Florida HEALTH

INSTITUTIONAL REVIEW BOARD (IRB) RESEARCHERS MANUAL

HUMAN RESEARCH PROTECTION PROGRAM
FLORIDA DEPT OF HEALTH

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Florida Department of Health

Human Research Protection Program (HRPP)
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Questions, concerns, complaints, or suggestions regarding the HRPP can be directed to the HRPP staff at 850-558-9620 or toll-free at (866) 433-2775. Information is provided under the “Institutional Review Board" (IRB) section of the biomedical research page on the Florida Department of Health website.

Anonymous comments can be submitted via a web-based form, also located on the website: http://www.floridahealth.gov/provider-and-partner-resources/research/irb/index.html.

More information about the HRPP can be obtained via a consultation with HRPP staff who can provide comprehensive information about the program, including laws governing research, requirements to conduct research for the Department, how the HRPP relates to other programs at the Department, and the types of research the Department does not allow.

A list of all Department IRB Polices is on the next page and are available from the HRPP program by request.

Please note that the information and guidance in this manual are subject to change.

Topic Area	ID	Title
Definitions	DOHP 5-D5-11.1	Definitions
Institutional Oversight of	DOHP 5-D5-1.1	Institutional Oversight of Assurance
Jurisdiction	DOHP 5-D5-1.2	Activities Subject to IRB Jurisdiction
	DOHP 5-D5-1.4	Differentiating Research from Practice
	DOHP 5-D5-1.5	Research Exempt from Institutional Review Board Review
Composition of IRB	DOHP 5-D5-3.1	Composition of the IRB
	DOHP 5-D5-3.2	IRB Member, Consultant, and Staff Conflicting Interests
Institutional Review Board Responsibility	DOHP 5-D5-10.1	Investigating Non-compliance
	DOHP 5-D5-10.2	Suspension or Termination of IRB Approval
	DOHP 5-D5-10.3	Reporting to Institutional Officials, Department or Agency Heads
	DOHP 5-D5-10.4	Complaints Regarding Human Subjects Research
	DOHP 5-D5-2.4	Data and Safety Monitoring Plans
	DOHP 5-D5-2.5	Certificates of Confidentiality
	DOHP 5-D5-4.1	IRB Review Responsibilities
	DOHP 5-D5-4.9	Review of Reliance Agreements
	DOHP 5-D5-4.10	HRPP Emergency Preparedness
Human Subjects	DOHP 5-D5-4.2	Conduct of Meetings by the Convened IRB
	DOHP 5-D5-4.3	Review of Human Subjects Research: Initial Review
	DOHP 5-D5-4.4	Review of Human Subjects Research: Continuing Review
	DOHP 5-D5-1.3	Human Research Protections in Funding Agreements
	DOHP 5-D5-8.1	Human Research Protection Program Records
	DOHP 5-D5-9.2	Community Involvement
Informed Consent	DOHP 5-D5-4.8	Monitoring of the Informed Consent Process
	DOHP 5-D5-5.1	Legally Effective And Prospectively Obtained Informed Consent
	DOHP 5-D5-5.2	Documentation of Informed Consent
	DOHP 5-D5-	Waiver and Alteration of Informed Consent

	5.3	
Vulnerable Subjects	DOHP 5-D5-5.4	Asset/Dissent by Children or Cognitively Impaired Adults
	DOHP 5-D5-6.1	Research involving Pregnant Women, Fetuses, Neonates
	DOHP 5-D5-6.2	Research Involving Prisoners
	DOHP 5-D5-6.3	Research involving Children
	DOHP 5-D5-6.4	Research Involving Adults Unable to Consent
Use of Drugs and Devices	DOHP 5-D5-7.1	Ensuring Regulatory Approval for Investigational Articles
	DOHP 5-D5-7.2	Storage, Handling, and Control of Investigational Articles
	DOHP 5-D5-7.3	Investigational Devices
	DOHP 5-D5-7.4	Investigational Drugs, Agents, and Biologics
	DOHP 5-D5-7.5	Humanitarian Use Devices
	DOHP 5-D5-7.6	Emergency Use and Emergency Use Authorizations
Researcher and Investigator Responsibility	DOHP 5-D5-2.1	Investigator Qualifications
	DOHP 5-D5-2.2	General Responsibilities of Researchers
	DOHP 5-D5-2.3	Identifying, Evaluating and Managing Researcher and Research Staff Conflicts of Interests
	DOHP 5-D5-4.5	Amendments to Approved Research
	DOHP 5-D5-4.6	Problems Requiring Prompt Reporting to the IRB
	DOHP 5-D5-4.7	Recruitment/Advertising
	DOHP 5-D5-9.1	Research Ethics Education and Training

INTRODUCTION

Purpose of the Manual

This manual serves as a comprehensive guide for researchers and research staff within the Florida Department of Health (Department) and other researchers who are conducting or involved in human subject research with and for the Department. As a public health agency to receive Full Accreditation from the Association for Accreditation of Human Research Protection Programs (AAHRPP), the Department maintains the highest standards for protecting research participants while facilitating ethical research that benefits Florida's citizens.

This manual outlines the policies, procedures, and ethical standards that govern research with human participants at our institution. Researchers should use this manual as a reference for understanding their own specific responsibilities and those within the Department ’s Human Research Protection Program (HRPP) to submit research for Institutional Review Board (IRB) review and approval.

All applicable researchers must read and understand the information in this manual before conducting human subject research.

Organizational Authority

The Department ’s HRPP operates under the authority of Florida Statute 381.86, which creates the Institutional Review Board within the Department to satisfy federal requirements under 45 CFR 46 and 21 CFR 50 and 56. The State Surgeon General serves as the Institutional Official (IO) with authority to:

- Determine and appoint IRB membership.
- Designate IRB Chairs.
- Commit institutional resources for effective HRPP operation.
- Ensure compliance with federal and state requirements.

The IRB has the authority to approve, require modifications, or disapprove research. The board also can suspend or terminate approval of research that is not being conducted in accordance with its requirements or that has been associated with unexpected serious harm to participants. Additionally, the board has the authority to observe, or have a third party observe, the consent process and the conduct of research. All research reviewed and approved may be subject to subsequent reviews and disapproval by Department officials, or by any institution for which the Department IRB is designated as the IRB of record.

The Department does not tolerate attempts to sway, pressure, manipulate, or otherwise influence the decisions of the IRB. Anyone with knowledge of attempts to influence the IRB, or who has questions or concerns, is encouraged to contact an IRB chair, IRB administrator, the Human Research Protection/IRB Coordinator, or the State Surgeon General. All reports will be investigated by the coordinator designated in the Department 's Assurance, in coordination with the program attorney and senior leadership.

Integration Throughout the Organization

The HRPP at the Department is integrated throughout the organization rather than being limited to

the IRB office. Various divisions, programs, and individual researchers share responsibility for protecting research participants, ensuring that human subjects protection is considered at all stages of research planning and execution.

Scope of the HRPP

Our HRPP applies to all research involving human subjects conducted by Department employees, contractors, or partners, regardless of funding source or location. Per Florida Statute 381.86(3), the Department 's IRB may also serve other state agencies at the discretion of the State Surgeon General.

Institutional Oversight of Assurance

The Department requires IRB review of all research involving human subjects to uphold its Assurance with the federal government's Office for Human Research Protections (OHRP). https://www.DHHS.gov/ohrp/register-irbs-and-obtain-fwas/fwas/fwa- protection-of-human-subjecct/index.html. By upholding its Assurance, the Department agrees to comply with the Federal Policy for the Protection of Human Subjects, also known as the "Common Rule," which outlines the basic provisions for IRBs, informed consent, and assurances of compliance. (The common rule was heavily influenced by the Belmont Report, which was written in 1979 and summarizes the ethical principles and guidelines for the protection of human subjects of research.)

The Department's Assurance is based on the following commitments:

- The Department agrees to safeguard the rights and welfare of human participants in research through the creation of an IRB.
- The Department's employees, contractors, and anyone acting as an agent of Department agree to comply with the Assurance when they are engaged in research under the jurisdiction of the Department's IRB. Agent includes Department employees, medical fellows and residents, students and interns, and others conducting research under a contract or memorandum of understanding with Department programs.
- The Department agrees to uphold the ethical principles of the Belmont Report for all proposed research. Those principles are as follows:
    - **Respect for Persons:** Recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy.
    - **Beneficence:** Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm; and
    - **Justice:** Fairness in the distribution of research benefits and burdens.
- Department agrees to follow other state laws relating to human subject's research.
- Department agrees that no research involving the Department can begin without prior approval from a health Department official and the Department IRB.

Activities Subject to IRB Jurisdiction

All research on human subjects must be reviewed and approved by the IRB whenever the Department is engaged in the study. Engaged can be defined as:

- Department employees or agents receive support directly from federal agencies (such as the Centers for Disease Control and Prevention) for the research. This applies even when all the research activities are carried out by agents or employees of another institution.
- Department employees or agents intervene or interact with study participants by performing invasive or noninvasive procedures, such as drawing blood, administering drugs or other treatment, or survey research.
- Department employees or agents intervene or interact with human subjects by manipulating the environment (e.g., controlling light, sound, or temperature).
- Department employees or agents obtain identifiable private information or identifiable biological specimens from study participants.
    - Obtaining includes but is not limited to observing and/or recording private behavior or using, studying, or analyzing identifiable private information or identifiable specimens already in the possession of the employees or agents of the institution.
- Department employees or agents are determined to be engaged in the research by the Institutional Official, the Human Research Protection Administrator, the director of the Office of Public Health Research (OPHR), or the IRB Administrator.

Additionally, the Department IRB must review the research if one or more of the following apply:

- The research is funded by Departments federal research appropriations, even if it is carried out by agents or employees of another institution.
- The research is conducted by or under the direction of any employee or agent of the Department in connection with his or her official responsibilities.
- The research is conducted using any Department property or facility.
- The research involves Department clients, including participants recruited at county health Departments.
- The research involves the use of non-public information maintained by Department; and
- The research is conducted in accordance with the Assurance filed with the Office for Human Research Protections in which the Department IRB is designated as the IRB of record.
- The Department IRB also must review and approve non-exempt research activities, such as employees or agents who acquire data by interacting with participants or obtain identifiable private information.

Involvement of Humans in Research

Investigators must provide to the IRB details of the proposed involvement of humans in their research protocols, including the characteristics of the subject population, anticipated numbers, age ranges, and health statuses. The proposed research should specify the gender and racial/ethnic composition of the subject population, as well as criteria for inclusion or exclusion of any

subpopulation. If ethnic, racial, and gender estimates and continuing review numbers are not included in the background data for a protocol, the Investigators must provide a clear rationale for exclusion of this information.

Activities Involving Residents, Interns, and Student Volunteers

Residents, interns, and student volunteers may not use data or information obtained through work for research without prior IRB approval. If there is a desire to use such information or the results of an analysis (e.g., the results of secondary analysis of data conducted while employed by the Department as part of an academic degree program), a request for review by the IRB should be submitted. Projects used in doctoral or master's programs or in residencies is normally considered research. Residents, interns, and student volunteers may not remove confidential data from the Department for research and other activities without first seeking review by the IRB.

Institutional Review Board Determinations Process for Making Determinations

The State Surgeon General or Human Research Protection Administrator has the authority to determine whether an activity covered by the human research protection program represents “Human Subject Research.” Department program managers, consultants, contractors, and investigators do not have the authority to make an independent determination.

If the Human Research Protection Administrator has direct involvement in the activity, then another person, usually an IRB chair, will make the determination. If the IRB chair has a conflict, another chair or the State Surgeon General will make a determination. Determinations are made using criteria in the “Human Subjects Research Determination Worksheet” and are communicated to the applicant via email or in an electronic application system. Determinations are normally made in less than one month.

The HRPP website specifies how program managers and researchers can request a consultation to determine whether an activity is research involving human subjects. The HRPP provides guidance on the process through regular presentations tailored to specific public health programs and through its website. While anyone can request a consultation about whether an activity is research involving human participants, requests normally come from the person responsible for the activity, such as a researcher or program manager.

Research Exempt from Institutional Review Board Review

All human subjects research under the jurisdiction Department Institutional Review Board (IRB) must be reviewed to determine whether it meets one or more of the exemption categories described in federal regulations 45 CFR 46.101(b) and 21 CFR 56.104(d) and complies with Department’s ethical standards. The IRB may create new categories if the research is not covered by federal regulations and if doing so increases the efficiency and effectiveness of the human research protection program.

The Human Research Protection/IRB Coordinator determines whether research is exempt from regulation and may authorize an IRB analyst to make exemption determinations under supervision. An investigator may request a particular category of exemption, but the final determination of applicability will be made by the IRB staff or committee member. An investigator must contact the Human Research Protection Program concerning the status of proposed research or changes in ongoing research.

Researchers complete an application form for determination of whether the research meets one or more of the exemption criteria. The staff generally make a determination in less than 14 days and notify researchers via email or an electronic review system. If all research activities involve procedures listed in one or more of the specific categories under 45 CFR 46.101(b), the Human Research Protection Administrator or authorized IRB analyst may grant exempt status.

Note: Under federal regulations, exemption categories do not apply to research involving prisoners. Under Florida Department policies and procedures, these categories do not apply to research involving deception. Categories at 45 CFR 46.101(b) permitting exemptions are:

- Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
    - Regular and special education instructional strategies.
    - The effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
    - Research that does not involve prisoners as participants; or
    - Non-FDA-regulated research.
- 45 CFR 46.101(b)(2): Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:
    - Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and,
    - Any disclosure of the human subjects' responses outside of the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
    - If the research involves children as participants, it must be limited to educational tests (cognitive, diagnostic, aptitude, achievement), and the Investigator must not participate in the observed activities. Research that uses surveys, interviews, or observation where the Investigator participates in the activities cannot be granted an exemption.
- 45 CFR 46.101(b)(4): Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens is exempt if:
    - These sources are publicly available, or the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. Data, documents, records, or specimens must have been collected before the research project begins. However, OHRP Guidance specifies limited conditions in which an Investigator may de-identify data prior to the initiation of research that would qualify for exempt status. See the below examples:
        - Investigator A wishes to screen blood samples at a rural hospital for incidence of HIV infection. She wants to use these specimens for another purpose. If Investigator A proposes to use specimens that had been drawn prior to the initiation of her research that are "on the shelf," the protocol may qualify as exempt, assuming the other requirements are met (i.e., the sources are either publicly available or the information is recorded by the Investigator in such a manner

that subjects cannot be identified, directly or through identifiers linked to the subjects).

- An investigator (with proper institutional authorization) may inspect private, identifiable records, but may only record information in a non-identifiable manner. The data must be permanently and completely de-linked at the time of extraction. A code may be used to organize data as it is collected. However, the code may not be a means of re-linking the data set to the original data source.
- Investigator B wishes to examine court records of involuntary commitments to psychological institutions. If he uses court records that were on file before the initiation of his research, the protocol may qualify as exempt.

- 45 CFR 46.101(b)(5): Research and demonstration projects, which are conducted by or subject to the approval of federal Department or agency heads, and which are designed to study, evaluate, or otherwise examine:
    - Public benefit or service programs; this exemption is for federally supported projects and is most appropriately invoked with authorization or concurrence by the funding agency. The following criteria must be satisfied to invoke the exemption for research and demonstration projects examining "public benefit or service programs:"
        - The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services under the Older Americans Act).
        - The research or demonstration project must be conducted pursuant to specific federal statutory authority.
        - There must be no statutory requirements that the project be reviewed by an IRB; or
        - The project must not involve significant physical invasions or intrusions on the privacy of participants.
- Procedures for obtaining benefits or services under those programs.
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs.

Note: This exemption is for projects conducted by or subject to approval of federal agencies and requires authorization or concurrence by the funding agency.

- 45 CFR 46.101(b)(6) and 21 CFR 56.104(d). Taste and food quality evaluation and consumer acceptance studies:
    - If wholesome foods without additives are consumed; or
    - If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Other Considerations Concerning Exempt Research

All research conducted under exempt review is subject to all applicable Department institutional and IRB policies and procedures, and the protections and ethical standards outlined in the Belmont Report.

Criteria Used to Make Determinations of Whether Research Involves Human Subjects

Research does not involve human participants, as defined by DHHS regulations, if the Investigator is not gathering information about living individuals through intervention or interaction with individual participants or collecting identifiable private information about living individuals. Information is considered "not identifiable" if the identity of the participant is not or may not readily be ascertained by the Investigator or associated with the information. For example, population-level registry data published by the Department is considered "not identifiable."

When the Investigator receives private information or specimens with no code or link to allow him or her to establish identity, the research does involve human subjects, unless it falls under FDA regulations. For example, a publicly available, unidentifiable, non-linked cell line qualifies as not involving human subjects.

The Investigator may receive coded private information or specimens and qualify for non-human subjects as defined by DHHS regulations if the following conditions are met:

- The research is not covered by FDA regulations.
- The code is not derived or related to HIPAA identifiers that must be stripped from private health information (e.g., patient medical record number and the last 4 digits of an individual's Social Security Number).
- The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
- The Investigator cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain, because:
    - The key to decipher the code is destroyed before the research begins.
    - The Investigator and the holder of the key enter into an agreement prohibiting the release of the key to the Investigator under any circumstances, until the individuals are deceased.
    - The private information is received from an IRB-approved repository or data management center that includes written operating procedures that prohibit the release of the key to the Investigator under any circumstances, until the individuals are deceased; or
    - There are other legal requirements prohibiting the release of the key to the Investigator until the individuals are deceased.

IRB Review for Non-Research Purposes

There are not universally accepted or completely specified criteria for determining when data collected for non-research purposes are being used for research. Thus, projects are reviewed

on a case-by-case basis. If after data collection is complete, an Investigator wants to access it to conduct research, IRB review and approval may be required. If an Investigator begins a non-research project and later finds that the data gathered could contribute to generalizable knowledge, he or she should contact the Department's HRPP for a determination as to whether IRB review is required.

Note: The IRB may not approve applications from investigators who attempt to circumvent its policies and procedures by collecting data as non-research and then applying to use it as existing data. It is therefore in an investigator's best interest to consider carefully the likelihood that he or she will want to use the data for research purposes in the future and seek IRB approval prior to starting the work.

The applicable regulations under which research determinations are made are 45 CFR 46 (DHHS regulations), 21 CFR 56 (FDA regulations), and 45 CFR 116 (HIPAA regulations). When research is not covered by a regulation, the Department follows the definition used in DHHS regulations.

To make the definition more precise, the Department further specifies the following (see also Glossary of Terms):

- **"Investigation"** means an inquiry, examination, or search for facts, usually involving the formulation or testing of a hypothesis.
- **"Systematic"** means conducted according to a plan, organized method, or procedure for testing or formulating a question or hypothesis and interpreting results.
- **"Designed"** means planned, purposed, or conducted to apply to phenomena outside the observed data, or to contribute to generalizable knowledge. "Generalizable knowledge" means observations, findings, information, or results that have been demonstrated with enough confidence and significance to confirm or alter the consensus within the professional norms of a community or discipline.

Other Regulation Definitions

- A "human subject" is defined at 45 CFR 46.102(f). When following FDA regulations, it includes an individual on whose specimen a device is used. This means medical device studies involving in vitro diagnostics and unidentified tissue specimens are classified as human subject's research.
- A "clinical investigation" is defined at 21 CFR 50.3(c) and 21 CFR 102(c).
- An "experimental subject" is defined 21 CFR 50.3(e) and 21 CFR 102(e).

Public Health Practice

To make determinations of whether research constitutes public health practice, Department relies upon criteria specified in "Public Health Practice vs. Research: A Report for Public Health Practitioners Including Cases and Guidance for Making Distinctions." Hodge and Gostin et al. 2004. Available at http://www.cste2.org/webpdfs/cstephresrpthodgefinal.5.24.04.pdf.

Public health investigations, when authorized and required by statute, such as investigations into acute or chronic infectious diseases, conditions, or environmental hazards, and activities explicitly required by statute, are generally not considered research involving human participants. However, a statute may require both public health reporting and authorize the use of information for research (such as the Florida Cancer Registry and Florida Vital Statistics).

Criteria used to make determinations and examples are provided in the "Human Subject Determination Worksheet."

Quality Improvement and Program Evaluation Activities

To make determinations of whether research constitutes quality improvement, Department relies upon criteria specified in Lynn J, Baily MA, Jennings B et al. "The Ethics of Using QI Methods to Improve Health Care Quality and Safety." Annals of Internal Medicine 2007; 146, 666-673. Available at: https://www.thehastingscenter.org/publications-resources/special-reports-2/the-ethics-of-using-qi- methods-to-improve-health-care-quality-safety/.

Quality assurance activities conducted as an ongoing part of program operations using a standard framework such as Plan-Do-Check-Act (PDCA) and Six Sigma are generally not considered research involving human participants.

Criteria used to make determinations and examples are provided in the "Human Subject Determination Worksheet."

Additional Requirements

Activities that are not research involving human participants must meet Departments ethical standards. These include acceptable risk-benefit relationships, equitable participant selection, consent where appropriate, protection of privacy interests of participants and the confidentiality of their data (under state law) where appropriate, transparency about the research process, proportionality, and where applicable, community involvement in quality improvement and public health efforts.

IRB Review of Research: The Application Review Process

Researchers must contact the Department IRB prior to starting a research project. IRB staff will determine if your project is research, and if it is determined to be research, staff will assist you along the way.

Research can begin when all required approvals have been completed. First, researchers complete a Research Determination Form at https://flhealth.my.irbmanager.com/ to ensure the following has occurred:

- Completion of an application for review prior to applying for a grant. Note: IRB approval is not required prior to the submission of grant applications.
- Approval from bureau chiefs, division directors, or office directors.
- Completion of a Data Use Agreement (DUA) for Department registry data. The contractual document allows for the transfer of non-public or restricted use data (people who have a specific disease, for example) by addressing issues such as ownership, permitted uses, publication of results, and disposal of the data.
- Approval from the administrator or director of research involving county health Department s by completing the "Research Site and Program Support" worksheet.
- Verification from the Bureau of Revenue Management or relevant budgetary unit that grant funding will not be released without IRB approval.
- A copy of the contract or funding agreement has been submitted to the Department.

The Department IRB may only review proposed research if a quorum is present, including at least one member whose primary interests are in nonscientific areas, at least one whose primary interests are in a scientific area, and at least one member who is not affiliated with the Department. HRPP staff are responsible for determining a quorum is established and maintained during the meeting, using the roster to document who is present. The information is recorded in the minutes for each meeting.

The staff, in consultation with an IRB chair, if necessary, evaluates each study and determines whether there is sufficient expertise or knowledge to review the research. Its evaluation is based on each member's curriculum vitae, and, when appropriate, by confirming with members that they are sufficiently knowledgeable to review a particular study. If no members are qualified, staff will reschedule the review or obtain a consultant to supplement the review. Reviews are not conducted when members do not have sufficient expertise or knowledge.

HRPP staff assign two primary reviewers to present each study, ensuring that at least one has appropriate scientific or scholarly expertise to conduct an in-depth review of the research. Video projections and video conference technology may be used to view specific parts of an application during the discussion of a study, such as the informed consent document. Chairs are responsible for ensuring and facilitating participation, providing opportunities for members to ask questions.

Presentations by Researchers

Researchers are encouraged to present a summary of their study and answer questions from IRB members. However, they may not be present for the IRB's discussion and vote and must leave the room or hang up if present on a conference call.

Consultants provide information to the IRB by completing either a reviewer comment worksheet or a form in the application review system. Additionally, they may present information at the IRB meeting. However, when a consultant attends a meeting, he or she does not vote.

Voting

A voice vote is taken for each action on the agenda and recorded for inclusion in meeting minutes. Members must vote either in favor (affirmative) or against (negative) regarding a protocol. Under Florida law (Ch. 119), a vote of "abstention" can only be recorded if there is a conflict of interest. Under federal regulations, IRB members with a conflict of interest may not participate in the review of any protocol except to provide information requested by the IRB. Department IRB members with a conflict of interest should leave the room during the discussion. The remaining members must vote either in favor or against the protocol. Approval requires a majority vote.

HRPP staff takes votes during the meeting and records them as part of the minutes. If quorum is lost during a meeting (e.g., recusals, early departures, or absence of non-scientists), the IRB cannot vote. If required members leave the room and quorum is lost, votes cannot be taken even if most of the members are still present.

Projects will be approved/disapproved under the following stipulations:

- IRB approval without changes: An approval is granted if the research meets the criteria for approval as defined in federal regulations and no changes are recommended.

- IRB approved pending verification of changes by the chairperson or his/her designee: The IRB may approve an application pending substantive alterations or requirements. For example, if the IRB needs more information about the plans for recruitment, or clarification about protections for confidentiality, the board must review those changes before granting approval.
- Minor prescriptive changes (changes that can be verified) or requirements may be reviewed by the IRB, the IRB chair, or his or her designee. Prescriptive changes are those that can be verified.

  For example, “drop the control group” is a specific prescriptive change; verification of whether the change was made can be done by the IRB chair. Similarly, “confirm that education materials are provided to everyone, not just those in the intervention arm” is a prescriptive change that also can be verified.
- The date of approval is the date the conditions were determined to have been met.

IRB Deferral

The IRB may defer a determination if the study does not meet the criteria for approval as defined in federal regulations, or the IRB committee recommends substantial revisions to the application, sponsor’s protocol, informed consent document(s), or other pertinent materials. The changes would be such that the IRB would be unable to assess the risk/benefit ratio without the completed revisions.

Approval may also be deferred if the information in the application or protocol is insufficient for the convened IRB to conduct an adequate review or in cases where the board requires additional expertise or does not have enough time to conduct an appropriate review.

Disapproval by the IRB

Disapproval is granted if the convened IRB determines the protocol does not meet specified criteria, or if the investigator is unable to revise the protocol to meet the criteria for approval as defined in federal regulations.

Process for Notifying Researchers

Researchers are notified of the IRB’s decision to approve, disapprove, or require modifications or clarifications to secure protocol approval through email or an electronic review system. If the IRB disapproves a proposed research study, researchers are given the rationale for its decision, and how they may respond in person or in writing.

If the study is reviewed at the convened IRB meeting and approved with minor changes, once the chair reviews and verifies the changes have been made, the approval period begins, retroactive to the date of the convened meeting. If the convened IRB requires substantial changes and defers the study, it is returned to the Investigator. When the Investigator resubmits the application, the study is reviewed again by the convened IRB (normally the same committee). If the convened IRB approves it, the approval date is the date of the meeting where the changes were reviewed and approved. The expiration date is 11:59 p.m. Eastern time on the expiration date. For example, if a study is approved through June 10, authorization to conduct research expires at 11:59 p.m. Eastern time on June 10.

Changes to approved research must not be implemented without prior IRB approval except to

eliminate immediate hazards to participants. Researchers should submit an application to modify or amend an approved research study electronically.

- Investigators must submit the exact text of an amendment or any other revisions to the IRB. Proposed changes (and a summary of those changes) to the consent document must also be submitted. Investigators should highlight the changes before submission.
- Modifications to the informed consent document must take into account both prospective research subjects and, if applicable, those already enrolled in the study.
- Investigators may modify research activities to avoid an immediate hazard to participants but must report this action to the IRB within five business days. (See "Problems Requiring Prompt Reporting to the IRB.")
- Any changes made without prior IRB approval, except to avoid an immediate hazard to participants, will be evaluated using specific criteria.

Review of Research Involving Vulnerable Populations

There are several research populations described in the federal regulations as "vulnerable" that require additional safeguards or protection. A group is generally considered vulnerable because there is reason to believe that the subjects of the research may have difficulty giving free and informed consent. Examples of vulnerable populations include pregnant women, human fetuses and neonates, children, cognitively impaired persons, prisoners, students and employees, and educationally disadvantaged individuals.

Researchers can successfully protect vulnerable populations by giving serious consideration as to why that population must be chosen, upholding the Belmont Report's ethical principles and guidelines, and engaging the community with whom the research will be conducted. For example, in some circumstances, the population is chosen because there is a social condition or circumstance that occurs only with that population, for example, to investigate the impact of long-term confinement in a correctional facility, the subjects need to be prisoners. Moreover, including affected members of the community, or potential participants' guardians, advocates, or family members, in research-related decisions paves the way for respectful discourse, encourages collective decision-making and helps identify the potential for exploitation so that it can be prevented.

On a case-by-case basis, the IRB or staff may request review by an individual with competence in an area not represented by the board membership. The Human Research Protection Administrator is responsible for identifying a consultant and should seek suggestions from entities, such as IRB members and chairs, relevant Department subject matter experts, bureau chiefs and division directors, federal partners such as the Centers for Disease Control and Prevention, university partners, or through a literature search

Additional Requirements for Activities Involving Vulnerable Populations

The IRB must review and approve the use of a vulnerable population in research activities. Special considerations are provided in the federal regulations and in Department IRB policies and procedures for the following populations:

- **Pregnant Women, Human Fetuses, Neonates, and Transplantation of Fetal Tissue:** The Investigator must ensure that all requirements are satisfied, and adequate

provisions have been made for monitoring the informed consent process.

- **Prisoners:** If a participant becomes a prisoner after enrolling in a research study that is not approved for inclusion of prisoners, the Investigator is responsible for immediately reporting the situation using the IRB application. He or she must cease all interactions or interventions with the prisoner-participant until approval has been received from the Department IRB and the OHRP. If the Investigator wants to enroll prisoners in research, then he or she needs to request an amendment. All research activities conducted or supported by the DHHS involving prisoners as participants require both Department IRB and OHRP approval.
- **Children:** The Investigator must ensure that all requirements in DHHS regulations or equivalent protections are satisfied. He or she is responsible for ensuring parental consent, as well as child assent/dissent, in accordance with the determinations of the Department IRB.
- **Cognitively Impaired:** Individuals who are or who may become decisional impaired may have diminished autonomy that limits their capacity to provide consent. Therefore, the Investigator is responsible for ensuring that informed consent is conducted in accordance with the determinations of the Department IRB.

Note: The IRB may also determine that other target populations identified in the research proposal are "vulnerable" and may impose additional protections not outlined in the federal regulations.

Research Conducted or Supported by DHHS

For research involving prisoners conducted or supported by the DHHS, two actions must occur:

- The institution engaged in the research must certify to the DHHS Secretary (through the OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305; and
- The DHHS Secretary (through the OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

When an Investigator wishes to engage in non-DHHS supported research, certification is not required. However, the IRB applies the standards of this policy and federal regulations in reviewing the research.

When either of the below are true, research should only proceed after the IRB has consulted with the appropriate experts:

- The research involves conditions particularly affecting prisoners as a class as explained; or
- The research does not satisfy the above stipulations.

Measures that are to be Taken When a Current Research Participant Becomes a Prisoner

When a participant becomes a prisoner after enrolling in a research study, the Investigator is responsible for immediately reporting the event using the "Problems Requiring Prompt Reporting" form. This is not required when the study was previously approved by the IRB for prisoner participation.

When interactions and interventions or obtaining identifiable private information will not occur during the incarceration, IRB review and approval under 45 CFR Part 46, Subpart C is not required.

When the study was not previously reviewed and approved by the IRB in accordance with the requirements of 45 CFR Part 46, Subpart C, all research interactions and interventions and obtaining identifiable private information must cease until the requirements of Subpart C (for DHHS-funded research) or equivalent protections are satisfied.

The Human Research Protection Administrator is responsible for certifying to the OHRP the duties of the IRB have been fulfilled.

Additional Approvals

The Federal Bureau of Prisons places special restrictions on research that takes place within the Bureau of Prisons under 28 CFR 512. 28 CFR 512 specifies additional requirements for prospective investigators (both employees and non-employees) to obtain approval to conduct research within the Bureau and the responsibilities of Bureau staff in processing proposals and monitoring research projects.

Additional Considerations

When a prisoner is also a child (e.g., an adolescent detained in a juvenile detention facility), special protections for children in research also applies. Research that would otherwise be exempt from the requirement of IRB approval is not exempt when it involves prisoners.

Equivalent Protections for Review of Research Involving Prisoners, Pregnant Women, and Children that are not Conducted or Supported by DHHS

Regardless of the source of funding:

- Researchers provide the same information for review.
- IRB members review the same materials.
- IRB members make the same protocol-specific determinations concerning the research.

Observational Research

The IRB may approve observational research involving children if it poses no more than a minimal risk and adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 40 CFR 26.406.

If the observational research poses more than a minimal risk but presents the prospect of direct benefit, to the individual participants, the IRB may approve the study only if it finds and documents that:

- The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to his or her well-being.
- The risk is justified by the anticipated benefit to the participants.
- The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
- Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 40 CFR 26.406.

When research involves secondary analysis of data from state registries, such as an

immunization registry, the Department may assign a reviewer whose expertise is more appropriate, such as a statistician or someone familiar with the database, as opposed to a reviewer with expertise in research involving children.

Review of Human Subjects Research: Continuing Review

All approved research proposals, except of those which qualify for exemption in accordance with federal regulations 45 CFR 46.101 and 21 CFR 56.104(d), must receive continuing review at intervals appropriate to the degree of risk as determined by the IRB. Continuing review must be conducted at least once per year. The Investigator must ensure that continuing review applications are submitted in a timely manner so that the review occurs prior to the study expiration date. Federal regulations do not allow a grace period.

Continuing review must be substantive and meaningful. Therefore, the Investigator must submit a comprehensive summary of the research activities and progress since the last continuing review, including a summary of adverse events and unanticipated problems, amendments, results of literature searches, publications, etc. The Investigator is responsible for staying abreast of the current literature in his or her field of study to ensure participants are no longer at risk if additional risks have been identified or no benefit has been proven.

- Researchers must submit all required application materials at least 60 days prior to the expiration of the IRB's authorization to conduct research. The expiration date is the last date that the protocol is approved.

Closures of Research

Researchers must submit a continuing review application to notify the Department that the research is completed, the study is closed, and IRB oversight is no longer needed. Failure to submit the form is considered non-compliance. Staff verify the study no longer involves human participants, including but not limited to the analysis or collection of private identifiable information. Once verification is complete, the researcher receives confirmation via email or electronic review system that the study is closed. No further action is required.

If staff determine the research involving human participants continues (for example, the researcher continues to analyze private identifiable information), the researcher is notified within 14 days that the study requires ongoing review and must submit the application to continue research.

Data and Safety Monitoring Plans

Research that poses greater than minimal risk, excluding "exempt" research, must include a data and safety monitoring plan (DSMP) to assure the safety and welfare of the study participants.

Research should include a DSMP if:

- The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention.
- Prior data suggest that the intervention under study has the potential to induce a potentially unacceptable toxicity.

- The study is evaluating mortality or another major endpoint and the inferiority of one treatment arm has implications for safety as well as effectiveness: or
- It would be ethically important for the study to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet been fully addressed.

The Principal Investigator establishes either a Data Safety Monitoring Committee (DSMC) or a Data and Safety Monitoring Board (DSMB), depending on the size, complexity, and level of risk involved in the research. (This requirement does not apply to industry-sponsored research, where the sponsor is responsible for safety monitoring.) Membership should be limited to those without significant conflicts of interest, whether they are financial, intellectual, professional, or regulatory in nature, and include physicians, biostatisticians, bioethicists, epidemiologists, and basic scientists.

The DSMC or DSMB will approve the safety measures to (a) preserve the study integrity and credibility; and (b) to facilitate the availability of timely as well as reliable findings to the broader clinical community.

Its responsibilities are as follows:

- Provide written documentation confirming members have read the protocol and agree with the study design and the DSMP.
- Review the progress of the study carefully and diligently.
- Review each enrolled subject's research chart monthly for side effects and tolerability of an investigational drug.
- Assure that all problems requiring prompt reporting (See "Problems Requiring Prompt Reporting to the IRB") are reported to the IRB.
- Be available to the Investigator for consultation concerning any adverse study events or any questions regarding consent issues.
- Provide a letter of predefined frequency to the IRB, through the Investigator, summarizing the oversight activities of the DSMC or DSMB during the monitoring period.

Additionally, the DSMC or DSMB is tasked with the following:

- Conduct initial review of the proposed research to assure quality of study conduct.
- Review procedures to assure quality of study conduct, including data management and quality control procedures.
- Assess the quality of ongoing study conduct by evaluating the accrual of study participants, compliance with eligibility, participant adherence to study requirements, and accuracy and completeness of data.
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study.
- Recommend early termination based on efficacy results.
- Recommend termination due to unfavorable benefit-to-risk ratio or inability to answer study questions.

- Recommend continuation of ongoing studies.
- Consider overall picture and primary and secondary analysis.
- Modify sample sizes based on ongoing assessment of event rates; and
- Review results.

The DSMC or DSMB is governed by a charter, which should be maintained in the study files and include:

- A detailed presentation of the membership composition, including qualifications and experience.
- Roles and responsibilities of the DSMC or DSMB and, if relevant, of Steering Committee members.
- The authority of the DSMC/DSMB (e.g., advisor to the sponsor, Principal Investigator);
- The timing and purpose of meetings.
- The procedures for maintaining confidentiality.
- The format, content, and frequency of DSMC or DSMB reports.
- Statistical procedures, including guidelines which will be used to monitor the identified primary, secondary, and safety outcome variables; and
- Plans for changing the frequency of interim analysis as well as procedures for recommending protocol changes.

Guidance for Data and Safety Monitoring Plans

The level of detail in a DSMP should be based on the degree of risk to the research participants. Low-risk studies may have simple plans but must contain at a minimum the following:

- Identification of a DSMC or DSMB.
- A description of the general data safety monitoring plan.
- A description of the plan to monitor progress and safety. (Depending on the complexity of the research, the plan may also include assessments of data quality, timeliness, participant recruitment, accrual, and retention.)
- A description of the plan to assure compliance with FDA and Department of Health and Human Services regulations concerning events that may present unanticipated problems to the participants or others. Such a plan should include:
    - A description of who will be monitoring and collecting problems requiring prompt reporting (e.g., Principal Investigator, research nurse).
    - Specification of who will be notified of problems requiring prompt reporting (e.g., the IRB, National Institutes of Health, FDA, Principal Investigator)
    - A reporting plan indicating the timing of reports.
    - A plan for reporting problems requiring prompt reporting if the study is longer than one year.
    - A description of the plan to ensure suspensions of funded trials are reported

to the grants program director; and

- A description of the plan to ensure data accuracy and protocol compliance.

Terminations, Suspensions, and Expirations of IRB Approval

All approved research is subject to modification or a change in approval status to protect participants. The IRB may suspend or terminate its approval if the research is not being conducted in accordance with its requirements or federal regulations or if it has been associated with unexpected serious harm to participants.

Examples where approval of research may be suspended or terminated include:

- Inappropriate involvement of human subjects in research.
- Inhibition of the rights or welfare of participants.
- Serious non-compliance, or continuing non-compliance, with federal regulations or IRB policies; or
- New information regarding increased risk to human participants.

Termination of the IRB's Approval

The IRB's approval of a study may be terminated if the research is not being conducted in accordance with the IRB policies, is not in compliance with federal regulations, and/or has been associated with unexpected serious harm to participants.

Only the convened IRB may terminate IRB approval. Prior to terminating approval, the board considers:

- Actions to protect the rights and welfare of currently enrolled participants.
- Whether procedures for withdrawal consider their rights and welfare (e.g., planning for their medical care, transferring them to another researcher, or allowing them to continue in the study under independent monitoring).
- And whether to inform current participants of the termination or suspension.

Suspension of the IRB's Approval

The IRB's approval of a study may be suspended if there is evidence of a possible increase in risk to participants or non-compliance by the investigator. Suspensions are made under full committee review procedures.

The convened IRB is authorized to suspend its approval of research at any time. If the suspension needs to be done urgently to protect research participants, an IRB chair, the Human Research Protection Administrator, or the State Surgeon General may do so. When research is suspended by someone other than the convened IRB, the IRB chair will be notified as soon as possible, and the convened IRB will be informed at the next meeting. In addition to notifying the convened IRB, the chair will alert the Deputy Secretary and State Surgeon General. They may require additional action be taken, such as reporting the suspension to the Office of Inspector General.

If someone other than the IRB suspends research, he or she should report any adverse outcomes or events to the board.

When research is suspended, the IRB or another authorized individual should protect the health and safety of research participants with actions such as:

- Transferring participants to another Investigator.
- Planning for clinical care outside of research; or
- Allowing the continuation of some research activities under the supervision of an independent monitor.

Sponsor-Imposed Suspensions

If a sponsor suspends the research for whatever reason, the IRB treats the notification as an unanticipated problem. (See "Problems Requiring Prompt Reporting to the IRB.")

Expiration of IRB Approval

There is no grace period extending authorization to conduct research beyond the expiration date of IRB approval. If the IRB does not reapprove the research by the specified expiration date, all study activities must cease, including recruitment, enrollment, interventions, interactions, and the collection and analysis of identifiable information.

If the IRB requires changes to the research at continuing review, the expiration period is not extended. Expiration is automatic and requires no decision, determination, or action by the IRB. Such expirations are not suspensions, terminations, or administrative holds.

Staff notify the researcher via email or using an electronic review system that authorization and approval to conduct research has expired. The researcher must immediately provide documentation to staff that all research has stopped and submit to the IRB chair a list of research subjects for whom expiration of the research would cause harm. The IRB chair reviews this list and allows individuals to continue participating only if there is an overriding safety concern or ethical issue such that it is in the best interests of individual subjects to continue participating. The convened IRB is informed of the chair's decision using the agenda for the next meeting.

Studies where approval has expired, and the Investigator has confirmed research has stopped may be closed administratively. Researchers typically complete a continuing review form to close their study. However, Florida Department of Health staff may close the study administratively if this is not possible (for example, the researcher is ill.) Reinstatement requires submission of a new research protocol for initial review.

Procedure for Reporting Suspensions and Terminations

The IRB reports all suspensions and terminations in writing promptly to the Investigator.

The letter includes the reasons for IRB's action and a list of requirements:

- The Investigator must submit procedures for the withdrawal of currently enrolled subjects. (The IRB may mandate oversight or transfer responsibility to another investigator to ensure implementation of these procedures.)
- The Investigator must submit a script or letter notifying all currently enrolled participants that are affected by the suspension. If a follow-up of study subjects is permitted or required by the

IRB, participants should be informed. The IRB may directly contact participants to fulfill this notification.

- The Investigator must notify the IRB or sponsor of any events that would have required reporting had the participants continued to be enrolled in the research.

Note: The IRB does not need to consider whether recurrent suspensions or terminations are serious or continuing non-compliance. All non-compliance that leads to a suspension or termination are evaluated according to specific criteria.

All suspensions and terminations will be reported according to DOPH 400-10.3-10, "Reporting to Institutional Officials, Department or Agency Heads."

Investigator Qualifications

The Florida Department of Health's (Departments) Assurance with the federal government specifies that all human subjects research that is conducted by or under the direction of any Department employee or agent (or other covered entity), in connection with his or her institutional responsibilities, must be reviewed by the Department IRB. (See "Institutional Oversight of Assurance.")

All investigators should meet the following requirements:

- Review the ethical principles of the Belmont Report, federal and state laws and regulations, institutional policies and procedures, Department IRB policies and procedures, and if applicable, Good Clinical Practice standards.
- Complete the required training (initial and continuing education) for the ethical conduct of human subject's research (See "Research Ethics Education and Training.")
- Maintain objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing, and reporting data. (Note: The IRB will consider conflict of interest issues in its deliberations of applications.)
- Be adequately qualified and, if necessary, licensed relevant to the scope and complexity of the research conducted.

General Responsibilities of Investigators Human Subjects Protection

The Investigator assumes responsibility for compliance with all federal, state, and local laws, institutional rules, regulations and policies, and Department IRB policies and procedures related to human subjects research, and, if applicable, with the FDA's Good Clinical Practice guidelines. He or she is the ultimate protector of the participant's rights and safety and is obligated to ensure that each subject is adequately informed and freely consents to participate in the research.

The Investigator may not initiate any research involving humans or amend or change an approved protocol without prior IRB review and approval, except when necessary to eliminate an apparent immediate hazard to participants. He or she is responsible for designing research studies that are sound enough to demonstrate outcome, minimize risks, and ensure that risks are reasonable in relation to the anticipated benefits.

The researcher should demonstrate adequate resources to protect participants. To that end, he or she should provide the IRB with the following information:

- The purpose of the research.
- The scientific or scholarly rationale.
- The procedures to be performed.
- A description of the procedures being performed already for diagnostic or treatment purposes.
- The risks and potential benefits of the research to participants, namely physical, psychological, social, economic, and legal risks.
- Description of the time for the researchers to conduct and complete the research.
- Description of the number and qualifications of staff.
- Description of research facilities.
- Whether the researcher has access to a population that will allow recruitment of the necessary number of participants.
- Description of the availability of medical or psychosocial resources that participants may need as a consequence of the research.

The Investigator must also disclose any interests specified in the application and, if applicable, complete the researcher and research staff conflict of interest worksheet. (See "Identifying, Evaluating, and Managing Researcher and Research Staff Conflicts of Interests.")

Investigator Training

Each Investigator must complete research ethics training consistent with requirements in "Research Ethics Education and Training." He or she should also ensure that other Investigators and key study personnel who are responsible for the design and conduct of the research are adequately trained in human research protections and complete continuing education requirements. Researchers are required to complete either the Collaborative Institutional Training Initiative (CITI) or the National

Institutes of Health (NIH) human subjects' protections training. NIH training must have been completed within the past three years. (See "Research Ethics Education and Training.")

Investigator and Key Study Personnel Conflicts of Interest

The Investigator must disclose all actual or perceived conflicts of interest, as defined by institutional policy, to the Department IRB. He or she must ensure that conflicts of interest are reviewed, that a determination is rendered by an Ethics Committee, and that the outcome of the review is submitted to the Department IRB prior to initiation of the research. (See "Identifying, Evaluating, and Managing Researcher and Research Staff Conflicts of Interest.")

Congruence with Funding Proposals

The Investigator must ensure that the IRB application is consistent with the proposal for funding for extramural or intramural support. He or she should act as a liaison between the IRB and the research sponsor.

Supervision and Auditing of Research Process

Each investigator must ensure that all procedures associated with the research are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified under Florida law and Department policies. He or she must ensure adherence to the study protocol and monitor the informed consent process. The Investigator must also ensure there are appropriate facilities and resources to conduct the research.

The Investigator must regularly review research processes and address any deficiencies identified. He or she should conduct and document auditing of research activities on a regular basis as well as audit external performance sites routinely, ensuring adequate staff and resources.

Confidentiality

The conditions for maintaining confidentiality of participants' research records are required for the life of the data. Research conducted with FDA-regulated articles must be kept in accordance with current FDA regulations. The Investigator must also ensure participant privacy and confidentiality in accordance with HIPAA guidelines and Institutional and IRB policies and procedures. (See "Certificates of Confidentiality.")

Research Ethics Education and Training

All investigators and key study personnel conducting human subjects research under the Department IRB must complete initial ethics and compliance training via the Collaborative Institutional Training Initiative (CITI) program prior to commencing research and recertify every three years.

CITI is a free online course in human subject's research protection and research ethics designed specifically for all personnel with significant involvement in the planning, conduct, and analysis of any scientific activity that employs human research participants. The course consists of training modules that are divided into two tracks: Biomedical Research and Social/Behavioral Research. The learning objectives of the CITI course are to:

- Provide an understanding of the historical perspectives, ethical principles, and federal regulations associated with the conduct of research with human participants.
- Provide a clear understanding of what constitutes informed consent and how it must be applied in research involving humans.
- Provide basic information on the regulations and policies governing research with investigational drugs, biologics, and devices.
- Provide a clear understanding of the ethical issues and federal regulations in force during the conduct of Social/Behavioral research, records-based research, and genetics research with human participants; and
- Provide Investigators conducting research at VA facilities a clear understanding of the special procedural and regulatory policies for human research at VA research facilities.

The IRB may not approve research without CITI certification for all researchers and key study personnel. Applications may be reviewed; however, the IRB will defer approval until education is complete.

Verification of completion represents only a minor change, and the study may be reviewed using the expedited procedure.

HRPP staff will confirm CITI training when new applications are submitted and the dates of completion at continuing review. The staff is also responsible for ensuring that certification is documented in an electronic system.

The IRB may not approve research without CITI certification for all researchers and key study personnel. Applications may be reviewed; however, the IRB will defer approval until education is complete.

Verification of completion represents only a minor change, and the study may be reviewed using the expedited procedure.

The IRB will send email notifications to all Investigators and key study personnel with active studies to alert them of pertinent IRB issues or decisions that may impact their research.

All investigators and key study personnel are encouraged to review the core training materials including Department 's Assurance, Department IRB policies and procedures, the Belmont Report, and the federal regulations, including 45 CFR 46, 21 CFR 50 and 56. Links to this information plus links to other federal agencies (e.g., National Institutes of Health, Food and Drug Administration, Office of Human Research Protections) governing human subjects research are available at the Department IRB's website: http://www.floridahealth.gov/provider-and-partner-resources/research/irb.html.

Unanticipated Problems Involving Risk to Participants or Others

The Investigator must report to the IRB, Data and Safety Monitoring Boards, sponsors, and appropriate federal agencies any problems requiring prompt reporting to the IRB. (See "Problems Requiring Prompt Reporting to the IRB.")

Research Records

At a minimum, investigators must maintain research records for at least three years from the date the research is closed with the Department IRB. Beyond three years, requirements for record retention vary depending on the type of research conducted and provisions of the Investigator's funding source. It is the Investigator's responsibility to have a clear understanding of the retention requirements of a

sponsor. All HIPAA-related documentation must be maintained for at least six years from the date of the last use or from the disclosure of the Protected Health Information (PHI).

All research records must be accessible for inspection and copying by authorized IRB representatives, federal regulatory agency representatives, and the Department or agency supporting the research.

If for any reason there is a change in the Principal Investigator (PI) on a protocol, the Department IRB must be notified. The Investigator may either have another researcher assume Principal Investigator responsibilities, close any research studies with the IRB, or take the research studies to a new location. The Investigator must notify the Department IRB in writing the plan for either destroying the data or transferring the data to another PI.

Use of Investigational Drugs and/or Investigational Devices

The Investigator is responsible for obtaining the Investigational New Drug (IND) or Investigational Device Exemption (IDE) from the FDA in accordance with federal regulations.

Additional Institutional Committee/Institution Approvals

The Investigator must seek review and approval from any other required Department central office programs, county health Departments, or other institutions (universities, hospitals, school districts, etc.) and provide documentation to Department IRB using the "Research Site and Program Support" worksheet, prior to initiation of any research.

Federal wide Assurances (FWA), Memos of Understanding (MOU), Other IRB Approvals, and Letters of Cooperation

The Investigator must ensure that the proper approvals and agreements are in place prior to the commencement of research. This includes research at performance sites, "engaged" or "not engaged," that are not a legal entity of Department or covered entity.

He or she is responsible for submitting copies of all IRB approvals or letters of cooperation, whichever is applicable, for all performance sites indicated in the IRB application that are not a legal entity of Department.

The Investigator must ensure that each performance site indicated in the IRB Application as "engaged" in research, has a current FWA and IRB approval, not just initially but throughout the conduct of the research.

If the Department IRB has agreed to serve as the IRB of Record for a performance site "engaged" in research as evidenced by an executed MOU, the Investigator must ensure that the MOU is current and that he or she upholds the terms and conditions defined within it.

Certificates of Confidentiality

The Florida Department of Health (Department) Institutional Review Board (IRB) is required to determine whether the risks to subjects are minimized, the informed consent is appropriate, and privacy and confidentiality protections are adequate. This may entail requesting a certificate of confidentiality from the Investigator.

Data collection about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices or preferences) requires the protection of confidentiality beyond preventing accidental disclosures. Under federal law, Investigators can obtain a Certificate of Confidentiality that will provide protection against the compulsory disclosure, such as a subpoena, of research data. The Investigator should describe in the IRB application any conditions under which confidential information might be disclosed and create an informed consent document that accurately reflects those conditions, including any voluntary disclosure by the Investigator.

What Research is Eligible for a Certificate of Confidentiality?

Any research that collects personally identifiable, sensitive information, and that has been approved by an IRB is eligible for a certificate.

Research can be considered sensitive if it involves the collection of information in the following categories:

- HIV, AIDS, and other STDs.
- Sexual attitudes, preferences, or practices.
- The use of alcohol, drugs, or other addictive products.
- Illegal conduct.
- Information that if released could reasonably be damaging to an individual's financial standing, employability, or reputation within the community.
- Information that might lead to social stigmatization or discrimination if it were disclosed.
- Information pertaining to an individual's psychological well-being or mental health.
- Behavioral interventions and epidemiologic studies; and
- Genetic information.

What Does not Need a Certificate of Confidentiality?

- Projects that are not research based.
- Projects that are not approved by an IRB in accordance with the National Institutes of Health (NIH) guidelines governing Certificates of Confidentiality.
- Projects that do not collect sensitive information or information that might harm the research participants; or
- Projects that do not collect personally identifiable information.

What Protections are Provided by a Certificate of Confidentiality?

A Certificate of Confidentiality protects Investigators and research participants from compelled disclosure of identifying information (Public Health Service Act §301(d), 42 U.S.C. §241(d)). Under the Public Health Service Act, the Department of Health and Human Services (DHHS) secretary may authorize individuals engaged in research to withhold the names or other identifying characteristics of participants from those not connected with the research. This means that Investigators may not be compelled in any federal, state or local civil, criminal, administrative, legislative, or other proceedings to identify their participants.

What are the Limitations of a Certificate of Confidentiality?

A Certificate of Confidentiality does not govern the voluntary disclosure of participants' identifying characteristics. It only protects them from compelled disclosure. Investigators, therefore, are not prevented from voluntarily disclosing certain information, such as child abuse or a subject's threatened violence to self or others. However, if an Investigator intends to make voluntary disclosures of such information, the consent form must clearly indicate this.

What is the Investigator's Responsibility for Ensuring Confidentiality?

Investigators are responsible for ensuring confidentiality of research data. If required, he or she

should submit a Certificate of Confidentiality to the IRB. The Certificate can be obtained from the National Institutes of Health (NIH). Additional information and submission instructions are located on the NIH website: https://humansubjects.nih.gov/coc/index.

Identifying, Evaluating, and Managing Researcher and Research Staff Conflicts of Interest

Financial interests related to the research must be disclosed, evaluated, managed, or eliminated to protect participants and maintain the credibility of the Florida Department of Health's Human Research Protection Program.

Related to the research refers to a financial interest in the sponsor, product or service being tested, or in a product or service that competes with the one being tested.

Investigators and all research personnel whose institutional responsibilities include the design, conduct, or reporting of research, or service on research-related Department committees such as the IRB, must report such interests, including those of their immediate family (spouse, domestic partner, and dependent children), as defined in this policy. Researchers should contact the Human Research Protection Administrator if there are questions about whether a financial interest must be reported.

Researchers and others covered by this policy must complete financial conflicts of interest training at least every three years immediately upon joining the Department; when the Department 's financial conflicts of interest policies are revised in a way that changes researcher requirements; or when there is non-compliance with financial conflicts of interest policies and procedures. Education is available through required IRB researcher training and occurs through completion of the Conflict-of-Interest module in the CITI training program. When a researcher informs HRPP staff of a change in reportable interests, HRPP staff will inform him or her of the need to retake the CITI conflict of interest education module.

Researchers must disclose the following financial interests using a Researcher and Research Staff Conflict of Interest Disclosure worksheet or online system within 30 days of discovering (e.g., through inheritance or marriage) it:

- Compensation or payments for services (e.g., consulting fees, lecture payments, bonus, royalties, paid authorship, honoraria, gifts, or in-kind products or services) related to the research of any value, except as otherwise excluded by this policy.
- Compensation or payments for services where an arrangement has been entered into such that the amount of compensation will be affected by the outcome of the research.
- Equity interests (stocks, stock options, security, or other ownership interests) related to the research of any value
- Equity interest related to the research in a non-publicly traded corporation of any value by the individual or a member of the individual's immediate family
- Equity interest related to the research of any amount to the researcher or any member of the researcher's immediate family where an arrangement has been entered into such that the amount of compensation will be affected by the outcome of the research.
- Intellectual property rights and interests (patents, copyrights, royalties, licensing agreements, and any other proprietary interest related to the research).
- Board or executive relationship related to the research, regardless of compensation.

- Any other interest that could be affected by the outcome of the research
- Travel related to the research, including the purpose of the trip, the identity of the sponsor or organizer, the destination, and the duration.

Researchers who are found not to have reported required interests are referred to the Office of Inspector General.

Non-reportable interests include:

- Publicly traded mutual funds, including the Florida Retirement System
- Salary from the Department or a University
- Income from seminars, lectures, or teaching engagements sponsored by Federal, state, or local government agency, an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education
- Income from service on advisory committees or review panels for federal, state, or local government agency, an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education (e.g., Centers for Disease Control and Prevention)
- Income from investment vehicles, such as mutual funds and retirement accounts, if the Individual does not directly control the investment decisions made in these vehicles

Financial interests meeting any of the following criteria are significant and thus require the development of a management plan:

- Compensation or payments for services (e.g., consulting fees, lecture payments, bonus, royalties, paid authorship, honoraria, gifts, or in-kind products or services) related to the research more than $5,000, except as otherwise excluded by this policy.
- Compensation or payments for services where an arrangement has been entered into such that the amount of compensation will be affected by the outcome of the research.
- Equity interests (stocks, stock options, security, or other ownership interests) related to the research more than $5,000.
- Equity interest related to the research in a non-publicly traded corporation of any value by the individual or a member of the individual's immediate family.
- Equity interest related to the research of any amount to the researcher or any member of the researcher's immediate family where an arrangement has been entered into such that the amount of compensation will be affected by the outcome of the research.
- Intellectual property rights and interests (patents, copyrights, royalties, licensing agreements, and any other proprietary interest related to the research).
- Board or executive relationship related to the research, regardless of compensation.
- Any interest concerning an officer or employee of the Department defined as a conflict of interest under Florida law.
- Any other interest that could be affected by the outcome of the research.

The Human Research Protection Administrator or the Department 's ethics officer will determine if an interest is related to the research and if the interest is significant enough to require review by a conflict-of-interest committee. The below guidelines apply:

- If the interest is non-reportable, the individual is informed via email or through an electronic system that no further action is required.
- If the interest is not related to the research or the person's institutional responsibilities, he or she is informed via email or through an electronic system that no further action is required.
- If the interest is related to the research but is not a significant financial interest, the individual is informed via email or through an electronic system that no further action is required.

The Human Research Protection Administrator will inform the researcher within 14 days that a significant financial interest related to the research exists. The researcher will then have an opportunity to propose a management plan to prevent the financial interest from interfering with the design, conduct, or reporting of the research, including interfering with the protection of participants. He or she will submit this information to the convened IRB using a form or online system. The convened IRB has final authority to determine whether the management plan is adequate.

The Human Research Protection Administrator is responsible for convening a conflict-of-interest review committee within 14 days after a determination is made. The committee is composed of the Human Research Protection Administrator, Ethics Officer, program attorney, and one or more IRB chairs, who read the researcher's application and all supporting materials such as the sponsor protocol, consent document, advertisements, and the disclosure form describing significant financial interests.

The conflict-of-interest committee has 30 days to develop a draft management plan; confirm the researcher's agreement to the plan; and develop a plan to monitor the research to ensure compliance. In developing such a plan, the committee will consider the value of the financial interest, the scope of the relationship, and the person's role in the research.

Examples of management actions include:

- Not conducting the research at Department.
- Severing the relationship that created the financial conflict.
- Reducing or eliminating the financial interest (e.g., sale of an equity interest) or other interests (not just those related to a particular research study).
- Changing personnel or responsibilities or removing personnel from all or some part of the project.
- Identifying an independent researcher to obtain informed consent.
- Appointing an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias.
- More frequent continuing review.
- Publicly disclosing the financial interest (e.g., when publishing or presenting the results of the research to the Institution's IRB or directly to participants in a clinical trial).
- A retrospective review and a mitigation report if necessary.

The researcher has 14 days to comment on the draft management plan and confirm agreement. If he or she does not agree to the plan, the research will not occur.

The Human Research Protection Administrator then submits the plan to a deputy secretary or other senior leadership It is then sent to the convened IRB, which reviews the plan but not the details of the disclosed interests. Research may not be approved prior to the IRB approving a management plan.

The IRB has final authority to determine whether a management plan is adequate, including one

developed by a researcher's organization outside of the Department. When researchers come from organizations that use personnel and committees external to the IRB to evaluate and manage financial conflicts of interest, they must report these determinations as part of their IRB application. For example, if a researcher's university has a conflicts of interest committee, the determinations of this committee must be submitted to the IRB as part of the application.

The convened IRB's determination is communicated to the researcher via email, or in an electronic system. Records of financial interest disclosures are maintained for at least three years from the completion date of the research.

Community Involvement

The Department IRB provides former, current, and prospective research participants with a toll-free number to contact the HRPP staff. Research participants are encouraged to contact the HRPP to discuss problems or concerns, file a complaint, obtain information, or offer input about how the Department can improve the process of participating in research.

The HRPP should make sure that its toll-free number appears on every informed consent document following a statement about who participants can contact independent of the research with questions or for additional information about their rights. The HRPP will maintain a clearly defined method for handling complaints in a confidential manner. Complaints may be communicated via the toll-free number or by using a web-based form.

Complaints Regarding Human Subjects Research

The Department IRB provides multiple mechanisms for participants, researchers, members of the public, and others to ask questions, discuss problems or concerns, file a complaint, request information, or offer suggestions. These safe, confidential and reliable channels include a website, toll-free phone number, consent document language, and a template for reporting concerns. The Human Research Protection/IRB Coordinator or other Human Research Protection Program staff will respond to these inquiries within two business days upon receipt.

The Human Research Protection/IRB Coordinator will investigate all complaints regarding human subjects in research under the Department IRB's jurisdiction. The level of investigation will depend on the seriousness of the situation and the potential risk to participants. Investigations should result in finding a suitable resolution and providing a response to the complainant in a timely manner.

Complaints may come from various sources, including IRB committee members, investigators, participants and their families, institutional personnel and committees, the media, anonymous sources, or the public. They may include anyone directly or indirectly involved in the research process/study.

All complaints will be handled in a confidential manner, including circumstances where an individual notifies the Department IRB of an alleged violation of Investigator compliance.

Those of a sensitive nature may be brought to the IRB chair for discussion and recommendation. They will be processed in accordance with "Problems Requiring Prompt Reporting to the IRB."

Problems Requiring Prompt Reporting to the IRB

Investigators must report the following problems to the Florida Department of Health (Department) Institutional Review Board (IRB) as soon as possible:

- An unexpected and related adverse event, regardless of whether the event was internal (on- site) or external (off-site), or a circumstance that meets the FDA definition of "serious adverse event." "Adverse events" not meeting these criteria do not need to be reported.
- Information that changes the risks or potential benefits of the research. For example:
    - An interim analysis or safety monitoring report that indicates the frequency or magnitude of harms or benefits different than initially presented to the IRB.
    - Any paper published from another study that shows that the risks or potential benefits of the research is different than initially presented to the IRB.
- Any breach of confidentiality.
- Any change in FDA labeling or the withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Any change to the protocol made without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- Any incarceration of a participant in a protocol not approved to enroll prisoners.
- Any event that requires prompt reporting to the sponsor.
- Any sponsor-imposed suspension for risk.
- Any participant complaint that indicates unexpected risks or cannot be resolved by the research team.
- Any protocol violation (an accidental or unintentional change to the IRB-approved protocol) that harmed participants or others or that indicated they may be at increased risk of harm or that has the potential to recur.
- Any unanticipated adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device that was 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.
- Any non-compliance identified by a Department of Health audit or monitoring.
- Any investigation by the FDA, the Office for Human Research Protections, or other federal agency of research.
- Any loss of license or hospital privileges by a researcher on the study.

Researchers are required to report problems to all IRBs with jurisdiction over the research and

provide documentation of their determinations to the Department using a form or an application review system. Problems should be reported regardless of whether they occur during the study, after study completion, or after participant withdrawal. For example, if the Investigator learns during data analysis of a breach in confidentiality that occurred during the recruitment phase, this information should still be reported to the IRB.

Criteria Used for Reviewing Unanticipated Problems Involving Risks to Participants or Other

Reviewers determine whether the report meets the definition of "unanticipated problem involving risks to participants or others" by evaluating whether the problem:

- Is unexpected (in terms of nature, severity or frequency) given (a) the research procedures and

  (b) the characteristics of the participant population being studied.
- Is related or possibly related to participation in the research (e.g., there is a possibility that the incident, experience, or outcome may have been caused by participation in the research); and
- Places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

These criteria will be applied to evaluate each item of information reported by researchers.

Process for Administrative Screening of Each Reported Problem

The IRB staff, when necessary, in coordination with the IRB chair or an IRB member with relevant subject matter expertise, conducts an administrative pre-review to screen all reports and assesses if the problem involves unanticipated risks to participants or others. If IRB staff determines the event is not unexpected and does not place participants or others at greater risk, then the problem is documented in records on a network drive or application review system as "no further action with justification." No further action is taken unless the problem involves non-compliance. If staff are unable to decide, or are unsure, the report is forwarded to an IRB chair.

Process for Review of Unanticipated Problems by the Chair

The IRB chair reviews the report to determine if the problem involves unanticipated risks to participants or others. If the chair determines the event is not unexpected and does not place participants or others at greater risk of harm, then the problem is documented in records on a network drive or application review system as "no further action with justification." No further action is taken unless the problem involves non-compliance.

If the chair determines the event is an unanticipated problem involving minimal risks to participants or others, then he or she may notify the IRB.

If the chair, staff, or subject matter expert is unable to make a determination, the report is forwarded to the convened IRB for review. The convened IRB will then review the report to determine whether the event is *not* an unanticipated problem involving risks to participants or others, or *not* non-compliance.

Process for IRB Review of Reported Problems by the Convened IRB

The convened IRB reviews reports using a primary and secondary reviewer system to determine if the event is an unanticipated problem involving risks to participants. Reviewers are assigned by the IRB staff, when necessary, in consultation with the IRB chair. Whenever possible, the report will be reviewed by the primary and secondary reviewers who conducted the most recent review of the protocol.

Reviewers will have relevant subject matter expertise and may request additional expertise if necessary.

All committee members have access to the report and supporting documents (including but not limited to safety monitoring board reports and sponsor reports) in addition to IRB protocol documents (including but not limited to the protocol, consent document, and supplemental information). One or more primary reviewers will review the report and all the related documents. All other committee members will review the report, the initial IRB application updated with any changes, any supporting documents, and the consent document.

If the IRB determines the event *is not* an unanticipated problem involving risks to participants, no further action will be taken if the problem does not involve non-compliance.

If the IRB determines the event *is* an unanticipated problem involving risks to participants, it will decide which of the following actions are appropriate regarding the protocol:

- Modification of the protocol.
- Modification of the information disclosed during the consent process.
- Providing additional information to past participants.
- Notification of current participants when such information might relate to participants' willingness to continue to take part in the research.
- Requirement that current participants re-consent to participation.
- Modification of the continuing review schedule.
- Monitoring of the research.
- Monitoring of the consent.
- Suspension of the research.
- Termination of the research.
- Referral to other organizational entities (legal counsel, county health Department director, division director, Deputy Secretary. and State Surgeon General in the role of Institutional Official.

The IRB's discussion is documented in minutes, including discussion of debated issues, if any, and their resolution. The Investigator is informed of the IRB's determination through email or the application review system.

Any unanticipated problems involving risks to participants or others will be reported to regulatory agencies, institutional officials, and others following the Department 's reporting policy. (See "Reporting to Institutional Officials, Department , or Agency Heads.")

Reporting to Institutional Officials, Department, or Agency Heads

The Florida Department of Health (Department) Human Research Protection Program ensures reporting occurs according to the federal regulations and Department policy.

This procedure applies when any of the following occurs:

- Determination from an IRB that a problem is an unanticipated problem involving risk to participants or others.
- Determination from an IRB that an incident of non-compliance is serious or continuing
- Any suspension or termination of IRB approval.

The process for reporting unanticipated problems involving risks to participants or others, serious or continuing non-compliance, and suspensions or terminations of research is outlined below:

- The Human Research Protection Administrator prepares materials within 30 days of the completion of an investigation or determination for reporting to organizational officials. Reporting to federal officials will generally take place within 60 calendar days.

Reports are made to the following Department officials:

- The bureau chief or division director
- The Deputy Secretary for Health
- The State Surgeon General

Reports also are made to the following organizations:

- The researcher's organization

Any other IRBs the researcher reported in the application at initial and continuing review as having jurisdiction over the research. (The Department will attempt to work collaboratively with other IRBs to coordinate reporting, when more than one IRB will be reporting.)

When research involves an FDA-regulated drug or device, the following will be reported to the FDA:

- Unanticipated problems involving risks to participants or others.
- Non-compliance determined to be serious or continuing; and
- Suspensions or termination of research.

When research is sponsored or supported by the Department of Health and Human Services (DHHS), the following will be reported to the Office for Human Research Protections (OHRP):

- Unanticipated problems involving risks to participants or others.
- Non-compliance determined to be serious or continuing.

Generally, the maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements is 90 days.

Any concerns regarding data integrity outside of the jurisdiction of the Department IRB will be referred to the Office of Inspector General, Office of General Counsel, Deputy Secretary, and State Surgeon General.

Informed Consent

The Investigator must ensure that the performance of the informed consent process is congruent with IRB policy and federal regulations. He or she may delegate obtaining informed consent to a member of his or her study team. However, he or she is responsible for monitoring the informed consent process and ensuring the consent documents have been provided to participants.

Monitoring of the Informed Consent Process

The Department IRB determines if a specific research project requires a monitor to observe the consent process or serve as an advocate to ensure the protection of study participants.

This may apply to:

- Situations where participation in research is the only available medical option and no standard of care is available or proven effective.
- Subjects who may, because of their illness or their hope at the prospect of receiving relief or "treatment" are too eager to participate (not make a voluntary decision) or consider the range of available treatment options, some of which may not include research.
- Subjects who may be vulnerable populations, including those with limited or no resources, diminished decision-making capabilities and those where sensitive surveys, interviews, interactions and/or interventions may pose more than minimal risk (e.g., runaways, refugees)
- Research where the risk is such that a second party (i.e., consent monitor) functions as a subject advocate to enhance the informed consent process.
- Situations where the IRB is concerned about the conduct of the study or the process of obtaining informed consent, such as:
    - Complaints from subjects or others regarding the conduct of the study.
    - Complaints from subjects or others regarding the consent process with the investigators.
    - An audit report identifying problems with the execution of the consent process and document; and
    - An audit review of violations or events of non-compliance identifying problems with the consent process or conduct of the study.

The convened IRB may determine at any stage of the review process the need for a consent monitor and require the researcher to provide the resources for monitoring. It will also determine whether to remove the requirement. If a consent monitor is required, the IRB will send correspondence to the investigator detailing the reasons why and indicate whether the board or the investigator will identify someone for the role. The IRB may seek the researcher's input in identifying a consent monitor; however, the selection is ultimately its decision. The Human Research Protection Administrator is eligible to serve as a consent monitor. IRB approval letters will include language specifying that research may only be conducted under the terms of the board's specified monitoring requirements.

Consent Monitoring

The consent monitor has five principal duties:

Listen: The consent monitor should listen to the consent process and exchange between the investigator and the subject and the subject's family.

Observe: The consent monitor should closely observe the communication between the investigator and the subject. The monitor should be prepared to ask questions of the investigator or the subject if it appears that things are not clear.

Ask Questions: The consent monitor should be prepared to ask questions to understand whether the subject fully comprehends the research and is making a knowledgeable decision about participation. Questions should elicit responses from the subject that require some deliberation and thought about the research rather than yes/no questions.

Document: The consent monitor should document the interactions, questions, answers, and the decision-making process.

Decide: The consent monitor should decide (with the investigator and the subject) whether the subject should be enrolled in the research or provided additional time to consider participation. He or she may determine that a subject does not understand the consent process or the research and request that the investigator re-review the materials with the subject. If the consent monitor does not think the subject understands the research or all items on the consent document, then the subject should not be enrolled in the study.

All potential consent monitor candidates will receive training from the Human Research Protection Program. Training will include a review of the following:

- The roles and responsibilities of a consent monitor.
- The "Evaluation to Sign a Consent Form."
- Reporting consent monitoring to the IRB.

Consent Monitoring Process

Prior to a session with a potential participant, the Principal Investigator or his or her designee will provide a copy of the informed consent document to the consent monitor. The monitor will use it to ensure that the investigator addresses all the elements of the consent process.

The Investigator will introduce the consent monitor to the potential subject and provide an explanation for the person's presence. At any time during the session, the monitor may be asked to review or clarify information and/or ask the subject questions to ensure he or she understands the study, its risks and benefits, and can express willingness to participate in the research.

At the end of the session, the consent monitor will use a checklist and ask questions on the "Evaluation to Sign a Consent Form" to assess the potential subject's comprehension of the consent process. He or she will then prepare a summary of the session that will be stored on the IRB network drive or in the application management system. The summary will be reviewed by the convened IRB.

Legally Effective and Prospectively Obtained Informed Consent

The Department ensures provisions are made to obtain informed consent prospectively from each research participant or the participant's legally authorized representative. However, the

IRB may grant a waiver of informed consent under certain circumstances, in accordance with federal regulations.

Presumption that Informed Consent will be Documented

The IRB reviews all consent documents to ensure the adequacy of the information and adherence to federal regulations regarding the required elements.

Presumption that Consent will be Obtained Prior to Research

Investigators must obtain consent prior to initiating research activities, including recruitment and screening procedures. The following guidelines apply to special populations and circumstances:

Children: Parents or guardians may consent to their children's participation in research.

Adults unable to consent: If a researcher intends to enroll adult subjects who lack the capacity to consent, he or she must consult legal counsel to determine who is authorized to grant permission on behalf of the participant.

Research over extended periods: Studies involving subjects who are decisional impaired may take place over extended periods of time. (Decisional impaired persons are those who have a diminished capacity to understand the risks and benefits of participating in research and to autonomously provide informed consent.) For such studies, the IRB considers whether and when obtaining consent again is required to ensure that a subject's continued involvement is voluntary. The IRB considers the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). The board also considers whether and when to require a reassessment of the subject's decision-making capacity.

Documentation of Informed Consent

Informed consent must be documented in writing and include information on who participants should contact questions, concerns, or information about their rights as research subjects. Contact information should be provided for:

- The Principal Investigator or a senior research team member.
- The Investigator's local IRB if it is not the Department IRB.
- Where to go and whom to contact in the event of a research-related injury when medical interventions are involved in the research.
- The Department IRB, including the toll-free telephone number; and
- If the research site is in a local health Department facility, the director, administrator, or medical director of the facility.

Three Options for Documentation of Informed Consent

The IRB may approve procedures for documentation of consent that involve either:

- A written consent form signed by the participant.
- A short form written consent with oral presentation; or

- In limited circumstances, a waiver of the signed written consent form.

Each of these options is described in detail below. The IRB determines which of the procedures described below is appropriate for documenting informed consent in research applications. Generally, only Option One will be appropriate.

Option One: Written Consent Form Signed by the Participant or Legally Authorized Representative

In most circumstances, the IRB requires that consent is documented using an IRB-approved written consent form that is signed and dated by the participant or the participant's legally authorized representative. This consent form must embody the required elements of informed consent and be in a language understandable to the subject. (See "Legally Effective and Prospectively Obtained Informed Consent.") The form may be read to the participant or the participant's legally authorized representative. However, the Investigator should allow the individual adequate opportunity to read and consider the consent document before signing it. A copy of the signed and dated document must be given to the person signing the form.

Option Two: Oral Presentation Using the Short Form

Oral presentation of informed consent information may be used and documented using the "short form" consent document. The short form consent document should generally only be used when the research poses no more than a minimal risk to subjects, or if it involves more than a minimal risk, presents the prospect of direct benefit to individual subjects. The short form consent document attests that the elements of consent have been presented orally. In such cases, the participant must be provided with both:

- A short form written consent document stating that the required basic and appropriate additional elements of consent (See "Legally Effective and Prospectively Obtained Informed Consent") have been presented orally to the participant or the participant's legally authorized representative; and
- A signed and dated copy of the written summary of the information, approved by the IRB, that is presented orally to the participant or the participant's legally authorized representative.

A witness to the oral presentation is required. The person obtaining the consent may not serve as the witness. For participants who do not speak English, the witness must be conversant in both English and the language of the participant. The participant or the legally authorized representative must sign and date the short form written consent document. The person obtaining consent (e.g., the Principal Investigator) must also sign and date a copy of the written summary of the information that is presented orally. A copy of the signed summary must be given to the participant or participant's legally authorized representative.

Participants Who Do Not Speak English

Written informed consent documents for non-English speakers should be in a language understandable to the participant and include all the required elements for legally effective informed consent. Federal regulations permit oral presentation of informed consent information in conjunction with a short form written consent document (stating that the elements of consent have been presented orally) and a written summary of what is being presented orally. However, a witness to the oral presentation is required, and the participant must be given signed and dated copies of the short form consent document and the summary.

When this procedure is used with participants who do not speak English, the following are required:

- The oral presentation and the short form consent document should be in a

language understandable to the participant. The IRB-approved English language informed consent document may serve as the summary; and

- A witness who is fluent in both English and the language of the participant should be present.

The IRB committee must review and approve all foreign language versions of the informed consent documents prior to use. Expedited review of these versions is acceptable if the convened IRB Committee has already approved the research study, the full English language informed consent document, and the English language version of the short form document.

Option Three: Waiver of Documentation (See "Waiver and Alteration of Informed Consent.")

No Verbal Consent: Verbal agreement to participate in a research study is not permitted unless the documentation or process of informed consent is waived by the IRB.

Use of Fax, Mail, or Email to Document Informed Consent

The IRB may approve a process that allows the consent document to be delivered by mail, fax, or email to the potential participant or the legally authorized representative. The Investigator may conduct the consent interview by telephone when the participant or the legally authorized representative can read the consent document as it is being discussed. A document may also be sent as an attachment via email for the participant to print out and sign and return. All other requirements for documentation of consent must also be met when using this procedure.

Waiver and Alteration of Informed Consent

The Department IRB must grant a waiver (or an exception) of informed consent for qualifying emergency research in accordance with federal regulations and Department IRB policies and procedures. The IRB follows the criteria in 45 CFR 46.116(c-d), 45 CFR 46.117, 21 CFR 177, 21 CFR 56.109(c)(1) and 21 CFR 56.109(d) to determine whether the requirement to obtain written documentation of consent process can be waived.

Exception from Informed Consent Requirements for Emergency Research Subject to FDA Regulation

Please note: Do not confuse with Emergency Use of FDA Regulated Products (See "Emergency Use of FDA Regulated Products and Emergency Use Authorizations.")

The IRB may review and approve a clinical investigation without requiring informed consent of all research subjects if the board (with the concurrence of a licensed physician who is a member of, or a consultant to, the IRB and who is not otherwise participating in the study) finds and documents each of the following:

- The target population for the research is in a life-threatening situation.
- Available treatments are unproven or unsatisfactory.
- The collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of interventions; and
- Obtaining informed consent is not feasible because:
    - The subjects will not be able to give their informed consent because of their medical condition.
    - The intervention under investigation must be administered before consent from

the subjects' legally authorized representatives are feasible; and

- There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- Participation in the research holds out the prospect of direct benefit to the subjects because:
    - The subjects are facing a life-threatening situation that necessitates intervention.
    - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects.
    - The risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects and the risks and benefits of the proposed intervention or activity; and
    - The clinical investigation could not practicably be carried out without the waiver.

- The Investigator has attempted to contact an authorized representative for each subject within the defined therapeutic window, and if feasible, asked for consent rather than proceeding without it. The Investigator must summarize efforts made to contact legally authorized representatives and provide this information to the IRB at the time of continuing review.
- The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with federal regulations and IRB policies and procedures. The procedures and document are to be used with subjects or their legally authorized representatives in applicable situations.
- Additional protections of the rights and welfare of the subjects will be provided, including, at a minimum:
    - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.
    - Prior to the initiation of the clinical investigation, public disclosure to the communities where the trial will be conducted and from which the subjects will be drawn to inform them of its risks and expected benefits;
    - At the completion of the clinical investigation plans for public disclosure of sufficient information to apprise the community and researchers of the study. Such information must include the demographic characteristics of the research population and the results of the clinical investigation.
    - Establishment of an independent data and safety monitoring committee to exercise oversight of the clinical investigation; and
    - Procedures to inform, at the earliest possible opportunity, each participant (or legally authorized representative or family member) the details of the study and other information in the informed consent document. The legally authorized representative or family member may discontinue the subject's

participation at any time without penalty or loss of benefits of which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as possible.

- If a subject is enrolled in a clinical investigation with waived consent and he or she dies, information about the clinical investigation is to be provided to the participant's legally authorized representative or family member.
- All clinical investigation records, including regulatory files, must be maintained for at least three years after completion of the study and be accessible to authorities for inspection and copying.
- Clinical investigations that are granted an exception to the informed consent requirement must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that the study may include subjects who are unable to consent. This is required even if an IND or IDE for the same drug or device already exists.
- If the IRB determines it cannot approve a request for exception from informed consent requirements because the clinical investigation does not meet the criteria in accordance with federal regulations and IRB policies or raises other relevant ethical concerns, the IRB must document its findings and provide them promptly in writing to the clinical investigator who will forward the information to the study sponsor.

No Deferred Consent or Un-Approved Waivers of Informed Consent

Informed consent procedures, which provide for other than legally authorized and prospectively obtained consent, fail to constitute informed consent under federal regulations. Therefore, waiving informed consent using a method other than those described in this policy is a violation of IRB policy and federal regulations and is subject to reporting to federal, state, and institutional officials. An exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

Assent/Dissent by Children or Cognitively Impaired Adults

The Department IRB must ensure that adequate provisions are made to protect children and cognitively impaired adults who lack decision-making capacity.

- In instances where the participant is not capable of giving informed consent (e.g., minors) or where he or she is cognitively impaired, the IRB must ensure procedures are in place to obtain assent, when in the judgment of the IRB, the subject can agree to participate in the study. The IRB will consider the age, maturity, and psychological state of the participant. This judgment may be made for all enrolled participants, or for each individual subject.
- Assent is not necessary if the capability of some or all the participants is so limited they cannot reasonably be consulted, or if the prospect of direct benefit is important to their health or well-being and available only in the context of the research. Even in situations where the IRB determines the participants are capable of assenting, the board may still waive the requirement under certain circumstances.
- When the IRB determines that assent is required, it should determine whether and how it should be documented.

- The IRB may approve minimal risk observational research if it finds adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 40 CFR 26.406.

When research involves secondary analysis of data from state registries, such as a registry about pregnancy and premature births, the Department may assign a reviewer whose expertise is more appropriate (i.e., a statistician) as opposed to someone with expertise in research involving pregnant women.

Recruitment/Advertising

The Department IRB must ensure that the appropriate safeguards exist to protect the rights and welfare of prospective and current research participants. In fulfilling this responsibility, the board must review the methods and materials that will be used to recruit participants.

The Investigator must obtain IRB approval for all television, radio, video or print advertisements, e-mail solicitations, Internet websites, and other recruitment methods and materials prior to their use. All methods require written approval from the facility where the research will be conducted. For example, if the research will be conducted at a county health Department, the Investigator must obtain permission from the director or administrator.

The following examples do not qualify as an advertisement:

- Communications intended only to be seen or heard by health professionals, such as “dear doctor” letters and doctor-to-doctor letters.
- News stories, so long as they are not intended for recruitment purposes (e.g., a news story would not include a phone number at the end to contact for more information to participate in a particular study, full details of inclusion/exclusion criteria of a particular study, etc.); and
- Publicity intended for other audiences (e.g., media releases regarding types of services available or offered by a particular clinic, institute, or physician).
- The IRB must review information contained in an advertisement and the mode of its communication to determine that:
    - The procedure for recruiting participants is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
    - The materials do not include exculpatory language.
    - The materials do not emphasize the payment or the amount to be paid, by such means as larger or bold type.

Before printing, posting or airing advertisements:

- The board must review the final printer-ready draft to evaluate the relative size of type used and other visual effects, the final audio or video, and the final versions of materials before they are posted to websites and on social media. The IRB may review and approve the wording of an advertisement prior to recording to avoid re-recording because of inappropriate wording. The review of the final taped message prepared from IRB-approved text may be accomplished through expedited procedures.

If the Investigator decides after initial approval to change the advertising methods or materials,

the changes are considered amendments to the ongoing study.

Any advertisement to recruit participants should be limited to the information the prospective participants need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:

- The name, address, and facility or institution of the Investigator or study coordinator (e.g., the Department);
- If applicable, include “investigational, meaning non-FDA approved;”
- The condition under study and the purpose of the research.
- In summary form, the criteria that will be used to determine eligibility for the study.
- A brief list of participation benefits, if any (e.g., a no-cost health examination).
- The time or other commitment required of the participants; and
- The location of the research and the person or office to contact for further information.

Advertising materials should not include:

- Claims, either explicitly or implicitly, that the drug, biologic, device or other type of intervention is safe or effective for the purposes under investigation.
- Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic, device, or intervention.
- Terms, such as "new treatment," "new medication," or "new drug," without explaining that the test article is investigational, meaning non-FDA-approved;
- Promises of "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the investigation.
- Compensation for participation in a trial offered by a sponsor to include a coupon for a product once it has been approved for marketing.

Advertising or Recruitment for Studies Involving Investigational Articles (See “Recruitment/Advertising.”)

Advertisements or recruiting tools for investigational articles must not include the phrase “new treatment” without explaining that the device, drug, agent, or biologic is “investigational,” meaning “non-FDA approved.” “Receive new treatment” implies that study participants will be given newly marketed products of proven worth. However, it is not a treatment because its effectiveness has not been proven or established. Moreover, the term “new” is misleading as it gives the participant hope of a new intervention when the outcome is unknown.

In addition, advertisements or recruiting tools must not include the promise of “free medical treatment” when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g., drug, agent, biologic). The use of the word “free” could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.

Incentives for Participation

The IRB must review payments for participation to determine that:

- The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
- Credit for payment accrues as the study progresses and is not contingent upon the participant completing the entire study.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
- All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.

Receptionist Scripts: The first contact prospective study participants make is often with a receptionist who follows a script to determine basic eligibility for the specific study. The IRB must review the script and procedures to ensure that they adequately protect the rights and welfare of the prospective participants. The IRB must have assurance that any information collected about prospective participants will be appropriately handled.

Internet Recruitment: All online recruitment advertisements must be reviewed and approved by the IRB prior to implementation, except for two specific clinical trial listing services: the National Cancer Institute's cancer clinical trial listing (PDQ) and the government-sponsored AIDS Clinical Trials Information Service (ACTIS). For all other online recruitment ads, IRB review and approval are required to ensure that the information does not promise or imply a certainty of a cure or other benefit beyond what is contained in the protocol and the informed consent document. In addition, the Investigator must ensure that the information shared for Internet recruitment is in accordance with his or her signed clinical trial agreement or grant.

Department of Health Mass Communication Email: Advertising submitted through mass email solicitation at Department should be simple, readable, and understandable and meaningfully and respectfully convey a message to a broad spectrum of the Department community. It should be text-based and written in paragraphs. The following format is recommended when utilizing this method of recruitment or advertisement:

A headline that describes the study and volunteers needed.

- Paragraph 1 – include enough information to help readers self-select.
- Paragraph 2 – purpose of the study.
- Paragraph 3 – requirements of participation.
- Paragraph 4 – benefit to the participant or a statement there is no benefit; and
- Paragraph 5 – a contact person “for more information.”

Students as Participants: The IRB exercises oversight with the use of students as participants in research.

Database/Primary Care Physician Recruitment: Oftentimes, Investigators request to search databases for potential participants who may be eligible for their research projects (e.g., by disease, age, sex, etc.), or they request to contact primary care providers (PCP) for access to potential participants from the PCP’s patient population. These recruitment methods require IRB approval prior to initiation.

Inclusion of Women, Children and Minorities: The inclusion of women, children, and minorities is important to ensure that these groups receive an appropriate share of the benefits of research and that they do not bear a disproportionate burden. To the extent that participation in research offers direct benefits to the participants, underrepresentation of women, children, or

minorities denies them the opportunity to benefit. Moreover, for purposes of generalizing research results, Investigators must include the widest possible range of population groups.

Finder's Fees and Bonus Payments: Research sponsors may offer to pay Investigators or study personnel an additional fee to encourage participant recruitment efforts and the timely or accelerated opening of research studies. Finder's fees and bonus payments are not allowed.

Legal Implications: The Council on Ethical and Judicial Affairs of the American Medical Association denounced the practice of finder's fees in December 1994. The federal Anti-Kickback Statute can also be implicated by this practice; and for physicians, Florida Statutes may prohibit certain recruitment incentives and may be subject to disciplinary action. (See, for example, Chapters 456.045 and 458.311.)

Recruiting Department Clients: During the process of recruiting Department clients or using a department facility to recruit participants, the Investigator must provide information on how a prospective research participant can contact the Department Human Research Protection Program, including the toll-free telephone number, or if applicable, the county health Department medical director, to voice concerns or ask questions.

Investigational Devices

The Department IRB must approve all research involving investigational devices in accordance with applicable laws and regulations.

Significant Risk (SR) vs. Non-Significant (NSR) Risk Devices

An investigational device must be categorized as either a Significant Risk (SR) device or a Non-Significant Risk (NSR) device unless it has an Investigational Device Exemption (IDE). While the sponsor determines the initial risk assessment, the IRB must make a determination regarding the appropriate SR/NSR category at a convened meeting.

- Research involving the use of an SR device must be conducted in accordance with the full requirements of the FDA and must have an approved IDE.
- Research involving the use of a NSR device must be conducted in accordance with the

  "abbreviated" requirements of the FDA as described in 21 CFR 812.2(b). In some cases, the FDA may notify the sponsor that it does not agree with the NSR determination and require submission of an IDE.

Exemptions from IDE Requirements

A claim that the device is exempt from IDE requirements must reference one or more of the seven exemption categories. Categories 1 and 2 pertain to a device in commercial distribution immediately before May 28, 1976, or a device the FDA has determined to be "substantially equivalent" to one that was in commercial distribution before May 28, 1976. Categories 3 and 4 are the most claimed and described below. Categories 5 and 6 pertain to the use of an investigational device on animals, while Category 7 applies to devices that are created or modified to comply with the order of an individual physician or dentist.

Category 3 applies to a diagnostic device so long as the testing:

- Is noninvasive.
- Does not require an invasive sampling procedure that presents significant risk.
- Does not by design or intention introduce energy into a subject; and

- Is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure.

Category 4 pertains to a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution. The testing must not be intended to determine the safety and effectiveness of the device and must not put participants at risk.

Note: It is the sponsor's responsibility to provide sufficient justification to support the exemption category being claimed. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

Informed Consent in Research That Involves an Investigational Device

Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures. (See "Legally Effective and Prospectively Obtained Informed Consent.")

- No claims should be made which state or imply, directly or indirectly, that the investigational device is safe or effective for the purposes under investigation or that it is superior to any other device.
- The informed consent document must contain a statement that the device is "investigational, "meaning "non-FDA approved;"
- The informed consent document must contain a statement that the FDA may have access to the participant's medical records as they pertain to the study; and
- The Investigator must ensure that throughout the consenting process and study, the participant understands that the device is experimental, and that its benefits for the condition under study are unproven.

Additional Reporting Requirements

Devices may have an unanticipated adverse effect on participants or others. An investigator must submit to the study sponsor and to the Department IRB any problems as soon as possible, no later than 10 business days after the Investigator first learns of the issue. (See "Problems Requiring Prompt Reporting to the IRB.") Should the IRB determine that the new information changes its risk assessment, it may reconsider its prior NSR decision and ask for FDA review.

A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to participants must terminate or suspend all or parts of the investigation as soon as possible, no later than five business days after the determination and no later than 15 business days after the sponsor first received notice of the adverse effect. He or she may not resume the investigation without IRB and FDA approval.

The Investigator must submit a final report to the sponsor and the Department IRB within 90 days after termination or completion of the investigation.

Investigational Drugs, Agents, and Biologics

The use of investigational drugs, agents, and/or biologics must be reviewed and approved for use in accordance with federal regulations.

IRB Requirements for the Use of an Investigational Drug, Agent, or Biologic

The Department IRB conducts the initial approval and ongoing monitoring of the use of investigational drugs, agents, and biologics in research that falls under its jurisdiction. Included in this process is a review by a pharmacist on the IRB committee. Prospective IRB review is required even if the FDA has granted a waiver.

FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

Compassionate Use: "Compassionate use" refers to giving investigational drugs (outside of an ongoing clinical trial) to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. However, the term "compassionate use" does not appear in FDA or DDHHS regulations. Therefore, it is preferable to use "expanded access" when discussing the use of investigational articles outside of formal clinical trials.

Group C Treatment Investigational New Drug (IND): The distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside of controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of efficacy in specific tumor types.

Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the Department IRB requires prospective IRB review and approval.

Open–Label Protocol: A study designed to obtain additional safety data, typically done when the controlled trial has ended, and treatment continues. The purpose of such a study is to allow participants to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. When open-label studies are conducted involving the Department, prospective IRB review and approval is required.

Parallel Track: A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to people living with HIV. These products are used in separate protocols that "parallel" controlled clinical trials. Parallel studies are essential to establishing the safety and effectiveness of products. Although the Secretary of the Department of Health and Human Services may waive provisions in 45 CFR 46, in which adequate protections of participants are provided through other mechanisms, when the Department is involved, prospective IRB review and approval is required.

Treatment IND or Biologics: A mechanism for providing eligible participants with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediate life- threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. When these studies are conducted involving the Department, prospective IRB review and approval is required.

There are four requirements that must be met before a treatment IND can be issued:

- The drug is intended to treat a serious or immediate life-threatening disease.
- There is no satisfactory alternative treatment available.
- The drug is already under investigation or trials have been completed; and
- The trial sponsor is actively pursuing marketing approval.

The FDA identifies two special considerations when a patient is to be treated under a Treatment

IND:

- **Informed Consent:** Informed consent is especially important in treatment situations because the participants are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven as either safe or effective, and their desperation may work against their ability to make an informed assessment of the risks involved. Therefore, the IRB must ensure that potential participants are fully aware of the risks involved.
- **Charging for Treatment INDs:** The FDA permits charging for the drug, agent, or biologic when it is used in a Treatment IND. Therefore, the IRB committee should pay particular attention to Treatment INDs in which the participants will be charged. Economically disadvantaged individuals will likely be excluded from participation. The IRB should balance this interest against the possibility that if the sponsor cannot charge for the drug, it may not be available for treatment use until it receives full FDA approval.
- **Single-Patient Use:** The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is not responding to other therapies or there is no approved or generally recognized treatment available. There is usually little evidence that the proposed therapy is useful. However, it may be plausible based on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a single patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use. When these studies are conducted involving the Department, prospective IRB review and approval is required. For example, the Department provides clofazamine for tuberculosis and other mycobacterium diseases. This drug can be provided under a single-patient use IND.
- **Emergency IND:** The FDA has established mechanisms and guidance for obtaining an Emergency IND license for the use of investigational drugs, agents, or biologics. Additional Department IRB guidance regarding emergency IND is provided in "Emergency Use of FDA-regulated Products and Emergency Use Authorizations."

When the protocol is subject to review under more than one Department or agency's regulations, the requirements of each must be met. This situation may arise, for example, with Treatment Investigational New Drugs where both the FDA and DDHHS have jurisdiction over the research.

Use of an Investigational Drug, Agent, or Biologic by an Investigator

For an investigational drug, agent or biologic to be used in clinical research at Department, an Investigational New Drug (IND) must be on file with the FDA and an IND number granted.

Clinical investigations of a drug, agent, or biologic that is lawfully marketed in the United States are exempt from the requirements of an IND, when the following conditions are met. The use is:

- Not intended to be reported to the FDA in support of a new indication for use nor support any significant change in labeling for the product.
- Not intended to support a significant change in the advertising of the product.
- Does not involve how the drug is introduced into the body, dosage level, and/or use in a subpopulation, or other factors that significantly increase the risks, or decrease the acceptability of the risks associated with the drug, agent, or biologic.

- Will be conducted in compliance with the IRB approval and informed consent procedures.
- Will be conducted in compliance with the requirements concerning the promotion and sale of the drug, agent, or biologic as described in FDA regulations 21 CFR Sec 312.7; and
- Does not intend to invoke exception from informed consent requirements for emergency use.

When a researcher asserts a study does not require an IND, the Department will require the researcher contact the FDA for a formal determination.

Research involving combinations of FDA-approved drugs, agents, or biologics that are currently approved as single use, do not require an IND. However, their use in research must still be prospectively reviewed and approved by the IRB.

The Investigator administering an investigational drug, agent or biologic must meet the following requirements to use the product in research conducted under the jurisdiction of the Department IRB:

- The drug, agent or biologic must be used only in accordance with the plan of investigation that is described in the FDA-approved IND application and the IRB-approved protocol.
- The drug, agent, or biologic may only be used in participants under the Investigator's personal supervision or under the supervision of physicians who are directly responsible for the Investigator; and
- Informed consent from the participant or the participant's legally authorized representative is prospectively obtained, unless a waiver of consent has been approved by the Department IRB.

Research involving an investigational drug, agent, or biologic must be conducted in accordance with the Department IRB policies.

Informed Consent in Research that Involves an Investigational Drug, Agent, or Biologic

Informed consent must meet the requirements outlined in the IRB informed consent policies and procedures. (See "Documentation of Informed Consent" and corresponding procedures.)

- No claims are to be made which state or imply, directly or indirectly, that the investigational drug, agent, or biologic is safe or effective for the purposes under investigation or that the drug is in any way superior to another drug;
- The informed consent document must contain a statement that the drug, agent, or biologic is

  "Investigational," meaning "non-FDA approved;"
- The informed consent document must contain a statement that the FDA may have access to the

  participant's medical records as they pertain to the study; and
- The Investigator must ensure that throughout the consenting process and study participation the participant understands that the investigational drug, agent, or biologic is under investigation, and that its benefits for the condition under study are unproven.

For Phase I studies, the informed consent document must disclose that the purpose of the research includes examining the drug's safety. For Phase II and Phase III studies, the informed

consent document must disclose that the purpose of the research includes examining the drug's safety and efficacy.

Ensuring Regulatory Approval for Research Use of Investigational Articles

Department requires that research using an investigational article (drugs or medical devices not FDA-approved or used for purposes not approved by the FDA) complies with federal regulations.

When the research involves an investigational article, researchers are required to obtain an IND or IDE prior to enrolling subjects in their study.

When the sponsor holds the IND or IDE, researchers are responsible for providing it to the IRB or including enough information in their application for the Human Rights Protection Program to determine whether the use of the article is exempt from regulatory requirements (21 CFR §312.2(b)) (21 CFR 812.2(b)(1)).

For investigator-initiated research, where the researcher holds the IND or IDE, he or she is responsible for arranging to have a contract research organization (CRO) accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) ensure the drug or device meets all regulatory requirements.

The IRB may approve investigator-initiated research by university researchers if documentation is provided that the university is responsible for ensuring all regulatory requirements are met.

Additionally, the university's human research protection program must be accredited by the AAHRPP. Investigators should not conduct FDA-regulated investigator-initiated research that is not monitored by a sponsor or CRO.

The process to confirm that the test article has an IND or IDE, or that the research protocol is exempt from FDA requirements is as follows:

For an IND:

Department staff confirms that the drug has an IND, or that the drug is exempt from the IND requirement (21 CFR §312.2(b)) using the "Investigational Drug" worksheet. The worksheet is stored on the network drive or application management system and serves as documentation of the validity of the IND or IDE. Acceptable forms of documentation are the presence of an IND on the sponsor protocol, communication from the sponsor, or communication from the FDA. Staff may require the sponsor to provide documentation from the FDA that an IND is not required. IRB review of the use of an investigational drug is conducted using the IND worksheet completed by the primary reviewer.

For an IDE:

Department staff confirms that the IDE is valid, or that the device meets requirements for an abbreviated IDE (used for non-significant risk devices) (21 CFR 812.2(b)(1)) or a full IDE exemption (21 CFR 812.2(c)) using the "Investigational Device" worksheet. Acceptable forms of documentation are the presence of an IDE on the sponsor protocol, communication from the sponsor, or communication from the FDA. Staff may require the sponsor to provide documentation from the FDA that an IDE is not required. IRB review of the use of an investigational device is conducted using the IDE worksheet completed by the primary reviewer.

Storage, Handling, and Control of Investigational Drugs and Devices

All investigational drugs and devices must be used only in approved research protocols and under the direction of approved researchers in accordance with applicable laws and regulations.

The IRB conducts protocol-by-protocol review and approval of the researcher's plans to control investigational drugs and devices. The following methods apply:

- For research at local health Department s, control may be provided by the pharmacy or by the Investigator in the research clinic.
- For research involving in vitro diagnostic devices, control may be provided by the Investigator in the laboratory.
- For other settings, control may be provided by the Investigator.

Storage of Investigational Drugs and Devices

For research in which investigational drugs (including controlled substances) are stored in a local health Department pharmacy, a licensed pharmacist must comply with all institutional, state, and federal laws regarding storage. If the investigational drugs are not controlled by a pharmacy, they must be stored under the direct supervision of the Investigator and in accordance with the sponsor protocol when applicable. In such cases, the Investigator must comply with all laws.

Investigational drug storage facilities must follow institutional, state, and federal (FDA laws). Pharmacy monitoring may be incorporated into the IRB auditing process to ensure compliance.

Dispensing of Investigational Drugs

Investigational drugs administered to research participants may be provided through a pharmacy, or by the Investigator or nurse in a research clinic. The Investigator must ensure that dispensing the drugs is in accordance with all institutional, state, and federal requirements.

The Investigator is responsible for the tracking and oversight of FDA-regulated devices in research. He or she must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the Department IRB:

- The investigational device must be used only by the Investigator or under his/her direct supervision and only as approved by the FDA and as described in the approved IRB documents.
- The Investigator must not supply the investigational device to individuals not authorized under the investigational device exemption (IDE); and
- Informed consent from the participant or the participant's legally authorized representative must be prospectively obtained.

Investigations of issues related to the potential mishandling of investigational drugs will be conducted by the Office of Inspector General, which will refer the issue to other Department offices, divisions, or agencies responsible for compliance and promptly (within seven business days) notify the IRB.

Humanitarian Use Devices

The Department IRB reviews and approves all humanitarian use devices (HUDs). A HUD is intended to benefit patients by treating or diagnosing a disease that affect fewer than 4,000 in the United States per year.

For a HUD to be used in treatment, diagnosis, or research, the Department IRB and the FDA must approve it, and a Humanitarian Device Exemption (HDE) must be issued. The IRB approval must confirm that the proposed use of the HUD is consistent with the current labeling of the device and does not exceed the scope of the FDA-approved indication. The IRB may impose more stringent restrictions for the HUD, as deemed necessary.

Additionally, the physician using the HUD may use it only in accordance with the labeling of the device, its intended purpose, and in the designated population for which the FDA approved its use.

The IRB committee must complete the initial review of a HUD and determine whether expedited review can be used for continuing review and minor modifications. Informed consent is required when the HUD is the subject of a clinical investigation; or the IRB requires its use.

Considerations for Prompt Reporting

When the healthcare provider receives or becomes aware of information that suggests a HUD has or may have caused or contributed to the death or serious injury of a patient, he or she must report the findings to the FDA and the IRB as soon as possible, but no later than 10 business days after the Investigator first learns of the issue. (See "Problems Requiring Prompt Reporting to the IRB.") This reporting is in addition to, not a substitute for, notifying the FDA and/or the manufacturer. Furthermore, the healthcare provider must promptly report modifications to the HUD or its use to the Department IRB.

Emergency Use of FDA Regulated Products and Emergency Use Authorizations

The Department IRB recognizes the provisions in the FDA regulations for the emergency use of investigational drugs, biologics, agents, and medical devices.

Note: Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care for patients to the extent he or she is permitted under FDA regulation and other applicable law.

Emergency use of a test article (an investigational drug or device) is not considered human subjects research under the DHHS regulations 45 CFR 46. Emergency use is defined as the use of a test article on a human participant 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 [21 CFR 56.102(d)]. The data may not be reported in a way that implies that the activity was a prospectively planned systematic investigation designed to develop or contribute to generalizable knowledge.

However, emergency use of a test article (an investigational drug or device) is subject to FDA regulations and the patient is considered a research participant. The FDA may require the data to be reported in a marketing application or published in a retrospective report. If the research involves an investigational drug, the FDA must issue an investigational new drug (IND) license.

The emergency use provision in FDA regulation [21 CFR 56.104(c)] is exempt from IRB review and approval when it meets several conditions. To ensure that emergency use complies with the

regulations, investigators should notify the Human Research Protection Administrator, Human Research Protection Program staff, or an IRB chair before using the test article. A licensed physician must determine whether the use is exempt from IRB review and approval.

The Human Research Protection Administrator or an IRB chair or member who is a licensed physician will review the request with the Investigator to make sure it meets FDA regulations and the Department 's policy concerning emergency use when the following are met:

- The patient is in a life-threatening or severely debilitating situation necessitating the use of the test article.
- No standard acceptable treatment is available.
- There is not enough time to obtain IRB approval.
- Permission of the sponsor exists prior to use.
- The activity does not meet the DHHS definition of “research involving human subjects”

The use is reported to the IRB within five days by the Investigator administering the test article. Any subsequent use is subject to IRB review.

Informed consent will be obtained and documented in accordance with FDA regulation 21 CFR 50. However, it may not be required if the circumstance meets the waiver criteria in 21 CFR 50.23, or one of the following are true:

- Informed consent cannot be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant.
- There is not enough time to obtain consent from the participant’s legal representative.
- There is no alternative method of approved or generally recognized therapy that will provide an equal or greater likelihood of saving the life of the participant.

Documentation that the situation is a life-threatening emergency should be included in the patient’s medical record and in a letter to the IRB.

The emergency use of an unapproved investigational drug or biologic requires an IND license. If the intended subject does not meet the criteria of an existing study protocol, the Investigator should contact the manufacturer of the drug/biologic to determine if the product can be made available under the company's IND license. If the IND license is not available through the manufacturer, the Investigator should contact the FDA for an emergency IND.

If there is no time to contact the Human Research Protection Administrator or IRB Chair prior to emergency use, either of them, or an IRB member who is a licensed physician, will determine whether the use is exempt retrospectively. The determination will be based on a report provided by the investigator within five days of the use. The Human Research Protection Administrator, IRB chair, or IRB member will issue a letter indicating whether the activity met the exemption requirements described in 21 CFR 56.103(c).

Note: Submitting notification to the Human Research Protection Administrator or IRB chair should not be construed as IRB approval. The Investigator is required to notify the IRB within five working days of emergency use. The notification is used to initiate tracking and ensure the Investigator files the report as described in FDA regulation 21 CFR 56.104(c).

If the IRB chair or the member who is a licensed physician determines, based on retrospective evaluation, that the activity does not meet the exemption requirements described in 21 CFR

56.103(c), the issue will be handled in accordance with “Investigating any Non-Compliance, Serious or Continuing Non-Compliance.”

If there is sufficient time to obtain IRB approval for emergency use, investigators will submit a new IRB application, which will be reviewed at the next meeting. FDA regulation [21 CFR 56.102(d)] permits one emergency use. Any subsequent use must have prior IRB review and approval [21 CFR 56.104(c)]. If an Investigator anticipates possible subsequent use of the agent, he or she should complete an IRB application.

Manufacturers or sponsors who agree to allow the use of the investigational drug, agent, biologic, or device, but will not ship it without “an IRB approval letter,” will be provided with a written statement that the IRB is aware of the proposed use and based on the information it has been provided by the Investigator, the use meets the requirements of 21 CFR 56.102(d).

During a public health emergency, it may be necessary to give a test article to more than one patient. The Project BioShield Act of 2004 gave the FDA the authority to provide Emergency Use Authorizations, or EUAs, which allow for the use of unapproved drugs, biologics, or medical devices to diagnose, treat, or prevent a serious or life-threatening disease or condition when no adequate, approved, or available alternatives exist. IRB review is not required for EUAs. However, the OHRP Program may assist in providing information and guidance to local hospitals about why review is not required.

An EUA will be in effect for the duration of the declaration under which it was issued, unless the authorization is revoked because the criteria for issuance are no longer met, or revocation is appropriate to protect public health or safety. The terms and conditions of an EUA preempt state laws governing the dispensing, administration, or labeling of unapproved medical products or cleared medical products for unapproved uses.

FDA Guidance specifies the information that should be submitted to the FDA for consideration of an EUA. Before an EUA can be issued, the Secretary of Defense, Homeland Security or DHHS must declare an emergency based on one of the following grounds:

- There is a domestic emergency, or potential for one, involving a heightened risk of attack with a specified biological, chemical, radiologic, or nuclear agent or agents.
- There is a military emergency, or potential for one, involving a heightened risk of attack on U.S. military forces with a specified biological, chemical, radiologic, or nuclear agent or agents.
- There is a public health emergency that affects, or has the potential to affect, national security, and that involves a significant biological, chemical, radiological, or nuclear agent, or a disease or condition that may be attributable to such an agent or agents.

The emergency use is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established product or procedure.

A declaration of emergency is issued under Section 564 of the Federal Food, Drug, and Cosmetic Act (FFDCA), allowing for the potential use of a product under an EUA if the FDA Commissioner certifies to the DHHS Secretary:

- The agent specified in the declaration of emergency can cause a serious or life-threatening disease or condition.
- Based on the scientific evidence available, including data from adequate and well-controlled clinical trials, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing (a) a serious or life-threatening disease or condition; or (b) a serious or life-threatening disease or condition caused by a product that was authorized or approved for diagnosing, treating, or preventing a disease or

condition caused by the agent specified in the declaration of emergency;

- That the known and potential benefits outweigh the known and potential risks of the product when used to diagnose, prevent, or treat the serious or life-threatening disease or condition that is the subject of the declaration; and
- That there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such a serious or life-threatening disease or condition.

The FDA Commissioner may establish conditions on the use of a product under an EUA. The provider may be required by the FDA to inform patients:

- That the FDA Commissioner has authorized the emergency use of the product
- Of the risks and benefits of the drug
- Of any alternative therapies available
- That they may refuse administration of the unapproved product

Glossary

To ensure and maintain consistency throughout human research protection program policies, the Department IRB uses the following definitions:

Administrative Rule: A statement of general applicability that implements, interprets, or prescribes law or policy or describes the procedure or practice requirements of an agency. The term also includes the amendment or repeal of a rule (see 120.55, Florida Statutes). Rules comprise the Florida Administrative Code.

Adverse Event: Any harm experienced by a participant regardless of whether the occurrence was internal (on-site) or external (off-site) or meets the FDA definition of "serious adverse event." The harm is both unexpected and related. “Adverse events” not meeting these criteria should not be reported.

(See “related” and “unexpected.”)

Advertising: A print or broadcast announcement that describes a research study. It is typically used to recruit subjects.

Agent: Any individual (employee or contractor) authorized to act on behalf of the Department of Health.

Allegation of Non-compliance: Written or verbal report of possible non-compliance involving research under the oversight of the Department.

Alternate Member: An individual appointed by the institutional official to substitute for an IRB member. The person counts toward a quorum in the absence of the IRB member whose expertise he or she is replacing. If the member and alternate are both present at a meeting, only one may vote.

Amendment: Any change to an IRB-approved study protocol regardless of the level of initial review. (See

also “minor amendment” and “major amendment.”)

Appearance of a conflict of interest: If a reasonable person with knowledge of the relevant facts would question the impartiality or the public interest duty of investigators, study personnel, IRB members, consultants, or IRB staff

Assent: A child’s affirmative agreement to participate in research. Failure to object to participation by

the child should not, absent affirmative agreement, be construed as assent.

Assurance: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).

Bonus Payment: Compensation tied to the rate or timing of recruitment. Examples include:

- The sponsor announces that the highest enrolling site in the nation will receive a $10,000 bonus
- The sponsor offers to pay an additional $10,000 to any site that enrolls five participants within a week.
- The sponsor offers to pay an additional $10,000 to any site that fulfills its recruitment target by the end of the month.
- The sponsor offers to pay an additional $1,000 for any subject who agrees to enroll within one day of initial contact.

Bonus payments are not allowed.

Certificate of Confidentiality: A document that provides additional protection of data from legal subpoena, such as compelled disclosure of identifying information of a participant enrolled in biomedical, behavioral, clinical, or other sensitive research.

Children: Individuals who have not reached the legal age to consent to the treatments or procedures involved in research or clinical investigation. Exceptions apply:

- A person under the age of 18 who has had the disability of nonage removed by a circuit court may consent to treatments and procedures in research; §743.015 F.S.
- A person under the age of 18 who is married or has been married, including one whose marriage is dissolved, or who is a widow or widower, may consent to treatments and procedures in research; §743-01 F.S.
- An unwed pregnant person under the age of 18 may consent to the performance of medical or surgical care or services relating to her pregnancy or her child, including not greater than minimal risk research; such consent is valid and binding; §743.065 F.S.
- A person under the age of 18 seeking medical care or services related to sexually transmitted diseases may consent to such treatments and procedures, including not greater than minimal risk research related to such diseases. The consent of the parents or guardians is not a prerequisite; §384.30 F.S.

Clinical Investigation: Any experiment involving a test article and one or more human subjects that meets the requirements for prior submission to the FDA under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act; or if it does not meet the requirements, the results will be submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations; (21 CFR 50.3(c), 21 CFR 56.102(c)).

Coded Information: Private information identifying an individual has been replaced with a number, letter, symbol, or a combination of the three along with a key to decipher the code linking the identifying information to the individual.

Cognitively Impaired: Having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavioral disorder), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished as determined by reasonable medical judgment. Individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interest.

Collaborative Institutional Training Initiative (CITI): An internet-based set of educational modules on the protection of human participants in research. It is sponsored by a consortium of IRB professionals and investigators from universities and medical schools across the country and is administered by the University of Miami.

Continuing Non-compliance: A pattern of repeated actions or omissions by an Investigator that indicates a deficiency in his or her ability or willingness to comply with federal and state regulations, Department IRB policy, or determinations or requirements of the Department IRB.

Continuing Review: Periodic review of research activities necessary to determine whether the risk- benefit ratio has changed, whether there are unanticipated findings involving risks to participants or others, and whether any new information regarding the risks and benefits

should be provided to participants.

Continuous Quality Improvement (CQI): A methodology to improve existing processes by identifying the root cause of a problem, developing and implementing an action plan, and evaluating the outcome to assure problem resolution. The PDSA cycle incorporates the following process: Plan, Do, Study, Act.

Data and Safety Monitor (DSM): An individual assigned to conduct interim monitoring of accumulating data from research activities to ensure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The individual should have expertise in the relevant medical, ethical, safety, and scientific issues.

Data and Safety Monitoring Board (DSMB): A formally appointed independent group consisting of at least three members assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. Membership should include individuals with expertise in the relevant field of study, statistics, and research study design.

Data and Safety Monitoring Committee (DSMC): Another term for DSMB.

Data and Safety Monitoring Plan (DSMP): Describes how the Investigator plans to oversee the safety and welfare of research participants and how adverse events will be characterized and reported. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the study.

Dead Fetus: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).

Delivery: Complete separation of the fetus from the woman by expulsion or extraction or any other means.

Department of Health and Human Services (DHHS): The United States government agency responsible for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.

Designed: Planned or conducted to apply to phenomena outside the observed data, or to contribute to such understanding.

Directed Audit: Audits of IRB-approved research that may be conducted by the IRB staff, Department Inspector General, or an outside third party to assess the Investigator's compliance with federal regulations, state and local laws, and Department IRB policies and procedures. These audits are generally conducted in response to concern(s) identified by an IRB committee, an external source (e.g., OHRP, FDA, or sponsor), or an internal source (e.g., participant, family member, or Department personnel, including IRB staff).

Dissent: An individual's verbal and/or non-verbal communication objecting to participation in research or research activities.

Document: A physical or electronic record submitted to the Department IRB.

Emergency Research: The use of an unapproved test article (drug, agent, biologic, or device) on 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.

Emergency Treatment IDE: An FDA mechanism providing eligible participants with investigational devices for the treatment of an immediate serious or life-threatening illness for

which there are no satisfactory alternatives.

Emergency Treatment IND: An FDA mechanism providing eligible participants with investigational drugs, agents, or biologics for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

Exempt Review: Studies determined to meet the exempt criteria as defined by the federal regulations. Exempt studies do not require periodic review unless a change in the project is planned.

Expired Study: When continuing review of the research does not occur prior to the end of the approval period specified by the IRB. IRB approval expires automatically and requires no decision, determination, or action by the IRB. No activities can occur after midnight on the last approval date specified on the approval letter and the informed consent document. Expirations are not suspensions or terminations of IRB approval, or administrative holds. Allowing a protocol to expire is considered non-compliance.

Family Member: Any one of the following legally competent persons: spouse; children (including adopted children); brothers, sisters, spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the participant is the equivalent of a family relationship.

Fetus: The product of conception from implantation until delivery.

Financial interest related to the research: Financial interest in the sponsor, product or service being tested, or a competitor of the sponsor.

Finder's Fee: Compensation of any type (cash, office or medical supplies, educational stipends, gift certificates, priority in authorship listings, travel reimbursement, or anything else of value) made in exchange for referral or recruitment of a participant. Such payments generally are made to residents, physicians, nurses, or others in a position to identify potential participants that might qualify for enrollment in a study. The fee is paid only for participants who are enrolled. Any financial interest related to research must be reported.

Food and Drug Administration (FDA): The United States government office under the Department of Health and Human Services (DHHS) responsible for implementing regulations governing drugs, devices, and biologics.

Generalizable Knowledge: Observations, findings, information, or results that have been demonstrated with enough confidence and significance to confirm or alter the consensus within the professional norms of a community or discipline.

Human Fetal Tissue: Tissue or cells obtained from a dead human embryo or dead fetus after a spontaneous or induced abortion, or after a stillbirth.

Human Participant: As defined by DHHS regulations, a living individual about whom an Investigator (whether professional or student) conducting research obtains data through intervention or interaction with an individual or identifiable private information.

Human Subject: As defined by FDA regulations, an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. He or she may be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used.

Human Subject Research: Any activity that either meets the DDHHS definition of "research" and involves "human subjects" (as defined by DHHS regulations) or meets the FDA definition of "research" and involves "human subjects" (as defined by FDA regulations).

Humanitarian Use Device (HUD): A device that is intended to benefit patients by treating or

diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.

Humanitarian Use Device Exemption (HDE): FDA approval for a physician to use a HUD in clinical treatment or as the subject of a clinical investigation.

Immediate Family Member: Spouse, domestic partner, children, and dependents.

Individual Conflict of Interest: A circumstance where an individual substantially involved with the research has a direct or predictable effect on a financial interest of the spouse, minor child, or organization in which the individual serves as an officer, trustee, partner, or employee.

Informed Consent: An individual's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.

Institutional Review Board (IRB): A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in research.

Interaction: Communication or interpersonal contact between an Investigator or his/her research staff and the research participant or his or her private identifiable information.

Intervention: Physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects' environment that are performed for research purposes.

Investigation: An inquiry, examination, or search for facts, usually involving the formulation or testing of a hypothesis.

Investigational Agents: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. Includes: products that already have a marketing authorization but are used or assembled (formulated or packaged) in a way different from the approved form; products used for an unapproved indication; or products used to gain further information about an approved use.

Investigational Device: A healthcare product that is either (a) not approved for marketing in the U.S. or

(b) is approved for marketing but is being clinically evaluated for a new intended use (e.g., a medical device designed to evaluate the effectiveness and/or safety of the device).

Investigational Device Exemption (IDE): Permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations on the device.

Investigational Drugs/Investigational Biologics (Test Articles): A new drug/agent or biologic that is used in a clinical investigation. Includes biological products that are used in vitro for diagnostic purposes; products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; and products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).

Investigational New Drug (IND): Permission that a new drug, agent, or biologic is safe and effective for a specific use and may be used in humans prior to FDA review of clinical data The FDA permission is evidenced by the assignment of an IND number or the granting of an IND exemption.

IRB Member: Individual appointed by the institutional official to serve as a voting member on a designated IRB who meets the requirements in terms of expertise or experience, or community representation; membership counts toward a quorum.

IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution and is designated to do so through an approved Assurance with the Office for Human Research Protections (OHRP). A Memorandum of Understanding (MOU) is required, designating the relationship, for Department to serve as the IRB of Record.

Joint Commission on Accreditation of Healthcare Organizations (JCAHO): A national accrediting body for hospitals and other healthcare delivery organizations.

Key Research Personnel: The Principal Investigator and all individuals responsible for the design or conduct of the study.

Guardian: Defined by DHHS as an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the research. LARs may not give permission for research involving children unless they are guardians.

Major Amendment: A proposed change in research-related activities that is not a Minor Amendment.

Memorandum of Understanding (MOU): A formal agreement between Department and another institution that identifies the Department IRB as the IRB of record for that institution.

Minimal Risk: 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. For research involving prisoners, minimal risk means the probability and magnitude of physical or psychological harm that is normally encountered in daily life, or in the routine medical, dental, or psychological examinations of healthy persons.

Minor Amendment: A proposed change in research-related activities that does not materially affect an assessment of the risks and benefits of the study or substantially alter the specific aims or design of the study and all the added procedures that qualify for review under expedited review per 21 CFR 50.110 and 45 CFR 46.110.

Neonate: A newborn

Non-compliance: Failure to comply with federal and state regulations, Department IRB policy, or the determinations or requirements of the Department IRB. Examples include conducting research without prior IRB approval; protocol deviations; making changes to the research protocol or study design without prior approval, except when necessary to eliminate immediate hazard to participants; and releasing confidential Department data for research without prior IRB approval.

Non-Human Subject Research: Any activity determined by the Institution to not represent “Human Subject Research.”

Non-significant Risk (NSR) Device Study: A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants.

Nonviable Neonate: A neonate after delivery that, although living, is not viable.

Not-Identifiable Information: The identity of the participant is not (or may not) readily be ascertained by the Investigator or associated with the information.

Not Less Than Once Per Year: All research proposals, with the exception of exempt

proposals, must receive IRB continuing review at a minimum of once every year, per federal regulations. There are no exceptions or grace periods allowed.

Office for Human Research Protections (OHRP): The U.S. government office under the Department of Health and Human Services (DHHS) responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.

Office of Public Health Research: The office responsible for research and human research protections at Department.

Parent: A child's biological or adoptive parent.

Pass-through funding: When Department receives support directly from federal agencies for non-exempt research and all research activities are conducted by community-based organizations or Department partners. For example, the CDC may provide research funding through Department to a community-based organization. This activity requires IRB review, even if the activity is conducted solely by Department agents or contractors.

Periodic Compliance Review: Random assessments of Department IRB-approved human research studies, including site visits, that may be conducted by internal or external compliance teams. Internal compliance teams monitor adherence to federal regulations, state and local laws, and Department IRB policies and procedures. Local compliance teams also monitor adherence to the study protocol, accurate documentation, reporting of study-related activities, and evaluation/observation of the informed consent process.

Permission: The agreement of parents or legal guardians allowing their child or ward to participate in research.

Policy: A statement defining a plan, guiding principle, or course of action intended to determine decisions, actions, and procedures as set forth by Department, the Office of Public Health Research, and the IRB as it pertains to Department's Human Research Protection Program (HRPP).

Pregnancy: The period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery.

Prisoner: 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. Probation and parole are treated the same but are usually NOT considered incarceration. Mental and substance abuse facilities are considered incarceration if someone is mandated to attend a program in lieu of jail or prison; however, an individual in such a facility is NOT considered incarcerated if he or she voluntarily commit themselves.

Privacy: Freedom from unauthorized intrusion or the state of being left alone and able to keep certain

personal information to oneself and control other's access to that information.

Private Information: Information disclosed in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information which has been provided for specific purposes that the individual can reasonably expect will not be made public (e.g., a medical record).

Private information must be individually identifiable to be considered research involving human participants. This may include identifiable private information obtained from a primary participant about a third party.

Procedure: A statement defining the internal process by which Department policies are administered by Departments Human Research Protection Program (HRPP).

Prospective: Research utilizing human participants' specimens/data that will be collected after IRB approval.

Public Meeting: The IRB is not exempt by the Florida Legislature from the requirements of public meetings. Members of the public may attend and observe IRB meetings.

Quality Assurance Reviews: May be conducted by internal or external personnel to verify that the application system is accurate, complete, and conforms to IRB policy and procedure.

Radiation Exposure: The quantity used to indicate the amount of ionization in the air produced by X- or gamma-ray radiation while conducting radiological procedures.

Radioactive Drug: Any substance defined as a drug under the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Includes any non-radioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products." Drugs, such as carbon- containing compounds or potassium-containing salts with trace quantities of naturally occurring radionuclides, are not considered radioactive drugs.

Radiological Procedure: Any procedure involving radiation (e.g., X-ray) or a radioactive agent (e.g., a radionuclide).

Recruitment: Seeking individuals to enroll or participate in a research project.

Related: An adverse event is "related to the research" if the Principal Investigator determines that it was more likely than not to be caused by the research procedures or if the event affects the rights and welfare of current participants.

Repository: A storage site or mechanism by which identifiable human tissue, blood, genetic material, or data are stored or archived for research by multiple investigators for multiple research projects.

Research: As defined by FDA regulations, any experiment that involves a test article and one or more human subjects. Must either meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Food, Drugs, and Cosmetics Act, or produce results that are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. For research involving drugs, an experiment is any use of a drug except for the use of a marketed drug during medical practice. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous.

- "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 during 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 activity that evaluates the safety or effectiveness of a medical device. [21 CFR 812.2(a)]
- "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)]

Research: As defined by DHHS regulations, any systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

Research Misconduct: Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results, or any attempt to unduly influence an IRB member or IRB staff.

Research Payments: Cash and non-cash payments for reimbursement of time and expenses associated with participation in research activities.

Retrospective: Research utilizing human participants' specimens/data that were previously collected (e.g., on the shelf) before the research was approved by the IRB.

Roster: Current listing of members appointed to serve on a designated IRB.

Secretary: The Secretary of Health and Human Services (DHHS) and any other officer or employee of DHHS to whom authority has been delegated.

Sensitive Information: Includes, but is not limited to, information relating to sexual attitudes, preferences, or practices; the use of alcohol, drugs, or other addictive products; illegal conduct. information, that if released, might be damaging to an individual's financial standing, employability, or reputation within the community, or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information.

Serious Non-compliance: An action or omission taken by an Investigator that any other reasonable Investigator would have foreseen as compromising the rights and welfare of, or harms, a participant.

Short Form Consent: A written informed consent document that summarizes the required elements of informed consent. Presented orally to the participant or his or her legally authorized representative

Significant Risk (SR) Device Study: A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life or otherwise prevents impairment of human health; 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or 4) presents a potential for serious risk to the health, safety, or welfare of a participant.

Sponsor-Imposed Suspension: A determination made by the sponsor of the study to place specific research activities on hold. May be made for interim data analysis; inadequate drug availability; response to a Data Safety Monitoring Board report/recommendation; or a pre-planned stopping point.

Standard Review: Studies reviewed by the full convened IRB committee with a recorded vote and corresponding minutes to document the discussion.

Suspension of Research: All interventions or interactions with living individuals cease until the IRB determines research may re-commence, except when the suspension of study drugs or other interventions would place participants at risk.

Systematic: Conducted according to a plan, organized method, or procedure for testing or formulating a question or hypothesis and interpreting results.

Termination of Research: All interventions or interactions with living individuals cease. If

terminating research would place participants at risk of harm, the IRB will work with the researcher to transition patients to a new study or take other appropriate action.

Test Article: Any drug (including a biological product for human use), human medical device, food or color additive, electronic product, or any other article subject to FDA regulation.

Third Party: Any person or vendor (external to Department) who receives payment for providing research- related services and/or products.

Treatment IDE: An FDA mechanism for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.

Unexpected: An adverse event is "unexpected" when its specificity and severity are not accurately reflected in the informed consent document.

Unanticipated Adverse Device Effect: Any serious adverse effect on health or safety or any life- threatening problem or death associated with a device that was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application). Also includes other unanticipated serious problems associated with a device that relates to the rights, safety, or welfare of participants.

Unanticipated Problem Involving Risks to Participants or Others: Any problem, event, or information, as determined by the Department that (1) was unforeseen, (2) indicates that participants or others are at increased risk of harm, and (3) is related to the research.

Viable: As it pertains to the neonate; being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.