CAPE FEAR VALLEY HEALTH SYSTEM
Policy – Procedure

Title: Human Research Protection Program Plan	**Current Effective Date:** 02/29/2024

Scope: Throughout this document "Institution" refers to Cape Fear Valley Health System.

Purpose:

The purpose of this policy is to describe the mission, scope, authority, and components of the Human Research Protection Program (HRPP) for ensuring the rights and welfare of all human subjects participating in research at the Institution are protected. The requirements of the HRPP apply to all research involving human subjects conduct on behalf of the Institution, irrespective of funding.

Policies and procedures for the HRPP are available on the IRB website. Any changes in these policies and procedures are communicated to all key individuals using various mechanisms such as: email, live training, and announcement on the IRB website.

Audience: All CFVHS Medical Staff, Allied Health Professionals, Staff, Residents and Students, Employees, and agents

Departments: Research, Human research Protection Program (HRPP), Institutional Review Board (IRB)

Keywords: Research, Human Subjects, Institutional Review Board (IRB)

Definitions:
Agent refers to individuals who (1) act on behalf of the institution; (2) exercise institutional authority or responsibility; or (3) perform institutionally designed activities. Examples of "employees and agents" include faculty, physicians, hospitalists, staff, students, contractors, volunteers, community IRB members, CFVHS faculty/physicians who are conducting research at another institution, a faculty/physician member performing research while on sabbatical or a resident/student conducting research at another institution as part of a course requirement.

Clinical Trial/Investigation [45 CFR 46.102(b), 21 CFR 50.3(c)] means a research project in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Cooperative Research [45 CFR 46.114] are human research projects covered by a signatory agency of the revised Common Rule (45 CFR 46) that involve more than one institution and/or site participating in the same research protocol, where each site completes a portion or portions of procedures.

Engaged in human subjects research as defined by the Department of Health and Human Services guidance document states that in general an institution is considered engaged in a

particular non-exempt human subjects research project when its employees or agents, for the purposes of the research project, obtain:

1. Data about the subjects of the research through intervention or interaction with them.
2. Identifiable private information about the subjects of the research.
3. Informed consent of human subjects for the research.

The Institution follows OHRP guidance on "Engagement of Institutions in Research" to apply this definition and exceptions to this definition.

Human Research means any activity that either:

- Is "Research" as defined by DHHS *and* involves "Human Subjects" as defined by DHHS; or
- Is "Research" as defined by USFDA *and* involves "Human Subjects" as defined by USFDA.

Human Subjects has reference to two definitions defined by federal agencies.

1. Department of Health and Human Services [45 CFR 46.102(e)] defines human subject as a living individual about whom the investigator conducting research:
    a. Obtains information or biospecimens through Intervention or Interaction with the individual and uses, studies, or analyzes the information or biospecimens; or
    b. Obtains, uses, studies, analyzes, studies, or generates identifiable private information or identifiable biospecimens.

    For the purpose of this definition:
    - **Intervention** means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
    - **Interaction** means communication or interpersonal contact between investigator and subject.
    - **Private Information** means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and the individual can reasonably expect will not be made public (for example, a medical record).
    - **Identifiable Private Information** means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
    - **Identifiable Biospecimens** means biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

2. Food and Drug Administration (FDA) [21 CFR 50.3(g)] defines human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Investigator [21 CFR 50.3(d)] is the individual responsible for the conduct of the human research at one or more sites. If the human research is conducted by a team of individuals at a site, the investigator is the responsible leader of the ream and may be call the principal investigator. Conduct of human subjects research includes activities such as:

1. Obtaining information about living individuals by intervening or interacting with them for research purposes.
2. Obtaining identifiable private information about living individuals for research purposes.
3. Obtaining voluntary informed consent of individuals to be subjects in research.
4. Studying, interpreting, or analyzing identifiable private information or data for research purposes.

Institutional Review Board (IRB) is the Committee authorized to review, approve, require modifications (to secure approval), or disapprove all human subject research at the Institution in accordance with applicable federal, state, and local regulatory requirements, as well as Institutional policies and procedures.

Multisite Study means non-exempt human research funded by the National Institutes of Health (NIH) involving more than one institution and/or site participating in the same research protocol, with each site completing all research activities outline in the protocol.

Research as defined by the Department of Health and Human Services [45 CFR 46.102(d)] means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Research is considered synonymous with Clinical Investigation as defined by the FDA. The following activities are considered not research by DHHS:

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, which focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.
    - Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
    - Including trends, signals, risk factors, patterns in diseases, or increased in injuries from using consumer products.

  - Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

Research as defined by the Food and Drug Administration [21 CFR 50.3(c)] means any experiment that involves a test article and one or more human participants, and that meets any one of the following:

- 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 meaning any use of a drug other than the use of an approved drug in the course of medical practice.
- Must meets the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device, OR
- Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Single IRB (sIRB) is the selected IRB of record that conducts the ethical review for each site participating in a Multisite or Cooperative Research study.

Policy:

The mission of Human Research Protection Program is to protect the rights, dignity, welfare, and privacy of the human subjects in all research conducted on behalf of the Institution (regardless of funding) by adhering to the principles outlined in the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research report entitled, *Ethical Principles and Guidelines for the Protection of Human Participants of Research* (*The Belmont Report*) and the regulations of the Department of Health and Human Services (DHHS), Food and Drug Administration (FDA), and other applicable agencies. The HRPP is committed to advancing the ethical treatment of research participants, promoting the responsible conduct of research, and ensuring and protecting the rights of every human research volunteer. The HRPP achieves its mission by:

- Ensuring that all research involving human subjects receives required approvals before research activities are initiated.
- Creating an environment at the Institution of respect for, and understanding of, the rights and welfare of research participants.
- Providing profession administrative support to the Institution's Institutional Review Board (IRB).
- Educating the Institutional community about federal, state, and Institutional research regulations, policies, and practice pertaining to human subjects protection.
- Conducting activities to enhance compliance with the requirements of the HRPP.

Applicability
Human subject research under the auspices of the Institution includes research:

- Conducted at this Institution
- Conducted by or under the direction of any employee or agent of this Institution in connection with their Institutional responsibilities
- Conducted by or under the direction of any employee or agent of this Institution using any property or facility of this Institution, and/or
- Conducted by or under the direction of any employee or agent of this Institution in collaboration with external researchers

Ethical Requirements
The Institutional HRPP adheres to the ethical principles and guidelines for the protection of research participants summarized in the *Belmont Report*, complies with federal regulations, guidance, and state laws related to human subjects protection, and for federally-sponsored research maintains a Federalwide Assurance of Compliance (FWA) with the Office for Human Research Protections (OHRP). The ethical and regulatory requirements of the HRPP apply to all research involving humans subjects conduct on behalf of the Institution and to all individuals and components of the HRPP.

The primary ethical principles guiding research for which the HRPP has overall responsibility, including protocols that are "exempt" from federal regulations pertaining to research involving human subjects, are provided in the *Belmont Report*.

Three basic principles of the *Belmont Report* are central to the ethics of research involving human subjects and guide the IRB in ensuring that the rights and welfare of research participants are protected. These are:

- **Respect for Persons** – applied by obtaining informed consent, and considering privacy, confidentiality, and additional protections for vulnerable populations.
- **Beneficence** – applied such that the potential benefits of research are maximized, and possible risks are minimized to the persons involved.
- **Justice** – evidenced in the equitable selections of research subjects.

Regulatory Requirements
For all human subject research conducted, funded, or otherwise subject to regulations by a federal department or agency who is a signatory of the Common Rule, the Institution applies the regulations of that agency relevant to the protection of human subjects, including, but not limited to:

- Common Rule, 45 CFR 46, Protection of Human Subjects
- 21 CFR 56, Institutional Review Boards
- 21 CFR Part 50, Protection of Human Subjects
- 21 CFR 312, Investigational New Drug Application
- 21 CFR 812, Investigational Device Exempts
- 34 CFR 50 and 56, Disability and Rehabilitation Research
- 34 CFR 98, Protection of Pupil Rights Amendment (PPRA); Student Rights in Research, Experimental Programs, and Testing

- 34 CFR 99, Family Educational Rights and Privacy Act (FERPA)
- 45 CFR 160 and 164, Standards for Privacy of Individually Identifiable Health Information; Security Standards for the Protection of Electronic Protected Health Information (HIPAA Privacy and Security Rules)
- Additional federal requirements, as applicable (e.g., DOD Directive 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DOD-Supported Research
- Applicable North Carolina laws.

Unregulated research must also be conducted in accordance with this policy.

All human research must undergo review by the Institutional Review Board (IRB) or the IRB Office, whether internal or external to the Institution. Activities that do not meet the definition of human research or meet the requirements of exempt research under the federal regulations do not require review and approval by the Institutional IRB and do not have to be reviewed by the IRB Committee unless there is a question regarding whether the activity is research.

The Institution's IRB approves research according to applicable federal and local law for the research conducted within the jurisdiction where the Institution resides. If the applicable law is inconsistent, the IRB will apply the most protective of the applicable laws.

The Institution's Legal Services assists the IRB Office in resolving conflicts among applicable laws and assists the IRB Office in determining who meets the definition of "legally authorized representative," "children" and "guardian" when human research is conducted in jurisdictions not covered by policies and procedures.

Any questions about whether an activity meets the regulatory definitions of human research should be referred to the IRB Office, who will provide a determination.

Other Requirements
When reviewing research that involves community-based research, the IRB obtains relevant expert consultation or training, as needed.

Institutional human research policies, guidelines, and operating procedures are intended to comply with applicable federal regulations, guidance, and state laws governing human subjects are followed for the review of all research regardless of whether the research is conducted domestically or in another country, including:

- Confirming the qualifications of investigators for conducting the research,
- Conducting initial review, continuing review (when applicable), and review of modifications to previously approved research,
- Post-approval monitoring, when necessary, handling of complaints, non-compliance and unanticipated problems involving risks to participants or others,
- Consent process and other language issue,
- Ensuring all necessary approvals are met,
- Coordination and communication with other IRBs.

For clinical trials, the Institution commits to apply the "International Conference on Harmonization – Good Clinical Practice E6" (ICH-GCP), when required by clinical trials sponsors.

The Institution prohibits payments to professionals in exchange for referrals of potential participants ("finder's fees") and payments designed to accelerate recruitment that are tied to the rate or timing of enrollment ("bonus payments.")

The Institution utilizes the IRB to review and approve the use of Humanitarian Use Device (HUD) before it can be used at a facility for clinical care (with the exception of emergency use).

The Institution utilizes the IRB to review and approve Expanded Access Use before it can be used at a facility for clinical care (with the exception of emergency use).

Federalwide Assurance of Compliance

The Institution maintains and supports a Federalwide Assurance of Compliance (FWA) with the OHRP that outlines processed by which the Institution protects research participants in federally sponsored research. The Cape Fear Valley Health System IRB #1 (00002987) is designed under the FWA for review of human subjects research. Additionally, in specific circumstances, the Institution designates and relies on external IRBs for the review of Institutional research involving human subjects. The Institution, in special circumstances, serves as the IRB of Record for external institutions or organizations.

Human Research Protection Program Oversight Components

Role of the Institutional Official (IO)

- The Institutional Official (IO) is the individual who is legally authorized to act for the Institution and, on behalf of the Institution, obligates the Institution to the Terms of the Assurance.
- The IO is responsible for ensuring that the HRPP functions effectively and the Institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO represents the Institution named in the FWA;
- The IO should be an individual of sufficient rank who as the authority to ensure that all obligations of the HRPP carried out effectively and efficiently. At CFVHS the Chief Medical Officer (CMO) is the person responsible for the legal entity that constitutes the Institution conducting research. The IO is at a level of responsibility sufficient to allow authorization of necessary administrative or legal action should it be required.

General administrative obligations and responsibilities of the IO

- Signatory authority for the FWA;
- Completing recommended Assurance training for the IO;
- Designating one or more IRBs that will review research covered by the Institution's FWA;
- "Setting the tone" by promoting an institutional culture of respect and conscience, so the ethical conduct of human subjects research is supported at the highest levels of the organization;

- Ensuring the IRB functions independently and its chair and members have direct access to the IO for appeal if they experience undue influence or if they have concerns about the function of the IRB;
- Ensuring adequate resources, including funds, space, and personnel are provided to support the operation of the HRPP;
- Appointing, suspending, or terminating the IRB membership of an individual;
- Appointing, suspending, or terminating the IRB chair or co-chair;
- Reviewing and signing memoranda of understanding and cooperative agreements between the Institution and other organizations, including those that establish reliance on IRBs of record for collaborative research (e.g., IRB Authorization Agreements and Individual Investigator Agreements);
- In accordance with 45 CFR 46.108, the IO will ensure the IRB has adequate meeting space and sufficient staff to support the IRB's review and record keeping duties. The resources provided for the IRB and HRPP office will be reviewed during the annual budget review process;
- By written memo, the IO may delegate certain responsibilities and authorities to appropriately trained individuals.

HRPP/IRB Office

The HRPP Office, which is responsible for supporting the administration of the IRB, works with the IRB and Other Institutional units to ensure compliance with the HRPP.

The HRPP/IRB Administrator and/or the IRB Office staff have the responsibility to:

- Developing, managing, and evaluating policies and procedures to ensure compliance with applicable state laws and federal regulations governing research. This includes monitoring changes in regulations and policies relating to human research protection;
- Overseeing all aspects of the human research protection program, including the HRPP office and the Institutional IRB(s);
- Day-to-day responsibility for the operation of the HRPP/IRB office;
- Advising the IO on key matters regarding research at the Institution;
- Implementing the Institution's policies, as they related to the conduct of research with human subjects;
- Submitting, implementing, and maintaining an approved FWA with the Office of Human Research Protection (OHRP);
- Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program;
- Developing raining requirements for IRB members, HRPP staff, and investigators;
- Serving as the primary contact at the Institution for OHRP and other federal regulatory agencies;
- Working closely with the IRB Chair(s) on the development of policy and procedures for review and approval by the IO;
- Working closely with the IRB Chair(s) in the preparation of, and follow up to, each convened meeting;
- Providing regulatory guidance to the IRB Chair(s) and members;

- Responsible for all aspects of processing protocols involving human subjects and providing administrative and clerical support to the IRB Chair as well as scheduling and coordinating all IRB functions;
- Responsible for record retention related to the program which includes maintaining complete IRB files, records of all research protocols, IRB correspondence, as well as research credentialing records of investigator and research staff.

IRB

All non-exempt human research must be approved by the Institutional IRB designated by the Institutional Official (IO). Officials of Institution may not approve human research that has not been approved by the IRB.

The IRB must follow applicable HRPP policies and procedures and has the authority/responsibility to:

- Determine whether an activity is human research;
- Approve, require modifications to secure approval, or disapprove all research activities overseen and conducted by the agents of the organization;
- Review the research in accordance with established policies and procedures to determine that research is ethically justifiable, according to all applicable laws, including initial review, continuing review (when applicable), review of modifications to previously approved research and unanticipated problems involving risks to subjects or others;
- Suspend or terminate approval of human research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants;
- Observe, or have a third party observe, the consent process and the conduct of the human research, and request audits of research reviewed;
- Evaluate financial interest of investigators and research staff and have the final authority to decide whether the financial interest and management plan, if any, allow the human research to be approved;
- Serve as the Privacy Board, as applicable, to fulfill the requirements of the HIPAA Privacy Rule for use or disclosure of protected health information for research purposes for non-exempt research;
- Report to the Institutional Official or designee any concern about attempts to unduly influence the independence of the IRB.

The Institutional IRB may serve as Single IRB or IRB of Record for another entity, organization, or individual investigator. When CFVHS provides IRB review for other organizations or individual investigators, the HRPP will follow established policies and procedures to ensure that the composition of the IRB is appropriate to review the research and will comply with appliable laws of the relying site.

CFVHS may also rely upon external IRBs of an AAHRPP accredited organization or of an organization that has been appropriately vetted by CFVHS. CFVHS will comply with the determinations of the reviewing IRB, follow reporting and conflict of interest disclosure requirements as specified in the authorization agreement, conduct monitoring, identify appropriate contact person, ensure researchers have appropriate qualifications and provide local context information (and any relevant updates) to the external IRB.

Investigators and Research Staff
The investigator has the ultimate responsibility for protecting the human subjects who participate in their research projects. The investigator is expected to abide by the highest ethical standards in the conduct and oversight of research and for developing ta protocol that incorporates the principles of the *Belmont Report*. Investigators are expected to conduct research in accordance with the approved research protocol and to oversee all aspects of the research by providing training for and supervision of all project team members.

In addition to complying with all the policies and standards of the governing regulatory bodies, the investigator must comply with Institutional and administrative requirements for conducting research. The investigator is responsible for obtaining all required approvals prior to initiating research.

Other Components of the HRPP

Legal Services provides the IRB and other components of the HRPP with counsel on an as needed basis, primarily on matters related to state laws, cooperative agreements, noncompliance, conflicts of interest, and contractual issues in human subjects research.

Radiation Safety Committee has the following responsibilities:

- Review an oversight of human subjects research involving radiation for research purposes (including x-rays, nuclear medicine studies, DEXA scans, CT scans);
- Oversight of an ensuring compliance with the radiation safety program;
- Establishment of institutional policies consistent with North Carolina Department of Health and federal regulations.

Corporate Compliance
The Institutional policies for Conflict of Interest and Conflict of Interest in Research promotes objectivity in research by establishing expectations and disclosure requirements to ensure the design, conduct and reporting of research will not be biased by Significant Financial Interest of an individual. Communication between the HRPP and Corporate Compliance is facilitated through the following mechanisms:

- Application that are received by the HRPP which include a disclosure of a conflict of interest are forwarded to Chief Legal Officer for review. The protocol file is accessible to the IO while under review and after it has been approved. IRB approval may be issued prior to a determination from the Chief Legal Officer if the HRPP has reviewed the relevant details and finds the matter is appropriately managed within the submitted protocol and, if applicable, the consent process.
- The HRPP Administrator is alerted to disclosures by Human Resources when they involve, or appear to involve, research with human subjects. Any resulting management plan is accessible to the HRPP and IRB members.
- The Corporate Compliance and the Research Director provides regular reports of all managed conflicts. The HRPP Administrator makes this report available to all HRPP staff and maintains a mechanism for reviewing the report against new submissions.

In accordance with Institutional policy provides advice to the Institutional research community to maximize compliance with statutory and regulatory requirements; regularly reviews the

compliance program to identify areas of risk and works with senior administration to secure solutions that will manage or eliminate threats to research integrity; and provides an education and outreach program to promote the responsible conduct of research.

Financial Office
The Corporate Director of Finance and Administration, with the assistance of Legal Services, reviews and approves all research proposals and agreement with external sponsors. This Institutional review ensures all terms of the award are in compliance with Institutional policies.

For all externally funded research, the HRPP Office will include Corporate Director of Finance and Administration on notices of exemption approval, expiration, suspension, termination, or closure sent to investigators.

Education and Training
Education and training requirements and resources are made available to the human research community via the IRB website. To maintain awareness of HRPP policies and procedures, the IRB Office communicates new information, revised materials, and opportunities for continuing education to the human research community by way of various email list-serve groups target to appropriate audiences.

IRB members, IRB Office staff, and others involved in the review of human research must complete the required initial and continuing human research training.

Investigators and research staff must complete the initial and continuing training described in the *IRB Investigator Manual and HRPP/IRB Policies and Procedures Manual*.

Reporting and Management of Concerns
Any person having concerns about the conduct of human research at Cape Fear Valley Health System is strongly encouraged to report incident so involving perceived noncompliance. Please see *CFVH Policy: Human Research Protection Program Compliance* for various reporting mechanisms.

Questions and For Additional Information
For questions, requests for additional information from the IRB Office and/or to provide feedback relating to the HRPP, please contact the IRB Office below:

Cape Fear Valley Health System
Medical Education - Research/IRB Office:
1638 Owen Drive
Fayetteville, NC 28304
910-615-5839

Monitoring and Auditing

In order to monitor and ensure compliance, internal or external auditors who have expertise in federal and state statutes, regulations and institutional requirements may conduct periodic audits. Audits will focus on areas of concern that have been identified by an entity, i.e., federal, state, local or institutional. Random audits may also be conducted.

Disciplinary Actions

The IO may place limitations or conductions on the investigator's or research staff's privilege to conduct human research whenever in the opinion of the IO such actions are required to maintain the HRPP.

Revision and Maintenance

The IRB office is responsible for maintaining and updating this policy annually. All new or revised information will be placed on the IRB website and updates will be communicated to the research community electronically.

Related Documents/Policies:

CFVH Policy: IRB Authority and Responsibilities
CFVH Policy: Human Research Protection Program Compliance
CFVH Policy: Conflict of Interest
CFVH Policy: Financial Conflict of Interest in Research
CFVHS HRPP/IRB Policies and Procedures Manual
CFVHS IRB Investigator's Manual

References:

The Belmont Report
45 CFR 46 (The 2018 Common Rule)
21 CFR 50
21 CFR 56
Final NIH Policy on the Use of a Single Institutional Review Board for Multi-site Research
OHRP Guidance: Engagement of Institutions in Human Subjects Research