designated alternates in the absence of a voting member) and the presence of at least one non-scientist. For research involving FDA-regulated test articles, a licensed physician must be present. At least one member should represent the general perspective of research participants (such as the community member, bioethicist, or other Board members who have participated in research as subjects). For VA research, the IRB will refer to the applicable VHA handbook for requirements for review of VA Research. For research involving prisoners, the prisoner representative must be present as a voting member.

The IRB Chair (or Vice-Chair sitting in for the Chair) calls the IRB Meeting into session when a quorum exists (as described above) based upon a count of members (voting and alternates in the absence of voting members) and the presence of a non-scientist. IRB decisions are made by a simple majority vote of the quorum. Should a quorum fail during a meeting for any reason, no further actions or votes may be taken until quorum is restored. IRB Members with a conflicting interest in any given protocol, will be asked to leave the room during the deliberation and vote, and will not be included in the quorum count. The IRB administrative staff continually monitors meetings to ensure that a valid quorum is maintained for each vote. Members for, against, and abstaining are counted for each motion. Each vote is recorded and entered into the IRB database. The names of members abstaining or not voting are recorded in the database. The minutes will document prior to each vote that a quorum existed for the vote and that at least one of each of the following types of Board members were present: licensed physician, non-scientist, and VA representative.

No proxy votes (written) are allowed. Members may attend a meeting via teleconference and may vote and be counted as part of the quorum if they have been provided all of the materials distributed to other members and are able to actively and equally participate in the discussion.

Communication from the IRB

All official correspondence from the IRB will be distributed to researchers by written hard copy sent via campus mail. Researchers may request that correspondence be held in the office and picked up by a member of the researcher’s staff. Some correspondence (e.g. Explicit Change Letters or Tabled Letters) may also be e-mailed to the researcher or their designee in order to facilitate a quicker response to the Board’s request. IRB Members and staff may communicate directly with researchers in person, via telephone, or e-mail in order to clarify issues, correct paperwork problems, or take other actions to expedite review of submissions. Copies of all written correspondence will be maintained in the IRB file.

Appeal of IRB Decisions

When the convened IRB disapproves or requires modifications to proposed research, Researchers may appeal the IRB decision in writing to the IRB. All appeals to full board decisions will be reviewed by the full Board. Only the IRB may change/overturn a previous decision.
Temporary Transfer of PI Responsibilities

The Principal Investigator is ultimately responsible for the conduct of any UF IRB approved study. All forms require original signature of the PI. If the PI will be unable to fulfill his/her role as obligated by the study, study activities may be temporarily transferred to another qualified individual. The PI must complete and submit the Temporary Transfer of Study Responsibility to the IRB.

Disposition of Research when Principal Investigator Leaves UF

Any principal investigator who has any active protocols at this Institution shall, within a reasonable time before leaving employment with the Institution do the following:

a. Notify the IRB, in writing, of the date the principal investigator is leaving, and identify, in writing, all of the Principal Investigator's protocols that will be active as of that date; and
b. Obtain IRB approval for closure or termination of the active protocols, or obtain IRB-01 approval of a new Principal Investigator on the active protocols.

The IRB shall, upon reasonable notification of the above, take prompt action to close or terminate the protocol or to approve a new principal investigator on the protocol.

If any principal investigator fails to comply, the IRB may, within a reasonable time following receipt of notice of such failure notify in writing the relevant departmental chair of the principal investigator's failure and request the departmental chair to take prompt appropriate action on the disposition of the Protocol. Additionally, the IRB may notify the principal investigator's gaining Institution of the principal investigator's failure. If the relevant chair fails to take prompt appropriate action in response to the IRB's request, the IRB may, in writing, notify the relevant college dean of the departmental chair's failure.

Administrative Changes to IRB Documents

Requests for administrative and technical corrections to IRB documents, including Informed Consent and Introductory Questionnaires, may be approved administratively by IRB office staff. The corrections must not be substantive or directly relevant to the determinations required by the IRB under 45 CFR 46.111, nor relate to any changes in research activity.

Examples of permitted changes include:

- spelling errors
- content of headers and/or footers
- bullet alignment
- font sizes and styles
- punctuation
- margins

These changes should be documented within the file by the inclusion of a redline/strikeout copy of the revised document and a line in the database indicating administrative corrections made by staff and approved by the IRB Assistant Director or IRB-01 Coordinator. The database record should indicate the date of the corrections, identity of the staff person making these corrections, the identity of the approver and a synopsis of the changes.
IRB Documentation and Records

Documentation

Correspondence to the IRB

Receipt of Documents from the PI

Upon receipt of an initial project submission, revision, continuing review, adverse event, emergency use or other paperwork, the office staff will:

a. Review to determine needed action.

b. Assign a project number to new submissions or verify the project number on secondary submissions.

c. Review the submission for completeness and accuracy.

d. Enter the information into the IRB database.

e. Forward the submission for review:

Chair/Vice Chair Review

Attach a comment sheet
Attach file information, as described
Forward for review

Full Board Review

Copy submission
Assign reviewers
Attach comment sheet for assigned reviewers
Attach relevant file information
Distribute to reviewers with meeting packet

Receipt of Comment Sheets from the Reviewer

Upon receipt of the comment sheet(s) from the reviewer(s) the office staff will:

a. Review the documentation of the action taken

b. Enter action information into database

c. Audit file as needed

d. Prepare informational letter(s) to the investigator (that is, approval, problem [tabled or explicit change], or disapproval letter)

e. Prepare office memorandum to investigators if the staff note that a project file needs an additional revision
f. Use signature stamp(s) and other IRB stamps as needed on original document(s)

g. Copy correspondence to the investigator for placement in the original file

h. Send the original correspondence to the investigator and keep the copy

i. Scan the submission

j. Enter final information into the database

k. File the documents

Required IRB Documentation

Membership Roster

The IRB-01 Administrative Office maintains a current list of Board members (voting and alternate). The official member roster indicates the voting member or alternate member’s name, gender, degree(s), classification as scientist or non-scientist, specialty area, representative capacities, and affiliation with the Institution (University of Florida, Shands, and/or NF/SG VHS). OHRP will be notified on at least a semi-annual basis on changes to the IRB membership or when there is a change in Chair. Copies of the IRB Membership Roster are available online at the IRB Website. Archival copies of member rosters are maintained in hard copy and/or electronically.

Membership Records

The IRB-01 Administrative Office maintains a member folder for each Board member. This folder contains a copy of the member’s cv/resume, contact information, training checklist, conflict of interest statement, representative capacity, confidentiality agreement, and any training certificates.

Convened Meeting Agenda

An agenda is prepared for each full Board Meeting by IRB-01 Administrative Staff (Program Assistant or others). Information about the submission (such as what kind of materials are included in the submission) is entered into the IRB-01 database. Submissions are organized into groups such as New studies, Tabled Submissions, Adverse Events, as well as some departmental groups such as Adult Oncology and Cardiology (departmental groups are created at the IRB Chair’s discretion). Agendas are distributed in advance to the members with the meeting packet and includes:

a. Project Number, Principal Investigator, Expiration Date, Risk Level, and Oversight

b. Project Name

c. Age range of subjects and Number of Subjects at UF and other sites

d. Special populations involved
c. Type of submission

d. Assigned reviewers (including identification of members with conflicting interest)

e. Summary of the submission including paperwork submitted by the Investigator and/or Administrative Office

f. Other pertinent information

There is no limit to the number of items that can be included on the agenda. Occasionally the full Board is unable to review all of the agenda items (e.g. if the Board loses quorum or runs out of time). Any leftover items will be placed at the beginning of the next meeting Agenda and reviewed at that time. If a substantial number of items remain the IRB may decide to hold an extra meeting.

Minutes

Informational Minutes

Informational minutes provide the convened IRB with information on: (1) actions taken outside the convened Board via an expedited review process including but not limited to approvals of new protocols, protocols undergoing continuing review, and modifications to previously approved research protocols, and (2) determinations of exemption. Informational minutes are distributed at each full Board meeting and consist of those items described above which have had their approval paperwork generated since the prior meeting.

Minutes of Convened Meetings

A written summary is recorded for each full Board meeting (meeting minutes). The minutes are generated from actual notes by office personnel present at the Board meeting in combination with the reviewer comment sheets. The recorded minutes include:

- Attendance including voting members and members in training (present and absent), alternate members when substituting for voting members, and non-members (including consultants, guests, visitors, staff members, and/or others) present. A sign-in sheet will be kept with the minutes to reflect the presence of members and/or alternates. In the event any members attend the meeting via conference call, see IRB Meeting Convened via Telephone Conference Call, page 88.

- Time meeting convened and adjourned;

- Discussion of IRB Business items;

- Protocol specific items reviewed at the meeting (from the Agenda)

- Actions taken by the convened Board;

- Separate deliberations for each action;
The number of members voting for, against and abstaining on each action, and when applicable, identification of abstaining and non-voting members by name;

Information on Members with conflicting interests and their status during the deliberation and vote on the applicable project;

The basis for requiring changes in or disapproving research;

A summary of protocol specific discussions including controverted issues and any resolution and/or determination;

For initial and continuing review, the approval period.

Determinations as required per regulation (e.g. waiver of consent, children, pregnant women, etc), including specific findings as required in VA guidance (e.g. enrollment of vulnerable subjects);

Information sent to the PI (content of explicit change, tabled, miscellaneous letters) that pertain to the project under discussion; and

Non-significant/Significant risk determination and rationale for the determination for studies involving investigational devices.

When following DHHS regulations or guidance: (1) justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document, and (2) that the required and additional elements of disclosure are included in the consent process.

Meeting and informational minutes are distributed to the full Board for review and/or corrections and approval, by a quorum at a convened Meeting and are maintained as part of the IRB record. Once approved by the IRB Membership at an IRB Meeting, IRB minutes may not be altered by anyone including higher authority.

Determination of risk level is documented in the IRB record for a given project.

IRB full board and informational minutes are sent to the NF/SGVHS Research Office per the regulations as outlined in the applicable VHA Handbook.

IRB Project Files

Project files will contain as applicable the following documents:

- Original submission including Introductory Questionnaire and applicable IQ addenda; Research protocols (initial and revised); any relevant merit review or grant application; Scientific evaluations, if provided; Proposed and approved consent form(s) (initial and revised); Subject recruitment and/or informational materials; Investigator brochure (or equivalent material such as the package insert); Questionnaire(s), survey instruments, or data collection forms; and any other information submitted by the Investigator for review. For DHHS-supported multi-
center clinical trials, any DHHS-approved protocol and sample informed consent documents.

- Progress and interim reports including but not limited to: Continuing review and progress reports submitted by investigators; Proposed revisions (memo and any affected paperwork) and corresponding IRB action; Any material sent to subjects and/or statements of significant new findings provided to subjects (i.e. letters); Adverse events reports; Reports of unanticipated problems (which may include reports of injuries); Significant new findings; Documentation pertaining to noncompliance (including protocol deviations/violations submitted by the PI); DSMB reports and safety updates;

- For studies involving the VA, copies of applicable VA Forms as required in VHA Handbook 1200.05 Handbook and any other correspondence with the VA (including the VA R&D committee).

- IRB documentation including but not limited to: Completed reviewer comment sheet(s) for each review (Full Board, Expedited, etc); Actions taken on submissions; Any findings required by laws, regulations, codes, or guidance; Correspondence between the IRB and the investigator including but not limited to all letters sent from the IRB and responses received from the investigator; and Miscellaneous items.

IRB determinations (based on information provided by the PI in the protocol submission) for waivers or alterations of informed consent or waiver of documentation of consent will be documented in the IRB record (minutes and/or applicable reviewer comment sheet).

For all research involving vulnerable or potentially vulnerable subjects, IRB records, including but not limited to, documents submitted by the PI and reviewed and approved by the IRB (or Executive Reviewer), minutes and/or comment sheets (for projects undergoing full board or expedited review) will document the inclusion of vulnerable subjects, and protocol specific findings, additional safeguards and determinations of the IRB for research involving pregnant women, human fetuses, neonates, prisoners, children and/or other vulnerable populations.

Organization of IRB Project File

IRB Project files are maintained in submission order with the most recent submissions on top. Some projects will consist of multiple folders and will be labeled “x of y” to alert office staff that there are multiple folders. The original submission will be the first item placed in the folder when the folder is started. The original submission will be in the following order: IRB-01 approval letter, Review Sheet(s), any intermediate submissions required prior to approval, Introductory Questionnaire, Protocol, Informed Consent Form followed by other study documents (such as advertisements, questionnaires, CD’s, videos, etc.). Each subsequent submission will be placed on top of the original submission. If a proposed Project Revision, Continuing Review Report/Study Closure Report, Serious and Unexpected Adverse Event and Safety Report Form, Protocol Deviations, or Cumulative Adverse Event Table is submitted, a copy is not placed in the file UNTIL the IRB-01 has generated correspondence regarding the submission (such as an approval letter or a review letter of some sort). At that time, the submission will be placed in the following order: IRB-01 correspondence, Review Sheet(s), any intermediate submissions required prior to approval, Project Revision Form, documents submitted with the Form, copies of stamped documents returned to Principal Investigator. Miscellaneous items are handled in a similar manner with appropriate
variations for the content. Non-reportable Adverse Events are signed by the appropriate office staff and placed in the file.

Policies and Procedures

Policies and procedures guiding activities of the IRB in compliance with federal regulations for the protection of human subjects, University Policy and State Law will be maintained in accordance with federal regulations and amended as necessary. Changes to the Policy and Procedure Manual will be approved by the convened IRB prior to implementation and version dates posted to identify revisions to pertinent materials.

Management of IRB-01 Forms and Comment Sheets

IRB-01 uses a variety forms such as our Introductory Questionnaires form or Continuing Review form to collect information from researchers. The IRB also uses Comment Sheets for IRB Reviewers to document the review of research submissions. These forms and comment sheets can frequently be revised in order to address regulatory or policy changes, new issues identified by the IRB, or simply to improve the way they obtain/record information. Form and Comment Sheet changes must be reviewed and approved before implementation. There are three levels of form review possible: IRB Administrative, Chair, and Full Board. Review will be documented on a sheet which will be filed along with a copy of the revised form or comment sheet.

- IRB Administrative review is intended primarily for changes involving spelling, grammar, formatting, numbering, instructions, or other changes which do not significantly alter the meaning or content of the questions form. The Administrative Review will be documented on the Form Review Sheet.
- IRB Chair review is intended primarily for: (a) the creation of forms relative to minimal risk research which would not otherwise require full Board approval, or (b) changes in forms (including adding new questions) which do not relate to greater than minimal risk to subjects. The Chair Review will be documented on the Form Review Sheet.
- Full Board review is required if: (a) Administrative or Chair review refers the form to the Full Board for approval, (b) the content relates to greater than minimal risk to subjects, or (c) the content relates to significant regulatory changes. The Full Board vote will be documented on the Form Review Sheet and in the meeting minutes.

The full Board will be notified of form changes approved outside of full Board by Administrative or Chair review.

Records

Record Maintenance

Record Access

Records of active IRB-approved protocols will be maintained in the IRB-01 Administrative Office in a secured area (locked room) with access limited to IRB Personnel. Investigators are asked to submit a “Request for Copying” to the IRB Office if any component of the IRB file is needed. Records of active files are not released from the Office unless needed to supplement a review by the Board. Office personnel and/or IRB members needing to review the contents of an active file should complete a sign-out record indicating the date, person, and project number.
IRB records pertaining to VA research will be accessible for inspection and copying by authorized representatives of VA including members of the Research and Development Committee.

Record Retention

Records, including, but not limited to, IRB project files, minutes, and policies and procedures, are retained in hard copy or electronically for a minimum of 3 years after completion, cancellation, or termination of the applicable study. IRB records relating to VA Research will be retained per the requirements as stipulated in the VHA Handbook 1200.05.

Projects are sent for record storage after closure and if there has been no file activity for six months.

At the time of storage or scanning, the IRB database will be updated to indicate final disposition of the project.

Record Inspection

All records shall be accessible for inspection and copying by authorized representatives of applicable Federal Agencies at reasonable times and in a reasonable manner.

Confidentiality of Records

Records of IRB activities will be maintained in a secured area with access limited to IRB Staff. Investigators are asked to remove direct references to subject’s protected information such as name, medical record number, birth date, driver’s license numbers, but may retain information, such as dates, as necessary, for Board determinations related to certain events.

Miscellaneous

Forms Updates

IRB Forms will be updated as needed. Changes in IRB Forms will be reviewed by the Chair and/or IRB Executive Committee. Version dates will be modified when forms are revised. Investigators will be notified through the IRB Website (announcements and links to forms will indicate “new”) and IRB Forum Events.

IRB Website

The IRB-01 website is a resource used to communicate information to investigators and research teams. The IRB-01 Website is maintained by the IRB-01 Coordinator and is updated as needed to disseminate new information relevant to the conduct of human subjects research under the purview of IRB-01.

Quality Assurance

Purpose
The Office of Research and Graduate Programs has created a Quality Assurance Program to assess the clinical research activities conducted under and in accordance with the University’s Assurance Agreement with the Office of Human Research Protections (OHRP), DHHS.

In order to best protect human subjects and maintain compliance with all applicable regulatory guidelines, the Office of Research and Graduate Programs created a Quality Assurance (QA) component of the University of Florida Institutional Review Boards to evaluate the current practices of the IRB and University of Florida Research community against the defined standards, of the DHHS (including OHRP), FDA, State of Florida, University of Florida, and the IRB Policy and Procedure Manual. The goals of the IRB QA Program are:

i. to enhance the protection of human subjects who participate in research programs at the University of Florida;
ii. to ensure compliance with the University of Florida FWA, federal regulations, state laws, and ethical guidelines;
iii. to establish a process for internal monitoring of human subjects research;
iv. to encourage continuous improvement in the conduct of human research at UF and its Affiliates;
v. to promote an institutional culture of responsible research and collaborative cooperation to improve the quality of research;
vi. to provide the institution with information about the quality of execution of clinical research;
vii. to proactively address potential issues and provide guidance in their resolution; and
viii. to offer Research Teams an opportunity to learn through external evaluation.

Activities of the QA Program may include, but are not limited to:

- Assessing and improving IRB and investigator compliance with federal regulations, state laws, and institutional policies through inspection of IRB files, monitoring of IRB meetings, review of OHRP Determination and FDA Warning Letters, and discussing with IRB Executive Committee
- Developing, maintaining, and revising IRB Policies and Procedures, forms, and guidance documents, in conjunction with the applicable IRB personnel, IRB Executive Committee and/or UF Research Administration, for compliance with applicable federal, state, and local laws and regulations;
- Conducting ongoing and/or directed audits of IRB operational procedures and compliance with applicable regulations;
- Conducting directed and random post-approval project inspections to ensure investigator compliance with relevant HHS and FDA regulations, institutional and IRB policies and guidelines for the protection of research participants and providing findings and feedback to research teams and the institution (Research Monitoring Program);
- Consent process monitoring as requested by the IRB and/or applicable Institutional Officials;
- Monitoring IRB workload and statistics for trends and areas that need improvement; and
- Providing education to the IRB Administrative Office, IRB members and Investigators as needed

Quality Assurance Research Monitoring Program

Federal regulations give the IRB the authority to observe or have a third party observe the consent process or the research. The Vice President for Research has designated a Quality
Assurance Coordinator to perform project inspections on behalf of the Institution and at the request of the University of Florida Institutional Review Boards.

Any human subjects' research under any UF IRB may be subject to “For Cause” or “Random” inspections. “For cause” inspections may occur as a result of known or suspected non-compliance in the conduct of human subject research reported to or identified by the Board, Executive Committee, or Administrative Office. Projects identified for “Random” inspections, will be generated through a query of the IRB database and will be based on the following criteria:

- Greater-than-minimal risk to subjects
- Federal or internally funded projects
- Projects that are actively enrolling subjects
- Projects that have local or no oversight
- Other Criteria that the QA Coordinator deems appropriate after approval by the EC

Additional criteria for random selection may include:

- Studies involving gene therapy
- Studies involving healthy volunteers
- Studies that are moderate to high risk

“For cause” inspections may be referred to the UF Research Monitoring Program by the Board, Executive Committee, or Administrative Office via phone, e-mail, or letter. Pertinent information will be obtained from the requesting source. The Principal Investigator will be notified of the inspection an “Inspection Notification Letter”, delivered through UF campus mail and copied by e-mail, and/or by phone. A mutually convenient time for the inspection will be scheduled with the PI.

If a project is identified for a random inspection, PIs will be notified in writing. Once notified, an on-site inspection will be scheduled within 6 weeks. Once the inspection is complete, the QA Coordinator will provide the PI and the AD of IRBs with a written report summarizing findings and providing recommendations. Any non-compliance will be handled per the IRB Noncompliance Policy. Results of Random Inspections will be maintained in separate QA Files, and not with the IRB Project File, unless referred for review by the Chair or Board.

Prior to “for cause” or “random” inspections, the corresponding IRB file will be inspected for appropriate records including initial submission (IQ, protocol, IC, advertisements, etc) and review, project approvals (including IC), modifications to protocol, reporting of AEs/SAEs, continuing review documents. An internal inspection checklist will be completed and compared to the findings of the on-site inspection or PI self-assessment. As part of for cause or random inspections, the consent process may be monitored, as needed, by the QA Coordinator or an experienced designee.

Inspections of VA Research will be conducted in conjunction with the NF/SG VHS Research Compliance Officer and findings communicated in writing.

Any findings of IRB noncompliance will be handled per the Noncompliance section of this manual.
IRB Review of HIPAA Documentation in Human Subjects Research

a. Purpose

The Office of Research and Graduate Programs in conjunction with the Privacy Office has established the position of HIPAA Coordinator to assist the IRBs, the IRB Executive Committee, and the Privacy Office in the review, analysis and approval of research projects covered under the HIPAA statute and done at the University of Florida.

b. Applicability.

The HIPAA Coordinator shall conduct a pre-review of HIPAA documents in accordance with the HIPAA regulations for IRB-01 and IRB-03 studies where appropriate. The HIPAA Coordinator will complete the “green sheet” documenting pre-review results for all new submissions as well as for subsequent HIPAA revisions. Such pre-review shall apply to all human subjects’ research covered under the HIPAA regulations. A study is covered under the HIPAA regulations if all of the following are true:

1. The study involves investigators and/or subjects from a HIPAA defined covered entity that uses IRB-01 or IRB-03 as its IRB. These covered entities include, but are not limited to, research conducted by employees of or in facilities owned by the colleges in the Health Science Center and Shands Teaching Hospital & Clinics Inc.;

2. The study involves the use, review, creation or disclosure of Protected Health Information (PHI);

c. Review of HIPAA documentation for research.

HIPAA certificates, authorizations and waivers shall be reviewed and documented in accordance with the following procedures:

1. Certificates

Certificates shall be available to allow Investigators to conduct (a) reviews preparatory to research or (b) decedent-only research. Requests for Certificates may be administratively reviewed and approved or denied, as appropriate, by the HIPAA Coordinator as the designated IRB administrative staff. Grant or denial of requests for certificates shall be documented to the file and to the Investigators through the completion of IRB Certificate forms and approval/disapproval letters.

2. Authorizations

1. The IRBs shall ensure that all studies incorporate HIPAA compliant authorization language into the body of the study's informed consent form unless the study does not involve the use of PHI for recruiting/identifying and/or enrolling human subjects.
   a. For VA research, the IRB will verify receipt of the separate HIPAA authorization that was reviewed and approved by the VA Privacy Officer and ensure that it is consistent with the informed consent document and protocol.
2. All HIPAA authorization language contained in the informed consent shall be reviewed and approved, amended, or denied, and documented as part of the standard IRB-01 protocol and informed consent review process (either expedited or full-board, as appropriate).

3. The standard IRB-01 approval letter is sufficient to document approval of the HIPAA authorization language incorporated into the informed consent. No HIPAA specific documentation is required for approval of authorization language.

3. Waivers of Authorization

1. Waivers of authorization may be available for a given study when appropriately requested by investigators on the IRB Introductory Questionnaire (IQ) or through the use of a separate HIPAA Waiver of Authorization form. Waivers are typically required for research studies for which a waiver of informed consent may be requested;

2. The IRB shall review, approve or deny, and document waivers of authorization under expedited or full-board review procedures, as appropriate.

3. The IRB shall review, approve or deny, and document waivers of authorization in strict accordance with HIPAA regulations, by completing and retaining in the file, the "University of Florida IRB-01 Checklist for Documentation of Approval/Disapproval of Waiver of HIPAA Privacy Authorization" (the "Green Sheet").


4. Duties of the HIPAA Coordinator

In addition to the above review of documentation, the HIPAA Coordinator shall also be responsible for the following:

1. The Coordinator, working with the Privacy Office, shall keep a log of investigators who have completed HIPAA for Research training.

2. The Coordinator will maintain the HIPAA folder found in the IRB-01 database and other pertinent parts of the IRB-01 database related to HIPAA regulations.

3. The Coordinator will act as a resource to the IRBs, investigators and staff concerning HIPAA matters by responding to questions and resolving issues.

4. The Coordinator shall prepare a report for IRB-01 and IRB-03 analyzing all studies to be discussed at the Full Board meeting for compliance with HIPAA. The report shall be emailed to the IRB prior to the meeting. If a HIPAA matter can be resolved prior to an IRB-01 full Board meeting, the Coordinator should do this through the use of a Full Board Correction form, or the use of other HIPAA forms as required.
5. The Coordinator shall provide HIPAA support to the Board as needed.

HIPAA non-compliance

The HIPAA Coordinator shall report allegations of non-compliance of HIPAA regulations to the University of Florida Privacy Office as well as the Assistant Director of IRBs. If these non-compliance allegations involve a research study approved by the Veteran’s Administration (VA), the VA Research Compliance and Privacy Officers and appropriate institutional officials will also be notified. The University of Florida Privacy Office will investigate the allegations and, upon conclusion of the Investigation by the Privacy Office, the IRB may defer to the Privacy Office regarding any remedial action or limitations regarding research involving the Investigator. Additionally, the IRB may take any action deemed appropriate for the protection of human subjects.

HIPAA Training for Researchers

In addition to the HIPAA Training required by the University of Florida Privacy Office, all Principal Investigators, co-principal and sub-investigators, all research coordinators, and all staff with access to research-related human health information are required to complete HIPAA for Research training by successfully completing the on-line HIPAA for Research training tutorial. Training must be completed prior to initiating human subjects research (that is, prior to IRB submission) and every two years thereafter, and/or as deemed appropriate by the IRB and/or the University of Florida Privacy Office. Failure to complete required HIPAA for Researcher Training may result in delayed approval of new research studies and/or suspension of previously approved research.