



Title	UNC-Chapel Hill Human Research Protection Program		
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1 Purpose

The University of North Carolina at Chapel Hill (UNC-Chapel Hill) fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the Organization. The review and conduct of research, actions by the Organization will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (referred to as the Belmont Report). The actions of Organization will also conform to all applicable federal, state, and local laws and regulations. In order to fulfill this policy, the Organization has established a Human Research Protection Program (HRPP). The UNC-Chapel Hill HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices. The research may be externally funded, funded from internal sources, or conducted without direct funding. The UNC-Chapel Hill HRPP is administered by the Office of Human Research Ethics (OHRE)

2 UNC Chapel Hill HRPP

2.1 HRPP Mission

The mission of the HRPP is to:

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- Provide guidance and support to the research community in the conduct of research with human subjects;
- Assist the research community in ensuring compliance with relevant regulations;
- To provide timely and high quality education, review and monitoring of human research projects; and
- To facilitate excellence in human subjects research.

The HRPP includes mechanisms to:

- Monitor, evaluate and continually improve the protection of human research participants

- Dedicate resources sufficient to do so
- Exercise oversight of research protection
- Educate investigators and research staff about their ethical responsibility to protect research participants
- When appropriate, intervene in research and respond directly to concerns of research participants

2.2 Organizational Authority

The UNC-Chapel Hill Human Research Protection Program operates under the authority of the Organization policy “Human Research Protection Program (HRPP)”. As stated in that policy, the operating procedures in this document “...serve as the governing procedures for the conduct and review of all human research conducted under the auspices of the UNC-Chapel Hill. The HRPP Policy and these operating procedures are made available to all UNC-Chapel Hill investigators and research staff and are posted on the OHRE website (<http://research.unc.edu/offices/human-research-ethics/>).

2.3 Ethical Principles

The UNC-Chapel Hill is committed to conducting research with the highest regard for the welfare of human subjects. With the exception of transnational research, where consideration of alternative ethical principles may apply (see SOP 2001.2), the UNC-Chapel Hill upholds and adheres to the principles of The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979). These principles are:

- 1) Respect for Persons, which involves obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.
- 2) Beneficence, which involves ensuring that possible benefits are maximized and possible risks are minimized to all human subjects.
- 3) Justice, which involves the equitable selection of subjects.

The UNC-Chapel Hill Human Research Protection Program (HRPP), in partnership with its research community, community including researchers and research staff, IRB members and chairs, IRB staff, the organizational official, employees and students, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

2.4 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law and organizational policies. All human subjects research at The UNC-Chapel Hill is conducted in accordance with the policy and regulations found in the Common Rule and 21 CFR 50 and 56. The actions of The UNC-Chapel Hill will also conform to all other applicable federal, state, and

local laws and regulations such as Department of Defense (DoD), Department of Education (DoE), EPA, Family Educational Rights and Privacy Act (FERPA). Research supported by the Department of Defense (DoD) is reviewed and conducted in compliance with part 219 of title 32 CFR, part 980 of title 10 USC, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s).

Research involving the use of Protected Health Information is reviewed and conducted in accordance with the Health Insurance Portability and Accountability Act (HIPAA), 45 CFR Part 160, 162, and 164.

Research involving the use of student educational records is reviewed and conducted in accordance with the Family Educational Rights and Privacy Act (FERPA), 34 CFR Part 99.

2.4.1 International Conference on Harmonization-Good Clinical Practice (ICH-GCP)

The UNC-Chapel Hill voluntarily applies the International Conference on Harmonization (“ICH”) Good Clinical Practices (“GCP”) Guidelines (sometimes referred to as “ICH-GCP” or “E6”) to clinical research conducted under its IRB. In general, UNC-Chapel Hill applies the ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations.)

2.5 Federalwide Assurance (FWA)

The federal regulations require that federally-funded human subject research only be conducted at facilities covered by a Federalwide Assurance (FWA) approved by the DHHS Office for Human Research Protections (OHRP). An FWA is an organization’s assurance to the federal government that human subject research conducted at that site is in compliance with federal regulations pertaining to the protection of human subjects. The FWA designates the Institutional Review Board that will review and oversee the research, specifies the ethical principles under which the research will be conducted, and names the individuals who will be responsible for the proper conduct of the research.

The UNC-Chapel Hill has an OHRP-approved Federalwide Assurance (FWA00004801) and has designated 6 IRB(s) (registered as 538, 539, 1648, 1649, 540, 9770).

In its FWA, The UNC-Chapel Hill has opted to limit the application of the FWA to non-exempt human subject research conducted or supported by DHHS or federal agencies that have adopted the Common Rule.

2.6 Research Under the Auspices of the Organization

Research under the auspices of the organization includes research conducted at this organization, conducted by or under the direction of any employee or agent of this organization (including students) in connection with his or her organizational responsibilities, conducted by or under the direction of any employee or agent of this organization using any property or facility of this organization, or involving the use of this organization's non-public information to identify, contact, or study human subjects.

Employee or Agent. For the purposes of this document, employees or agents refers to individuals who: (1) act on behalf of the organization; (2) exercise organizational authority or responsibility; or (3) perform organizationally designated activities. “Employees and agents” can include staff and students, among others.

Engagement. The Department of Health and Human Services (DHHS) regulations [45 CFR 46.103[a]] require that an institution “engaged” in human subject research conducted or supported by a Federal Department or Agency provide the Office for Human Research Protection (OHRP) with a satisfactory assurance of compliance with the DHHS regulations, unless the research is exempt under 45 CFR 46.101(b). “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; or (3) the informed consent of human subjects for the research.” In general, institutions that receive an award through a grant, contract, or cooperative agreement directly from DHHS for the non-exempt human subjects research (i.e. awardee institutions), are also considered engaged in research even where all activities involving human subjects are carried out by employees or agents of another institution.

FDA regulations are oriented to the responsibilities of IRBs, investigators, and sponsors as opposed to institutions. In general, FDA-regulated research conducted in The UNC-Chapel Hill facilities or by The UNC-Chapel Hill Principal or Sub-Investigators (as defined on the FDA 1572 or delegation of responsibilities log) requires review by an UNC-Chapel Hill designated IRB. Exceptions to this requirement may be granted on a case-by-case basis (e.g., when The UNC-Chapel Hill’s involvement in the research is limited to the provision of a common diagnostic procedure and associated reading or analysis).

The IRB Compliance Manager with the assistance of the OHRE Director and staff as needed, will determine whether the UNC-Chapel Hill is engaged in a particular research study. Investigators and other institutions may not independently determine the UNC-Chapel Hill engagement.

When the UNC-Chapel Hill is engaged in research, the Institutional Official may choose to enter into an agreement to cede review to an external IRB. (See SOP 901 for details on ceding review.)

For additional information on determining engagement please refer to Guidance on Engagement on Institutions in Human Subjects Research, <http://www.hhs.gov/ohrp/policy/engage08.html>

2.7 Written policies and procedures

The UNC-Chapel Hill Standard Operating Policies and Procedures for Human Research Protection detail the policies and regulations governing research with human subjects and the requirements for submitting research proposals for review by the UNC-Chapel Hill IRB. This is not a static document. The policies and procedures are annually reviewed and revised by the OHRE Director or his/her designee. The OHRE Director will approve all revisions of the policies and procedures.

The OHRE Director will keep the Organization research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists. The policies and procedures will be available on the UNC-Chapel Hill IRB website and printed/electronic copies will be available upon request. Changes to the policies and procedures are communicated to investigators and research staff, and IRB members and IRB staff by way of the OHRE website, town hall meetings, email and other methods as appropriate.

2.8 The UNC-Chapel Hill HRPP Structure

The HRPP consists of various individuals and committees such as: the Institutional Official, the Director of the OHRE, the IRB Managers and staff, the IRB(s), the Institutional Biosafety Committee (e.g., for gene transfer research), Radiation Safety Committee, Radioactive Drug Research Committee, Conflict of Interest Committee, Office of Sponsored programs, Legal Counsel, investigators, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the organization in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

The following officials, administrative units and individuals have primary responsibilities for human subject protections:

2.8.1 Institutional Official

The ultimate responsibility of the HRPP resides with the Institutional Official (IO) of the program. The IO is legally authorized to represent the UNC-Chapel Hill. The IO is the signatory of the FWA and assumes the obligations of the FWA. At the UNC-Chapel Hill, the Vice Chancellor for Research is the Institutional Official. The IO is responsible for ensuring that the UNC-Chapel Hill HRPP and IRB(s) have the resources and support necessary to comply with all organizational policies, laws, and regulations that govern human subject research. Such resources include, but are not limited to:

- Staffing commensurate with the size and complexity of the research program;
- Appropriate office space, equipment, materials, and technology;
- Resources for the production, maintenance, and secure storage of HRPP and IRB records;
- Resources for auditing and other compliance activities and investigation of non-compliance;
- Access to legal counsel; and
- Supporting educational opportunities related to human research protections for IRB members, relevant administrative staff, and all members of the research team.
- Support for evaluation of Conflict of Interest; and

- Support for Community Outreach.

The IO conducts and documents an annual review of HRPP and IRB function, requirements, and resources and makes adjustments as needed.

The IO is also responsible for:

- Fostering, supporting and maintaining an organizational culture that supports the ethical conduct of all research involving human subjects and the adherence to regulations and organizational policies;
- Ensuring that the IRB functions independently by, among other mechanisms, being directly accessible to the IRB Chair(s) and members if they experience undue influence or if they have concerns about the function of the IRB;
- Oversight of the Institutional Review Board (IRB);
- Oversight over the conduct of research conducted by all UNC-Chapel Hill investigators;
- Assuring the IRB members are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations;
- Assuring that all investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations; and
- Oversight of the development and implementation of an educational plan for IRB members, staff and investigators.

The IO must complete the OHRP Human Subject Assurance Training and any other appropriate training on human research protections. The OHRE Office will provide ongoing continuing education for the IO concerning human research protections.

The designated IO is made known to employees of the organization and is accessible by phone, email, in person or other methods of communication. The IRB Chairs and OHRE Director have access to the IO for any concerns or issues related to the HRPP.

In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to effectively administer the program. However, the IO is ultimately responsible and is expected to be knowledgeable about all human subject protections responsibilities at the organization.

2.8.2 The Office of Human Research Ethics (OHRE)

The **Office of Human Research Ethics (OHRE)** is responsible for ethical and regulatory oversight of research at UNC-Chapel Hill that involves human subjects. The OHRE administers, supports, and guides the work of the Institutional Review Boards (IRBs) and all related activities.

2.8.3 Director of the OHRE

The Director of the OHRE is selected by and reports to the Institutional Official (IO) through the Associate Vice Chancellor for Research Compliance and is responsible for:

1. Developing, managing and evaluating policies and procedures that ensure compliance with all state, and federal regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protection and overseeing the administration of the IRB.
2. Advising the IO on key matters regarding research at the UNC-Chapel Hill.
3. Implementing the organization's HRPP policies and procedures.
4. Submitting, implementing and maintaining an approved FWA through the IO and the Department of Health and Human Services Office of Human Research Protection (OHRP).
5. Managing the finances of the UNC-Chapel Hill OHRE.
6. Assisting investigators in their efforts to carry out Organization's research mission.
7. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.
8. Developing training requirements as required and as appropriate for investigators, subcommittee members and research staff, and ensuring that training is completed on a timely basis.
9. Serving as the primary contact at the UNC-Chapel Hill for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services, the Food & Drug Administration (FDA) and other federal regulatory agencies.
10. Day-to-day responsibility for the operation of the HRPP office, including supervision of HRPP and IRB staff.
11. Responding to questions regarding the protection of human subjects.
12. Working closely with the Chairs of the IRBs on the development of policy and procedures, as well as organizing and documenting the review process.

2.8.4 OHRE Staff

In addition to the leadership structure described above, other support staff members for the OHRE and IRB include Compliance Manager, Education and Training Manager, QA/QI Manager, Data and Information Manager, IRB Senior Analysts, IRB Analysts, Business System Analysts, Office Manager, and Administrative Assistants. The OHRE and IRB staff for the UNC-Chapel Hill must comply with all ethical standards and practices. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis. The UNC-Chapel Hill OHRE staff reports to the OHRE Director, who has day-to-day responsibilities for its operations.

2.8.5 Institutional Review Board (IRB)

The UNC-Chapel Hill has six on-site IRBs, appointed by the Institutional Official (IO). The IRBs prospectively reviews and makes decisions concerning all human research conducted at the UNC-Chapel Hill facilities, by its employees or agents, or under its auspices unless another IRB

has been designated to do so. The IRB is responsible for the protection of rights and welfare of human research subjects at the UNC-Chapel Hill through review and oversight of safe and ethical research. It discharges this duty by complying with the requirements of federal and state regulations, the FWA, and organizational policies. (See SOP 401 for a detailed discussion of the UNC-Chapel Hill IRB and external IRBs.)

The IRB functions independently of, but in coordination with, other organizational committees and officials. The IRB, however, makes its independent determination whether to approve or disapprove a research plan based upon whether or not human subjects are adequately protected.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the organization. However, those officials may not approve human research that has not been approved or has been disapproved by the IRB.

2.8.6 Counsel's Office

The UNC-Chapel Hill HRPP relies on the Office of University Counsel for the interpretations and applications of state law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research. Legal Counsel will also advise the IRB about other legal issues such as who is a child, and who can serve as a legally authorized representative or guardian. When there are any conflicts between federal or national law and other applicable laws, the Legal Counsel will determine the appropriate resolution.

2.8.7 Department Chairs and/or Organizational Leaders

Department Chairs and organizational leaders are responsible for ensuring that the investigator is qualified by training and experience to conduct the proposed research. For each research study submitted to the UNC-Chapel Hill IRB for approval, the department chair or leader must certify that s/he accepts responsibility for supporting adherence to the federal and state regulations and organizational policies governing the protection of human subjects of research, including applicable organizational credentialing requirements. Department chairs/leaders are responsible for assuring that investigators have the resources required to conduct the research in a way that will protect the right and welfare of participants. Such resources include but are not necessarily limited to personnel, space, equipment and time.

Department chairs/leaders are required to review all proposals before they are submitted to the IRB for review. The signature of the Department chair or leader indicates that (1) the investigator is qualified and has the necessary resources to safely conduct the study, and (2) attests to the scientific merit of this study, which means

- The research uses procedures consistent with sound research design;
- The research design is sound enough to reasonably expect the research to answer its proposed question;

2.8.8 The Investigator

The investigator is ultimately responsible for the protection of the human subjects who participate in research. The investigator is expected to abide by the highest ethical standards when developing a research plan that incorporates the principles of the Belmont Report. The investigator is expected to conduct research in accordance with the IRB approved research plan and to oversee all aspects of the research by providing training and supervision of support staff, including oversight of the informed consent process. All subjects must give informed consent unless the requirement has specifically been waived by the IRB. Investigators must establish and maintain an open line of communication with research subjects within their responsibility. In addition to complying with all applicable policies and standards of regulatory bodies, investigators must comply with organizational and administrative requirements for conducting research. The investigator is responsible for ensuring that all research staff complete all organizational required training as well as training for their responsibilities in any given specific research study. When investigational drugs or devices are used, the investigator is responsible for providing a plan for their storage, security, dispensing, accounting, and disposal.

2.8.9 Other Related Units

2.8.9.1 Office of Sponsored Research and Office of Industry Contracting

Office of Sponsored Research (OSR) and Office of Industry Contracting (OIC) staff review all research agreements with all sponsors including federal, foundation, and non-profit sponsors. This review ensures that all terms of the award (grant or contract) are in compliance with organizational policies. Only designated senior individuals within the Office of Sponsored Research and OIC have the authority to approve research proposals and to execute research agreements on behalf of the organization.

The OSR and OIC ensure that required AAHRPP language (see SOP 1601) is included in contracts. The Office of Sponsored Research and OIC have access to the IRB submission to confirm that the contract and the consent documents are consistent in terms of costs to subjects and who pays in case of injury. OSR, OIC and the IRB office coordinate efforts to ensure that all applicable individuals have filed appropriate COI disclosures to meet investigator COI policies.

When the grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of the UNC-Chapel Hill a subcontract is executed between the UNC-Chapel Hill and the collaborating institution. The subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval. The collaborating institution must also ensure that key personnel involved in human subject research are in compliance with the NIH policy on education in the protection of human research subjects and provide documentation of education of key personnel to the UNC-Chapel Hill, when required.

2.8.9.2 UNC Hospitals Investigational Drug Services Pharmacy

A pharmacist from UNC Hospitals Pharmacy serves on the IRB, allowing the Pharmacy to have complete information about all IRB approved research that takes place at the UNC-Chapel Hill and under its jurisdiction. The Pharmacist member assures that information about all studies involving drugs used in research is shared with both the Pharmacy Staff as appropriate and that the UNC Hospitals Investigational Drug Services and the Pharmacy and Therapeutics Committee is made aware of IRB approved research involving drugs.

The UNC Hospitals Investigational Drug Services Pharmacy is responsible for storing, accounting for, dispensing, and compounding of most investigational drugs used in research, whether conducted inpatient or outpatients. The manufacture/compounding of drug products not commercially available is coordinated by the UNC Hospitals Investigational Drug Services Pharmacy. Waivers from use of the UNC Hospitals Investigational Drug Services Pharmacy for handling investigational drugs will be considered on a case by case basis by the UNC Hospitals Investigational Drug Services Pharmacy, with required information regarding storage, accounting, dispensing etc. provided within the IRB application.

The Pharmacy is available to provide guidance to investigators in relation to the management of the study drugs.

2.8.10 Relationship Among Components

The Research Compliance Steering Committee will meet to ensure a dialogue is maintained between the various compliance entities at the Organization. Membership is comprised of Directors and members from Office of Industry Contracting, Office of University Counsel, Office of Sponsored Research, Office of Human Research Ethics, Conflict of Interest, Office of Clinical Trials, Environmental Health and Safety, Institutional Animal Care and Use Committee, HIPAA Office, Office of Technical Commercialization, and UNC Hospitals Compliance and Research Integrity with the Associate Vice President for Research Compliance as chair. The committee will act in an advisory capacity to the Vice President for Research, monitoring the effectiveness of existing compliance programs, developing new or revised policies as changes in requirements occur, and disseminating updated compliance information to the research community.

2.8.10.1 Study-Specific Coordination

In addition to IRB approval, the Investigator must obtain and document the approval, support, or permission of other individuals and departments or entities impacted by the research as well as approval by other oversight committees, including, but not limited to:

- Pathology
- University Hospital/Affiliated Hospital/s
- Pharmacy
- Radiology/Imaging
- Nuclear Medicine

- Nursing
- Confirmation that permission to enter classrooms or hospital units will be obtained
- Confirmation that permission from external research locations (sites) will be obtained
- Departmental approvals
- Database access permissions (e.g., Medical/Educational Records)
- Institutional Biosafety Committee
- Radiation Safety Committee
- Radioactive Drug Research Committee
- Conflict of Interest Committee
- Scientific/Scholarly Review Committee

For any that are indicated, a letter of support, collaboration, permission, or approval from the designated authority, should be included in the Initial Study Application to the IRB. The application will be reviewed in the IRB Office to ensure that all necessary letters are included. Final IRB approval will not be given until all necessary letters are received. The IRB may request review or consultation with any of the above listed or other organizational committees or components even when such review or consultation is not technically required by policy.

Other committees and officials may not approve research involving human subjects to commence that has not been approved or has been disapproved by the IRB.

3 Definitions

Common Rule. The Common Rule refers to the “Federal Policy for the Protection of Human Subjects” adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Human Subject Research. Human Subject Research means any activity that meets the definition of “research” and involves “human subjects” as defined by either the Common Rule or FDA regulations.

Note: The terms “subject” and “participant” are used interchangeably in this document and have the same definition.

Research. The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

For the purposes of this policy, a “systematic investigation” is an activity that involves a prospective study plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a study question. Investigations designed to develop or contribute to generalizable knowledge are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

The FDA has defined “research” as being synonymous with the term “clinical investigation.” A clinical investigation, as defined by FDA regulations, means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration 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)]

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act means any activity that evaluates the safety or effectiveness of a 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)]

Human Subject. A human subject as defined by the Common Rule is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or through identifiable private information [45 CFR 46.102(f)].

- Intervention means both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.
- 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 which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

- Identifiable information means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

For research covered by FDA regulations, human subject means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject also includes any individual on whose specimen an investigational device is used or tested or used as a control. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Test Article. The FDA defines "Test article" as meaning any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act [42 U.S.C. 262 and 263b-263n]. [21 CFR 50.3(j)]

Test articles covered under the FDA regulations include, but are not limited to:

- a) **Human drugs** – The primary intended use of the product is achieved through chemical action or by being metabolized by the body. A drug is defined as a substance recognized by an official pharmacopoeia or formulary; a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; a substance (other than food) intended to affect the structure or any function of the body; a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process.)
<http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>
- b) **Medical Devices** - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm>
- c) **Biological Products** - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and

tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.

<http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>

- d) Food Additives - A food additive is defined in Section 201(s) of the FD&C Act as any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristic of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use); if such substance is not Generally Recognized As Safe (GRAS) or sanctioned prior to 1958 or otherwise excluded from the definition of food additives.
<http://www.fda.gov/Food/IngredientsPackagingLabeling/Definitions/default.htm>
- e) Color Additives - A color additive is any dye, pigment or substance which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color. Color additives for use in food, drugs, and cosmetics require premarket approval. Color additives for use in or on a medical device are subject to premarket approval, if the color additive comes in direct contact with the body for a significant period of time.
<http://www.fda.gov/Food/IngredientsPackagingLabeling/Definitions/default.htm>
- f) Foods - Foods include dietary supplements that bear a nutrient content claim or a health claim.
- g) Infant Formulas – Infant formulas are liquid foods intended for infants which substitute for mother’s milk.
- h) Electronic Products - The FDA regulates certain classes of electronic products including radiation-emitting electronic products such as microwaves and x-rays.

Institutional Review Board (IRB) - An IRB is a board designated by UNC-Chapel Hill to review, approve the initiation of, and conduct periodic review of research involving human participants, as defined above. The primary purpose of such review is to assure the protection of the rights and welfare of the human participants. The IRB may be assigned other review functions as deemed appropriate by UNC-Chapel Hill.

4 REFERENCES

- 4.1 DHHS Regulations: 45 CFR 46
- 4.2 FDA Regulations: 21 CFR 50 and 56.
- 4.3 DoD Instruction 3216.02, DoD Directive 3210.07
- 4.4 Health Insurance Portability and Accountability Act (HIPAA), 45 CFR Part 160, 162, and 164.
- 4.5 Family Educational Rights and Privacy Act (FERPA), 34 CFR Part