

1 Human Research Protection Program

The University of Virginia 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 University of Virginia 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.

1.1 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

1.2 Organizational Authority

University of Virginia Human Research Protection Program operates under the authority of the Organization policy “University of Virginia Human Research Protection Program (HRPP)”

adopted on July 7, 2017. 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 University of Virginia.” The HRPP Policy and these operating procedures are made available to all University of Virginia investigators and research staff and are posted on the HRPP website (<http://www.virginia.edu>).

1.3 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 throughout the materials and guidance for the University of Virginia’s HRPP program.

Research. The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized 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.

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 the University of Virginia 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 the University of Virginia.

1.4 Ethical Principles

The University of Virginia is committed to conducting research with the highest regard for the welfare of human subjects. With the exception of international research, where consideration of alternative ethical principles may apply (see Section 25), the University of Virginia 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 University of Virginia’s 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.

1.5 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law and organizational policies. All human subjects research at the University of Virginia is conducted in accordance with the policy and regulations found in the Common Rule and 21 CFR 50 and 56. The actions of the University of Virginia will also conform to all other applicable federal, state, and local laws and regulations such as those specific to the Department of Defense (DoD), Department of Education (DoE), US Department of the Army, Department of Transportation National Highway Traffic Safety Administration, Department of Justice (DoJ), and the 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.

1.6 International Council on Harmonization-Good Clinical Practice (ICH-GCP)

The University of Virginia voluntarily applies the International Council on Harmonization (“ICH”) Good Clinical Practices (“GCP”) Guidelines (sometimes referred to as “ICH-GCP” or “E6”) to human subject research in a clinical trial conducted under a UVA IRB only to the extent that they are compatible with FDA and DHHS regulations.

The following procedures will be followed:

- Manufacturing, handling, and storage of investigational articles will be conducted in accordance with applicable good manufacturing practice.
- The available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.
- Where allowed or required, the researcher may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the researcher.
- The researcher, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial subjects.
- Researchers should maintain records that document adequately that the subjects are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.

1.7 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 University of Virginia has an OHRP-approved Federalwide Assurance [00006183] and has designated three IRB(s) to review all human research plans.

- IRB-HSR:IRB#1 Registration # 00000447
- IRB-SBS:IRB#2 Registration # 00000448
- IRB-HSR:IRB#3 Registration # 00010459

In its FWA, the University of Virginia has opted to voluntarily apply the Common Rule (i.e., Subpart A) to all of its human subject research including all non-federally funded research. Subparts B, C, and D of 45 CFR 46 are applied to all research regardless of funding with the exception of Subpart B which will not be applied to social, behavioral, educational and non-therapeutic medical research.

1.8 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, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

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 University of Virginia facilities or by University of Virginia Principal or Sub-Investigators (as defined on the FDA 1572 or delegation of responsibilities log) requires review by a University of Virginia- designated IRB. Exceptions to this requirement may be granted on a case-by-case basis (e.g., when the University of Virginia's involvement in the research is limited to the provision of a common diagnostic procedure and associated reading or analysis).

An experienced member of the IRB staff in consultation with the IRB Chair, Vice Chair, and/or legal counsel as needed, will determine whether the University of Virginia is engaged in a particular research study. Investigators and other institutions may not independently determine University of Virginia engagement.

When the University of Virginia is engaged in research, the Institutional Official may choose to enter into an agreement to cede review to an external IRB.

For additional information on determining engagement please refer to Guidance on Engagement on Institutions in Human Subjects Research, <http://www.hhs.gov/ohrp/policy/enqag08.html>

1.9 Written policies and procedures

The University of Virginia 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 University of Virginia IRB. This is not a static document. The policies and procedures are annually reviewed and revised by the IRB Directors and reviewed by the IRB Chairs prior to approval by the Institutional Official.

The Institutional Official 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 electronic mailing lists. The policies and procedures will be available on the University of Virginia HRPP website. Changes to the policies and procedures are communicated to investigators and research staff, and IRB members and IRB staff by way of emails and postings on the HRPP and IRB websites.

1.10 University of Virginia HRPP Structure

The HRPP consists of various individuals and committees including but not limited to:

- The Institutional Official,
- The HRPP Director,
- The IRB Directors, Staff, and Committee Members,
- The Institutional Biosafety Committee (IBC),

- Human Investigations involving Radiology Exposure (HIRE) Committee,
- The Radioactive Drug Research Committee (RDRC),
- University Conflict of Interest Committee (UCOI),
- School of Medicine Conflict of Interest Committee (SOM COI),
- Office of Sponsored Programs (OSP),
- School of Medicine Grants and Contracts office (SOM-OCG),
- School of Medicine Clinical Trials office (SOM-CTO),
- General Counsel,
- Office of Environmental Health and Safety (EHS),
- Investigational Drug Services (IDS)
- Information Security (InfoSec),
- Group on Research in Medical Education (GRIME) and Graduate Medical Education Committee (GMEC), and
- Researchers and support 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:

1.10.1 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 University of Virginia. The IO is the signatory of the FWA and assumes the obligations of the FWA. At the University of Virginia, the Vice President for Research serves as the IO. The IO is responsible for ensuring that the University of Virginia HRPP and IRBs 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;
- Support for Community Outreach;
- Support for an organizational culture that fosters and maintains the ethical conduct of research involving human subjects and adherences to regulations and organizational policies; and,
- Support for the oversight of the conduct of research by all University of Virginia investigators.

The IO must complete the OHRP Human Subject Assurance Training, the University of Virginia's required CITI Training, and any other appropriate training on human research protections. The HRPP Director will provide on-going 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.

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.

1.10.2 Director of the HRPP

The HRPP Director is selected by and reports to the Institutional Official (IO).

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

The HRPP Director responsible for:

- 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 for Health Sciences Research (IRB-HSR) and the Institutional Review Board for the Social and Behavioral Sciences (IRB-SBS);
- 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;
- Oversight of the development and implementation of an educational plan for IRB members, staff and investigators;

- Oversight of the budgetary processes of the University of Virginia's HRPP;
- Completing the OHRP Human Subject Assurance Training, the required CITI training and any other appropriate training on human research protections.
- 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.
- Assisting investigators in their efforts to carry out Organization's research mission.
- Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.
- Serving as the primary contact at the University of Virginia 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.
- Responding to questions regarding the protection of human subjects.
- Working closely with the IRB Directors and Chairs on the development of policy and procedures, as well as organizing and documenting the review process.
- Developing and monitoring timely completion of training requirements for Conflict of Interest (COI), Embryonic Stem Cell Research Oversight (ESCRO), and Responsible Conduct of Research (RCR) as required and as appropriate for subcommittee members, investigators and research staff;
- Advising the IO on key matters regarding research at the University of Virginia.

The HRPP Director has access to the IO for any concerns or issues related to the HRPP.

1.10.3 HRPP Staff

In addition to the leadership structure described above, other HRPP staff members include IRB Directors, Associate and Assistant Directors, IRB Compliance Coordinators, a Compliance Content Specialist, Post Approval Monitors, IRB Educators and Office Administrators. The HRPP and IRB staff for the University of Virginia 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 University of Virginia HRPP staff report to the HRPP Director who has responsibilities for its operations.

The IRB Directors have responsibility for implementing the organization's HRPP policies and procedures under the direction of the HRPP Director and guidance of University General Counsel. The IRB Directors also oversee the day-to day operations of the IRB offices.

1.10.4 Institutional Review Board (IRB)

The University of Virginia has three on site IRBs, appointed by the Institutional Official (IO). The IRB prospectively reviews and makes decisions concerning all human research conducted at

University of Virginia 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 University of Virginia, 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 Section 4 for a detailed discussion of the IRB.)

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.

1.10.5 General Counsel's Office

The University of Virginia HRPP relies on the General Counsel's Office for the interpretations and applications of state law and the laws of any other jurisdiction where research is conducted as they apply to human subject research. General 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 General Counsel will determine the appropriate resolution.

1.10.6 Department Chairs and/or Organizational Leaders and their Designees

Department Chairs and organizational leaders and their designees 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 University of Virginia IRB for approval, the department chair, leaders, faculty advisor or designee 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/faculty advisors/designees 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/faculty advisors/designees are required to review all proposals before they are submitted to the IRB for review. The signature of the Department chair, leader faculty advisor or designee 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;

1.10.7 The Investigator

The investigator is the 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 if applicable, which includes 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.

1.10.8 Other Related Units

1.10.8.1 Sponsored Programs Administration

Sponsored Programs Administration 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 Sponsored Programs Administration have the authority to approve research proposals and to execute research agreements on behalf of the organization.

Sponsored Programs Administration ensures that required AAHRPP language (see Section 20.2) is included in contracts as appropriate. Sponsored Programs Administration has access to the relevant documents to confirm that the contract and the consent documents are consistent in terms of who pays in case of injury. Sponsored Programs Administration 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 University of Virginia, a subcontract is executed between the University of Virginia 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 University of Virginia. . *This requirement is waived if Sub-*

recipient's FCOI Policy is PHS compliant.] If the contrary, then the Sub-recipient is required to adhere to UVA's FCOI Policy, is provided with the Financial Disclosure Form, and is asked to submit the form to VPR Office for review and COI determination.

1.10.8.2. University of Virginia Investigational Drug Service (UVA IDS)

A pharmacist from the University of Virginia Investigational Drug Service (UVA IDS) serves on the IRB, allowing the IDS to have complete information about all IRB approved research that takes place at the University of Virginia 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 University of Virginia Hospital Pharmacy and Therapeutics Committee is made aware of IRB approved research involving drugs.

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

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

1.10.8.3 University of Virginia Cancer Center Protocol Review Committee (PRC)

The Protocol Review Committee (PRC) serves as the UVA Protocol Review and Monitoring System as required by the National Cancer Institute (NCI). The PRC is charged with providing institutional peer-review of the scientific merit of all cancer related clinical research protocols. The primary goal of the PRC is to ensure that cancer-related studies involving human subjects conducted at the UVa Cancer Center are:

- Scientifically and statistically sound;
- Appropriately designed;
- Feasible for completion; and
- In compliance with NIH guidelines for human studies.

As part of the review process, the PRC:

- review and approve protocol-specific data and safety monitoring plans on cancer-related trials prior to protocol review by the IRB and
- determine if a protocol competes with existing or pending protocols for a particular subject pool. The PRC will not approve protocols that directly compete with an open or pending institutional or NCI-sponsored trial.

1.10.8.4 University of Virginia Neonatal ICU Protocol Review Committee

The Neonatal ICU Protocol Review Committee serves as the scientific review committee for all research that is conducted in the UVA Neonatal ICU. The primary goal of the NICU clinical trials research scientific review is to ensure NICU studies are performed safely, accounting for unique characteristics of preterm and full term newborns, is feasible, family friendly and the consent form accurately reflects the protocol for the family or person giving consent.

1.10.9 Relationship Among Components

The UVA Research Steering Committee will meet to ensure a dialogue is maintained between the various research compliance entities at the University. Membership is comprised of the following with the Senior Associate Vice President for Research serving as chair:

1. Office of the Vice President for Research: Senior Associate Vice President for Research
2. Institutional Review Boards: IRB Directors and Education Director
3. School of Medicine Clinical Trials Office: Director
4. Office of the General Counsel: Associate General Counsel
5. School of Medicine Office of Grants and Contracts Director; Assistant Dean for Research Administration
6. Office of Sponsored Programs: Assistant Director of Contracts
7. Office of Sponsored Programs: Assistant Vice President for Research

The committee will act in an advisory capacity to the Senior Associate 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. The committee may consult other University personnel with expertise in critical areas as needed.

1.10.10 Study-Specific Coordination

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

- Clinical Engineering (new medical devices in health system)
- Conflict of Interest Committees (University and School of Medicine)
- Embryonic Stem Cell Research Oversight (ESCRO) Committee
- Graduate Medical Education Committee (GMEC)
- Group on Research in Medical Education (GRIME) Committee
- Human Investigations Involving Radiology Exposure (HIRE) Committee
- Institutional Biosafety Committee (IBC)
- Investigational Drug Services (IDS)

- Information Security (InfoSec) (data security approval)
- Permissions from internal or external research locations
- Permissions from internal or external offices or sites providing archived data
- Radioactive Drug Research Committee(RDRC)
- Scientific & Scholarly Review Committees (e.g., Cancer Center Protocol Review Committee (CC PRC), Neonatal ICU Protocol 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. The study will not be allowed to enroll subjects 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.

1.11 Multi-Site Research Projects and IRB Reliance Agreements

UVA researchers are often engaged in non- exempt human subject research that may involve collaborators and/or human subjects at other institutions. In accordance with 45CFR46.114, a UVA IRB may serve as the IRB of Record only for the UVA site, UVA may rely upon the review of a qualified non- UVA IRB or a UVA IRB may serve as the IRB of Record for all sites involved in the multi-site research study. Reliance on another IRB is accomplished through the use of an IRB Authorization/ Reliance Agreement. The scope of the Reliance Agreement may be limited to a specific protocol on a case-by-case basis or to any group of protocols agreed upon by both parties.

A signed IRB Reliance Agreement must be in place before a University of Virginia IRB will serve as the IRB of Record for another institution or rely on the review of a non- UVA IRB.

Information regarding IRB Reliance Agreements may be found below. Information regarding the protocol submission process for a protocol that will be overseen by a non- UVA IRB may be found in section 9.

Definitions

IRB of Record: A reviewing IRB that assumes IRB responsibilities for another organization. May also be called the Central IRB (CIRB) or Single IRB (sIRB).

IRB Reliance Agreement: A formal, written agreement in which the reviewing IRB agrees to serve as the IRB of Record for a Relying Organization.

Relying Institution: A relying Institution is the institution that has entered into an IRB Reliance Agreement with another institution's IRB to serve as the IRB of Record.

Non-Exempt Human Subject Research- any human subject research that does not meet the Exempt criteria in 45CFR46.

Engagement of Organizations in Non-Exempt Human Subject Research: An organization is considered engaged in human research when its employees or agents, for the purposes 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; OR 4) a direct federal award to conduct human subject research, even when all activities involving human subjects are carried out by subcontractors (i.e. employees or agents of another organization). HHS Guidance: [Engagement in Human Subjects Research](#)

1.11.1 UVA engaged in only a part of a Multi-Site Research Project

When the University of Virginia is engaged in only part of a cooperative research project, UVA may rely on a non-UVA IRB for the part of the study being conducted at UVA. If the study will be reviewed by a UVA IRB, the UVA IRB only needs to approve the part(s) of the research in which the University of Virginia investigator is engaged. For example, if the University of Virginia is operating the statistical center for a multi-site trial that receives identifiable private information from multiple other institutions, the UVA IRB reviews and approves the research activities related to the receipt and processing of the identifiable private information by the statistical center.

1.11.2 Each research site obtains IRB Approval from their IRB

It is the policy of the University of Virginia to assure that all facilities participating in a study involving human subjects receive adequate documentation about the study in order to protect the interests of study participants. Before a study can begin, it must be approved by the IRB of each participating site. The lead Principal Investigator must identify all institutions participating in the research, the responsible IRB(s), and the procedures for dissemination or collection of study information (IRB initial and continuing approvals, relevant reports of unanticipated problems, study modifications, and interim reports) between all participating institutions.

Prior to signing of sub contracts with each research site the Office of Sponsored Programs/ School of Medicine Office of Grants and Contracts will obtain the IRB approval from each site.

1.11.3 UVA Relies on a non- UVA IRB as the IRB of Record

The decision for UVA to rely on a non- UVA IRB is made on a case by case basis. The decision will include such factors as:

- Risk level of the study
- Qualifications of proposed IRB of Record
- Location of subject enrollment
- Requirement to rely on a single IRB from a funding source /sponsor
- Requirements of federal regulations or policies of federal agencies.

UVA has joined SMART IRB and encourages the use of the SMART IRB Reliance Agreement template and SOP's when possible.

1.11.4 UVA IRB serves as IRB of Record for non-UVA Sites

Requests for a new reliance agreement to allow another institution or independent investigator to rely on the UVA IRB for IRB review are considered on a case-by-case basis. The Researcher requesting the reliance agreement must submit a request for an IRB reliance agreement _ to the IRB.

The requests to add relying sites will be handled as modifications. The modification to add a relying site will not take place until the UVA IRB approves the main protocol, consent and other relevant study documents for non-exempt studies.

The UVA IRB follows the same criteria for consideration of a modification meeting the criteria of expedited or full board review. The addition of a relying site is considered an expedited modification so long as there are no content revisions to the document(s) that would be greater than minimal risks and therefore require the modification to add a relying site go before a convened IRB.

The UVA IRB will review the relying site local content revisions to the consent document and ensure that no changes have been made outside of the applicable sections outlined in the request form. Any additional revisions required for a particular relying site, will be outlined specifically in the relying site request form.

Once review is complete and the relying site is added to the protocol via a modification, the UVA study team will notify the relying sites of all determinations and communications from the UVA IRB. This includes those decisions for initial review, continuing review, modifications, and reportable events.

The UVA IRB will make available upon request, relevant IRB minutes. In addition, the Relying institutions are provided with the website links for the UVA IRB membership rosters, and standard operating procedures.

All applicable policies governing research at UVA are available via the UVA HRPP website as well as the UVA IRB website. HRPP staff are noted on the website pages including contact information.

UVA researchers are made aware of significant policy changes via a site wide email from the IRB offices. Should a policy change directly affect specific studies (e.g. COI management plan), the PI and study team are emailed with information and guidance on how to submit revisions if applicable. The UVA study teams are required to communicate relevant information directly to outside study teams.

1.11.5 UVA PI serves as Overall PI or UVA serves as the Data Coordinating Center

If a UVA investigator serves as the overall PI they or the Data Coordinating Center is responsible for:

- documenting how the conduct of the research plan and the protection of human subjects will be communicated to and among the other participating facilities engaged in the research study.
- serving as the liaison with regulatory and funding agencies, with other participating facilities, and for all aspects of internal review and oversight procedures.
- ensuring that all participating facilities obtain review and approval from their IRB of record and adopt all research plan modifications in a timely fashion.
- ensuring that the research study is reviewed and approved by any other appropriate committees at the coordinating facility and at the participating facilities prior to enrollment of participants.

The University of Virginia investigator must follow these procedures when University of Virginia is the coordinating facility or overall PI:

- During the initial IRB submission of the multi-site study, the investigator indicates in writing on the application form or in an application letter that the University of Virginia PI is the overall PI for all sites in the study and/or is the coordinating facility of a multi-site study.
- For health sciences research, the School of Medicine Clinical Trials office will verify the items noted below prior to the initial IRB review. The IRB will not open the protocol to enrollment until it has received verification from the SOM CTO.
 - Method for assuring all participating facilities have the most current version of the research plan

- Method for confirming that all modifications to the research plan are communicated to participating sites
 - Method for communicating to participating facilities any serious adverse events and unanticipated problems involving risks to subjects or others
 - Method of communicating regularly with participating sites about study events
 - When appropriate, the plan for monitoring the conduct of the research at participating facilities
 - Method for communicating interim analyses, including data safety reviews, to participating facilities, as applicable
 - In addition, throughout the course of any federally funded study verify the investigator has the appropriate IRB approvals on file from each site and verify the FWA for each site is current.
- The IRB will verify the items noted below prior to approval is granted:
 - Name of each participating facility
 - Confirmation that each participating facility has an active FWA (including FWA number and expiration date) for all federally funded studies
 - Contact name and information for investigator(s) at each participating facility
 - Contact name and information for IRB of record at each participating facility with the IRB/ethics committee approval
 - The UVA Office of Sponsored Programs will verify the items noted below before a contract is signed.
 - If applicable: IRB approval from local in country IRB/Ethics Committee for international research for each site
 - IRB approval from IRB of Record for each site
 - The investigator will:
 - maintain documentation of all correspondence between participating sites and the IRB of Record.
 - maintain a copy of the IRB approval from all sites prior to enrollment of subjects at a site